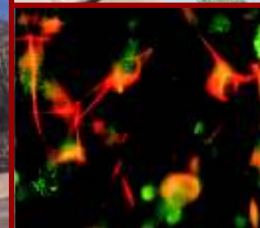
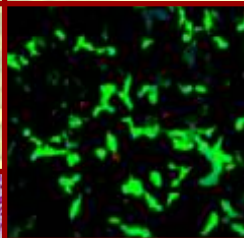


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**Industrial Toxicology Research Centre
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Annual Report

2005-2006



**Industrial Toxicology Research Centre
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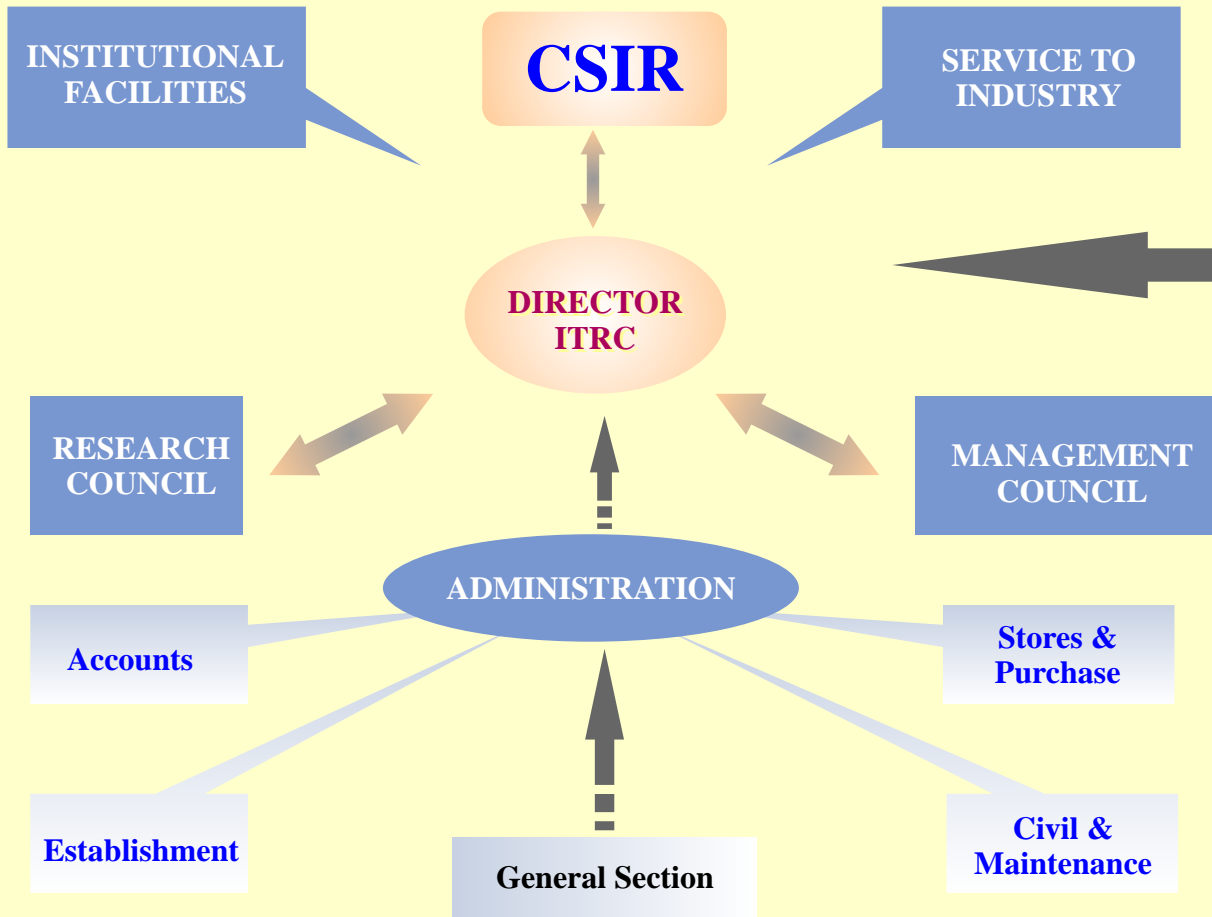
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ITRC

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- Research Planning & Business Development
- Toxicology Information Centre & Library
- Bioinformatics
- Quality Assurance Unit
- Computer Cell
- Instrument Service & Maintenance
- Biomedical Illustration & Photography
- Animal House

- Analysis of Pollutants
- Water Quality Analysis
- Environmental Impact Assessment
- Specialized Toxicity Tests
- Safety Evaluation of Chemicals & Products
- Regulatory Toxicology
- Toxicology Database
- Human Resource Development



R & D Areas

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TOXICOGENOMICS & PREDICTIVE TOXICOLOGY

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ITRC, a constituent laboratory of CSIR, New Delhi, is the only institution of its kind in South-East Asia

The Motto :
Safety to environment & health and service to industry

ASSESSMENT, MAPPING & REMEDIATION OF GROUND WATER CONTAMINATION

NATIONAL S & T MISSIONS

निदेशक की रिपोर्ट

मुझे आई.टी.आर.सी. की उपलब्धियों से भरे एक और उत्पादकतायुक्त वर्ष को आपके समक्ष प्रस्तुत करने में अपार प्रसन्नता हो रही है। मुझे हर्ष है कि मैं संस्थान की शोध एवं विकास में सम्पूर्ण वृद्धि, सामाजिक कार्यक्रम और उद्योगों की सेवा से संबंधित जानकारी आपसे बाँट रहा हूँ। वर्ष 2005-2006 में हमारे संस्थान ने विषविज्ञान शोध और औद्योगिक स्वास्थ्य के क्षेत्र में उल्लेखनीय रूप से निरन्तर योगदान दिया है। इस केन्द्र के वैज्ञानिकों ने जीवविज्ञान और जैव प्रौद्योगिकी पारिस्थितिकी और पर्यावरण, स्वास्थ्य सुरक्षा और औषधि, जल स्रोत और प्रौद्योगिकी के क्षेत्र में शोध कार्य किया है। प्रयोगशाला ने नियमित रूप से नेटवर्क आधारित कार्यक्रमों में प्रयास किया है जिसमें यह सुनिश्चित किया गया है कि विश्लेषणात्मक आंकड़ों के साथ-साथ यांत्रिक उपलब्धता का सामूहिक ध्येय हो। हमारे शोध का यह भी उद्देश्य है कि सुरक्षित और अच्छी गुणवत्ता के उत्पाद हों इससे हम अन्तर्राष्ट्रीय बाजार में प्रतिस्पर्धा कर सकें। समन्वित प्रयास से विश्वसनीय सूचना उत्पन्न कर सकें जिससे पारिस्थितिकीय रूप से सुदृढ़ जीवन सुनिश्चित हो सके।



नयी वैज्ञानिक सूचना तैयार करने की हमारी प्रबल इच्छा से हमने विषविज्ञान शोध में नये क्षेत्रों की पहचान की है। हमारी शोध परिषद् ने पाँच नये क्षेत्रों को संस्थागत शोध गतिविधियों में शामिल किया है इसके अलावा 13 सी. एस. आई. आर. नेटवर्क आधारित कार्यक्रम और अन्य बाह्य निधि प्राप्त परियोजनाएं चल रही हैं। यह क्षेत्र हैं:—प्रणाली विषविज्ञान और जोखिम आंकलन; पर्यावरण विषविज्ञान; टॉक्सीकोजीनोमिक्स तथा निवारक विषविज्ञान; खाद्य, औषधि और रसायन विषविज्ञान, तथा आंकलन, मापन और कानपुर क्षेत्र में भूमि जल में पुनः निदर्श करना है।

आई.टी.आर.सी. ने नेटवर्क आधारित परियोजना "औद्योगिक रसायनों से भारतीय जनसंख्या में पॉलीमार्फिज्म का टॉक्सीकोजीनोमिक्स और बायोमार्कर का विकास" को समन्वित किया है। इसके अलावा हमारी ज़्यादातर नेटवर्क परियोजनाओं ने समन्वित प्रयास का 4 वर्ष पूरा कर लिया है और संबंधित शोध क्षेत्र में उल्लेखनीय नतीजे/ संकेत मिलने लगे हैं।

वर्ष की शोध एवं विकास की उल्लेखनीय उपलब्धियाँ हैं :-

- आई.टी.आर.सी. ने घरेलू प्रोटीन और डी.एन.ए. आधारित नैदानिक जाँच विकसित की है इससे जी.एम-फसलों और खाद्यों की जाँच की जा सके। इससे जी.एम. फसलों में प्रचलित ट्रांसजेन्स की जाँच में यह परीक्षण उपयोगी सिद्ध होगा।
- संस्थान ने जी.एम. फसलों और खाद्यों के एलर्जिक संभाव्यता के मूल्यांकन हेतु समर्थता विकसित है (एक सिमूलेटेड गैसट्रिक फ्लूड डाइजेसन असे) जी.एम. फसलों में इस प्रकार का आंकलन उत्पाद के विपणन के लिए उपयोगी होगा और जनता के खपत योग्य होगा।
- सी.वाई.पी.131 में एस.एन.पी.,1 ए 2, एरिल हाईड्रोकार्बन रिसेप्टर (ए.एच.आर.) तथा ए.आर.वाई. एल. हाईड्रोकार्बन्स न्यूक्लियर ट्रांसलोकेटर (ए.एच.एन.टी) जीन्स की पहचान की गयी है। जो



भारतीय जनसंख्या में प्रो-कार्सीनोजेन्स तथा प्रो-म्यूटाजेन्स के मेटाबोलिक कार्यकलाप में युक्त होते हैं। एकत्र की गयी जानकारी से यह पता चला कि कौकेशियन और एशियन जनसंख्या में कार्यात्मक महत्वपूर्ण एस.एन.टी का पता चला है। जो पर्यावरण रसायनों के कार्सीनोजेनिक प्रभावों में लोगों को पूर्वानुकूल करते हैं, ये भारतीय जनसंख्या में भी पाये जाते हैं।

- वैज्ञानिक रूप से विधिमान्य स्वास्थ्य प्रोन्नत को विकसित करने के लिए अध्ययन किये गये जो कि परम्परागत जानकारी पर आधारित हैं। यह पाजिटिव हेल्थ प्रमोटर (पी.एच.पी.) फार्मूलेशनस जी.एम.पी.मानक के अन्तर्गत विकसित किये जा रहे हैं, जोकि नेटवर्क परियोजना के अन्तर्गत की गयी खोजों पर आधारित हैं।
- जिंजीबर आफिसीनेल एक व्यापक रूप से प्रयोग में लायी जाने वाली हर्बल औषधि हैं जो चिकित्सा की परम्परागत प्रणाली में भी है। पारिस्थितिकीय क्षेत्रों से प्राप्त नमूनों की तुलना में भारत के दक्षिण क्षेत्र से प्राप्त राइजोम में उच्चतर एण्टी-आक्सीडेन्ट, एण्टीमाइक्रोबियल गतिविधियाँ और बायो-एक्टिव घटक पाये गये हैं। यह सूचना नैदानिक फार्मूलेशनस की तैयारी में मूल्यवान हो सकती है।
- 6-जिंजिरोल, जो अदरक का एक महत्वपूर्ण घटक है और जिसमें यह संभावना है कि यह प्रोस्टेट कैंसर में प्रभावी कीमोप्रीवेंटिव और नैदानिक कारक के रूप में कार्य कर सकता है। इसी प्रकार लूपियोल, एक ट्राईटरपिन जो आम में उपस्थित रहता है उसने यह दर्शाया है कि इसमें कैंसर कीमोप्रीवेंटिव गुण होते हैं। इस अध्ययन ने यह दर्शाया है कि लूपियोल और आम के पल्प एक्सट्रैक्ट सप्लीमेंटेशन प्रोस्टैट को बढ़ने से रोकते हैं और सीरम प्रोस्टैट विशिष्ट एण्टीजेन के स्तर को कम करते हैं जो कि टेस्टोस्टेरान द्वारा प्रेरित होता है जैसा कि प्रोस्टैट कैंसर सेल में एपॉपटोटिक सेल पापुलेशन में वृद्धि के रूप में देखी गयी है।
- समय के अनुसार एण्टीआक्सीडेंट क्षमता के स्थायित्व में परिवर्तन और फिनोलिक कंटेंट से इसके संबंध का लोकप्रिय हर्बल चाय में मूल्यांकन किया गया। उच्च फिनोलिक कंटेंट युक्त नमूनों के समुचित भंडारण समय के दौरान एण्टीआक्सीडेंट क्षमता में थोड़ी कमी दिखाई दी। यह अध्ययन यह दर्शाता है कि इस बात की आवश्यकता है कि निर्माताओं को हर्बल चाय के लाभकारी प्रभावों में कमी के बगैर उपयोग की अवधि के बारे में सूचना उपलब्ध कराने की आवश्यकता है।
- काली चाय पॉलीफिनॉल्स जिसमें कैटेचिन्स, थियारूबिन तथा थियाफ्लेविन्स होते हैं उन्होंने मैमरी और इसोफेगल ट्यूमर को बढ़ाया है, ऐसा प्रदर्शित हुआ है।
- आयुर्वेद में उपयोग में लाये जाने वाले 1400 पौधों में से 700 पौधों के बारे में विषविज्ञान मापदण्ड, सक्रिय घटक और एण्टीडोट संभाव्यता पर सूचना संकलित की गयी है और इसका विधिमान्यकरण किया जा रहा है। नोडल प्रयोगशाला निसकेयर से उपलब्ध कराये गये साफ्टवेयर पर इस सूचना का डिजिटल प्रलेखन किया जा रहा है। डेटाबेस में 340 पौधों से संबंधित सूचना पहले ही जोड़ ली गयी है।
- आई.एल-6, टी.एन.एफ., आई.एल-30 के संबंध में म्यूरिन एयरवेज में स्टैट 3 की भूमिका का परीक्षण किया गया। जो कि एस्थमा पैथोजेनेसिस में महत्वपूर्ण भूमिका निभाता है। यह प्रदर्शित किया गया कि इनफ्लेमेशन संबंधित साइटोकाइन्स के एक्सप्रेशन को स्टैट 2 सिरना के ट्रांसफेक्शन संचालित कर सकते हैं और थेरापी में उपयोग में लाया जा सकता है।



- डोपामाइन डी.ए.-डी 2 रिसेप्टर जो कि एस.एच.वाई.-एस.वाई.-5 वाई ह्यूमन न्यूरोब्लास्टोमा सेल लाइन में बंधा होता है उसका उपयोग पर्यावरिक रसायनों की न्यूरोविषालुता के आंकलन में मॉडल के रूप में किया जाता है। यह परिणाम दर्शाते हैं कि डी.ए.-डी 2 हेतु रिसेप्टर व्यक्त किये गये हैं और मानव न्यूरोब्लास्टोमा सेल लाइन फिजियोलॉजिकली कार्य कर रहे हैं और चेताविषालुता के आंकलन हेतु इन विट्रो मॉडल के रूप में प्रयोग में लाये जा सकते हैं।
- एक वैकल्पिक एनीमल इन विवो मॉडल के विकल्प के रूप में ड्रोसोफिला मेलानोगेस्टर का उपयोग किया गया क्योंकि मैमल्स की तरह इस आर्गेनिज्म में जीन्स की होमोलॉजी विद्यमान थी। सेलुलर स्ट्रेस की रचना को समझने के लिए उदा. एच.एस.पी. 70 और पर्यावरिक रसायनों के विरुद्ध स्ट्रेस-एन्जाइम जिसमें डिक्लोरवोस और क्लोरोपाइरीफोस जाँच रसायनों के रूप में प्रयोग किया गया था, उस अध्ययन ने सुझाया कि क्लोरोपाइरीफोस की तुलना में डिक्लोरवोस ज़्यादा संकटमय है।
- एक अध्ययन ने दर्शाया कि ओ.सी.पी. के रेसीड्यू जो कि पी.ओ.पी.-पेस्टीसाइट समूह का निर्माण करते हैं और उन्हीं निर्माण के लिए पिछले कई वर्षों से प्रतिबंध लगा दिया गया था और देश में यह उपयोग में लाया जा रहा है और गंगा के एलूवियल भूमिजल एक्वीफर्स में अभी भी विद्यमान हैं, जिससे स्थानीय जनसंख्या के स्वास्थ्य को खतरा है जो इसे जल स्रोत के रूप में प्रयोग करते हैं।
- कानपुर शहर के चयनित स्थलों में गंगा नदी के सतह को जल में एसरीचिया कोलाई और एन्ट्रोकोची के मल्टीड्रग रेजिस्टेंट वाइरुलेंट इन्वार्नमेन्टल आईसोलेट्स का पता चला है।
- भारतीय जनसंख्या में डी.एन.ए. क्षति की मात्रा में जीनोविषालुता हेतु मानव अनुवीक्षण अध्ययनों ने उल्लेखनीय लिंक और जीवनशैली संबंधी भिन्नताओं को दर्शाया है। यह देखा गया है कि सामान्यतया भारतीय जनसंख्या में महिलाओं की तुलना में पुरुषों में डी.एन.ए. क्षति का सतह स्तर ज़्यादा था। आगे यह पाया गया है कि धूम्रपान, मांसाहारी भोजन और कठोर शारीरिक क्रिया-कलाप से पुरुषों में डी. एन. ए. क्षति ज़्यादा होती है।
- हमारे संस्थान के वैज्ञानिकों ने रिफाइनरी और उद्योगों द्वारा उत्पन्न संकटमय रद्दी के प्रबंधन की तकनीक विकसित की है। संकटमय रद्दी के इन-सिटू रिमिडिएशन हेतु मानव मृदा और हाइड्रोआक्सीएपेटाइट का उपयोग इमोबीलाइजिंग एजेंट के रूप में किया गया है जो संदूषित मृदा में भारी धतुओं को इमोबीलाइज करता है और भूमि जल में इनके निक्षालन को रोकता है।

वैज्ञानिकों के उपर्युक्त योगदान में से कुछ को विभिन्न शैक्षिक निकायों द्वारा पुरस्कार और सम्मान से मान्यता प्रदान की गयी है। डॉ. ए. के. अग्रवाल को इंडियन एकेडमी ऑफ न्यूरोसाइंसेस, बंगलौर की वार्षिक बैठक में न्यूरोसाइंसेस के क्षेत्र में उनके द्वारा प्रकाशित सर्वश्रेष्ठ पेपर हेतु “ज्योत्सना माई रघुनाथ भट्टाचार्य अवार्ड” दिया गया।

डॉ. आर. के. उप्रेती को एकेडमी ऑफ साइंसेस फार एनीमल वेलफेयर द्वारा “सूरजाबेन जेटालाल ठाकेर अवार्ड-2005” दिया गया।

डॉ. ए. पी. साहू को सामान्य रूप से पर्यावरण विज्ञान में और विशेष रूप से विषविज्ञान के क्षेत्र में नवम्बर, 2005 में जयपुर में उनके मूल्यवान योगदान को मान्यता देने हेतु इंडियन एकेडमी ऑफ इन्वार्नमेन्टल साइंसेस, हरिद्वार द्वारा स्वर्ण पदक और मानद फेलोशिप प्राप्त हुई।



डॉ. कृष्ण गोपाल को फरवरी 2006 में बायोव्द रिसर्च सोसायटी द्वारा "वर्ष का वैज्ञानिक" 2006 प्रदान किया गया।

डॉ. आलोक धवन को 2005 में बायोमेडिकल शोध के क्षेत्र में "आई.सी.एम.आर. का शकुन्तला अमीर चन्द पुरस्कार-2002" प्रदान किया गया।

कई वैज्ञानिकों को विभिन्न शैक्षिक सोसायटी के सदस्य के रूप में चुना गया और सलाहकार बैठकों में प्रतिभागिता, समिति, सम्मेलन, वर्कशॉप में विशेषज्ञ के रूप में आमंत्रित किया गया।

हमारे वैज्ञानिकों ने विभिन्न सरकारी विभागों जैसे:- बी.आई.एस.,आई.सी.ए.आर.,आई.सी.एम.आर.,सी.आर.आर.आई.,सी.पी.सी.बी.,डी.एस.टी.,डी.जी.एच.एस. की समितियों में कार्य किया है। उन्होंने रसायनों एवं उत्पादों के विषालुता आंकलन के दिशा निर्देश को बनाने में सहायता प्रदान की है। खाद्य और पैकिंग सामग्री में विभिन्न संदूषण और अपमिश्रक की अनुमेय सीमा निर्धारित किया। खाद्य और जल में पेस्टीसाइड रेसीड्यू मूल्यांकन किया है। शोध की खोजों के आधार पर वैज्ञानिकों ने विभिन्न उद्योगों और सरकारी अभिकरणों रसायनों की संभाव्य विषालुता के नियामक और उनके उपयोग पर परामर्श दिया है। आई.टी.आर.सी. ने जीवन की सामान्य गुणवत्ता में सुधार लाने के लिए वायु एवं जल अनुवीक्षण का नियमित सर्वेक्षण संचालित किया है।

आठ पुस्तकों के अध्याय के साथ अद्वितीय पुनरीक्षित जर्नल्स में कुल 88 पेपर प्रकाशित हुए। औसत इम्पैक्ट फैक्टर 1.545 था।

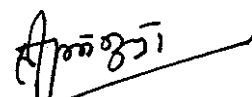
आई.टी.आर.सी. ने इस वित्तीय वर्ष के दौरान बाहर से 250 लाख नकद के रूप में उत्पन्न किया।

5 रिसर्च फेलो को पी. एच. डी. की उपाधि प्रदान की गयी। दो पेटेंट आवेदन और एक कॉपीराइट फाइल किये गये।

संस्थान ने मानव संसाधन विकास में महत्वपूर्ण भूमिका निभाई है। जिसमें प्रशिक्षण-कार्यशाला, संगोष्ठी और सम्मेलन, विभिन्न विश्वविद्यालयों के छात्रों हेतु ग्रीष्मकालीन प्रशिक्षण और मानव और पर्यावरण स्वास्थ्य संबंधी जोखिम की सुरक्षा से संबंधित कार्यक्रमों द्वारा जन-जागरण आयोजित किया गया है।

मैं, डॉ. आर. ए. माशेलकर, महानिदेशक, सी.एस.आई.आर. का हृदय से आभारी हूँ। मैं शोध परिषद के चेयरमैन प्रो. वी. एस. वेलियाथन और सदस्यों के सुझाव और नियमित उत्साहवर्धन हेतु कृतज्ञता ज्ञापित करता हूँ। स्थानीय प्रयोगशालाओं के निदेशकों के सहयोग की भूरि-भूरि प्रशंसा करता हूँ। संस्थान के वैज्ञानिकों और कर्मियों के समर्पित प्रयास अत्यधिक प्रशंसनीय हैं और मैं इसे हृदय से स्वीकार करता हूँ।




सी. एम. गुप्ता

Director's Report

It gives me immense pleasure to present before you the achievements of ITRC for yet another productive year. I am happy to share with you the all round growth of the Institute in R&D, societal programmes and services to industries. During 2005-06 our Institute continued contributing significantly in the field of toxicological research and industrial health. The scientists of this centre pursued research in the sectors of **Biology and Biotechnology, Ecology and Environment, Health Care and Drugs, Water Resources and Technology**. The Laboratory continued its efforts in networked mode programmes with collective vision to ensure availability of mechanistic as well as analysis data. Our research is also aimed at safe and good quality products to enable us to compete in international market. Concerted efforts were made to generate reliable information for ensuring ecologically sound life.

In our quest to generate new scientific information we identified newer areas of cutting edge toxicological research. Our Research Council approved 5 new areas as institutional research activities, in addition to ongoing 13 CSIR network mode and other externally funded projects. These areas are : Systems Toxicology and Risk Assessment; Environmental Toxicology; Toxicogenomics and Predictive Toxicology; Food, Drug and Chemical Toxicology, and Assessment, Mapping and Remediation of Ground Water Contamination.

ITRC coordinated the Networked Project "Toxicogenomics of polymorphism in Indian population to industrial chemicals and development of biomarkers". Besides this, most of our networked projects completed fourth year of concerted efforts and significant outcomes/indications started appearing in respective research areas.

Significant R&D highlights of the year are:

- ITRC has developed indigenous protein and DNA based diagnostic tests for detection of GM-crops and food. These tests would be useful in detection of transgenes that are introduced in GM crops.
- The institute developed capability for the evaluation of allergenic potential of GM crops and foods (a Simulated Gastric Fluid Digestion Assay). Such an evaluation in GM crops will be useful for marketing the product for public consumption.
- SNPs in CYP1A1, 1A2, Aryl hydrocarbon receptor (Ahr) and aryl hydrocarbons nuclear translocator (Ahnt) genes were identified, these are involved in the metabolic activation of pro-carcinogens and pro-mutagens in the Indian population. The information generated revealed that functionally important SNPs reported in Caucasian and Asian populations, which predispose individuals to the carcinogenic effects of environmental chemicals, are also found in the Indian population.
- Studies were carried out for the development of a scientifically validated health promoter, based on traditional knowledge. Three Positive Health Promoter (PHP) formulations are being developed under GMP norms, based on findings under a networked project.



- *Zingiber officinale* is a widely used herbal drug in traditional system of medicine. The rhizome obtained from Southern region of India was found to have higher anti-oxidant, antimicrobial activities and bio-active constituents as compared to the samples procured from other ecological zones. The information is valuable for preparation of therapeutic formulations.
- An important constituent of ginger, 6-gingerol was found to have the potential to act as an effective chemopreventive and therapeutic agent for prostate cancer. Similarly, lupeol, a triterpene present in mango has been shown to possess cancer chemopreventive properties. The study showed that lupeol and mango pulp extract supplementation prevents enlargement of prostate and decreases levels of serum prostate specific antigen induced by testosterone as evident from an increase in apoptotic cell population in prostate cancer cells.
- Changes in the stability of antioxidant capacity with time and its relation to phenolic content was evaluated in popular herbal teas. Samples containing high phenolic content showed lesser decline in antioxidant capacity over a considerable storage time. The study indicates a need to provide information by the manufacturers regarding period of use without decline in beneficial effects of herbal teas.
- Black tea polyphenols that include catechins, thearubin and theaflavins were shown to inhibit mammary and esophageal tumors.
- Of the 1400 plants used in Ayurveda, information on toxicology parameters, active constituents, and antidote potential of 700 plants has been compiled and is being validated. Digital documentation of this information is being carried out on the software provided by NISCAIR the nodal lab. Information of 340 plants has already been added to the database.
- Role of STAT3 in murine airways was examined in response to IL-6, TNF, IL-13 which plays a major role during asthma pathogenesis. It was demonstrated that transfection of STAT2 SiRNA can regulate the expression of inflammation associated cytokines and may be of use in therapy.
- Dopamine DA-D2 receptor binding in SHy-Sy-5y human neuroblastoma cell line was used as a model for the assessment of neurotoxicity of environmental chemicals. The results indicate that the receptors for DA-D2 are expressed and physiologically functional in this human neuroblastoma cell line and could be used as *in vitro* model for the assessment of neurotoxicity.
- *Drosophila melanogaster* was used as an alternate animal *in vivo* model because of homology of genes present in this organism with that of mammals. To understand the mechanism of cellular stress viz. hsp70 and oxidative stress-enzymes against environmental chemicals, studies using dichlorvos and chlorpyrifos as test chemicals, suggest that dichlorvos is more hazardous as compared to chlorpyrifos.
- A study showed that the residues of the OCPs which constitute POP-pesticides group and were banned for last several years for manufacture and use in the country are still present in the alluvial ground water aquifers of Gangetic plains, which may pose health risk to the local population using these water resources.



- Multi-drug resistant virulent environmental isolates of *Escherichia coli* and *Enterococci* were detected in surface waters of river Ganga at selected sites in Kanpur city.
- Human monitoring studies for genotoxicity have shown significant gender and lifestyle related differences in the extent of DNA damage among Indian population. It was observed that basal level of DNA damage in males was higher than females generally in Indian population. Further, smoking, non-vegetarian diet and strenuous physical activity were found to enhance DNA damage in males.
- Scientists of our institute explored the techniques for managing hazardous waste produced by refineries and industries. Humus soil and hydroxyapatite have been used as immobilizing agents for *in-situ* remediation of hazardous waste that immobilizes heavy metals in contaminated soil and prevents their leaching into the ground water.

Various academic bodies by way of awards and honours recognized some of the above contributions of the scientists. Dr. A.K. Agarwal received “Jotsana Mai Raghunath Bhattacharya Award” for the best paper published in the area of neuroscience at the Annual Meeting of Indian Academy of Neurosciences, Bangalore.

Dr. R.K. Upreti received the “Surjaben Jethalal Thaker Award-2005” from Academy of Sciences for Animal Welfare.

Dr A.P. Sahu received a Gold Medal and Honorary Fellowship (FIAES) of Indian Academy of Environmental Sciences, Haridwar in recognition of his valuable contributions to environmental sciences in general and toxicology in particular, in November 2005 in Jaipur.

Dr. Krishna Gopal received the “Scientist of the year” 2006 award from Bioved Research Society, in February 2006.

Dr. Alok Dhawan was awarded “Shakuntala Amir Chand Prize-2002 of ICMR” in the field of Biomedical Research in 2005.

Many scientists were elected members of various academic societies and invited to participate in consultative meetings as experts in committees, conferences & workshops.

Our scientists also served on committees of various government departments like BIS, ICAR, ICMR, CRRI, CPCB, DST, DGHS. They also helped in formulating the guidelines for toxicity evaluation of chemicals and products, setting up permissible limits of various additives and contaminants in food and packaging material, evaluation of pesticide residues in food and water. Based on research findings, scientists advised various industries and government agencies about the potential toxicity of chemicals for regulating their use. ITRC undertakes regular surveys for air and water monitoring to improve the general quality of life.

Eighty eight papers were published in peer reviewed journals along with 8 book chapters. The average Impact Factor was 1.545.

ITRC generated Rs 274 lakhs as External Cash Flow during this financial year.



Five Research fellows were awarded Ph.D. degrees. Two patent applications and one copyright were filed.

The Institute also played a significant role in Human Resource Development by organizing training-workshops, seminars and conferences; conducting summer training for students of various universities and organization of public awareness programmes related to safeguarding human and environmental health associated risks.

I wish to express my gratitude to Director-General, CSIR Dr. R.A. Mashelkar, Chairman Prof. V.S. Valiathan and members of the Research Council for their advice and constant encouragement and Directors of local laboratories for their cooperation. The dedicated efforts of scientists and staff of the centre are highly appreciated and acknowledged.


(C.M. Gupta)



Industrial Toxicology Research Centre

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R & D Highlights

Networked and Related Projects

Project : Toxicogenomics of polymorphisms in Indian population to industrial chemicals for the development of biomarkers

Single Nucleotide Polymorphisms (SNPs) in Human Microsomal Epoxide Hydrolase

Microsomal epoxide hydrolase (mEH) primarily metabolizes epoxides which are generated via the metabolism of xenobiotics by Cytochrome-450. Many of the epoxides interact with DNA and cause cancer. In the event of altered activity of human mEH, the levels of epoxides are expected to vary, affecting their capability for cancer activation. To understand the cancer causation in individual due to varied pattern of altered activity of mEH in humans, the mEH genotype of different individuals in a population is important to be determined.

Polymorphism in exon 3 of human mEH (Tyr/His 113) in 49 lung cancer patients and 137 healthy case controls was evaluated by capillary DNA-sequencing. The frequency of His 113 was 0.375 in controls and 0.418 in lung cancer patients but no statistically significant association was found, possibly due to small sample size. The results are in contrast with an earlier study, where His allele at codon 113 was associated with a significantly decreased risk of lung cancer (0.21) compared with controls (0.29).

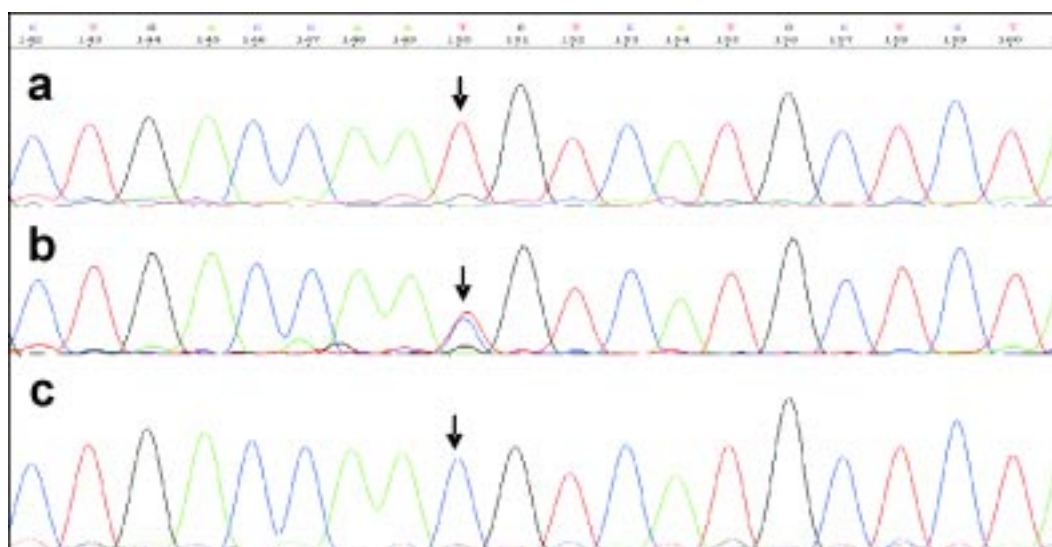


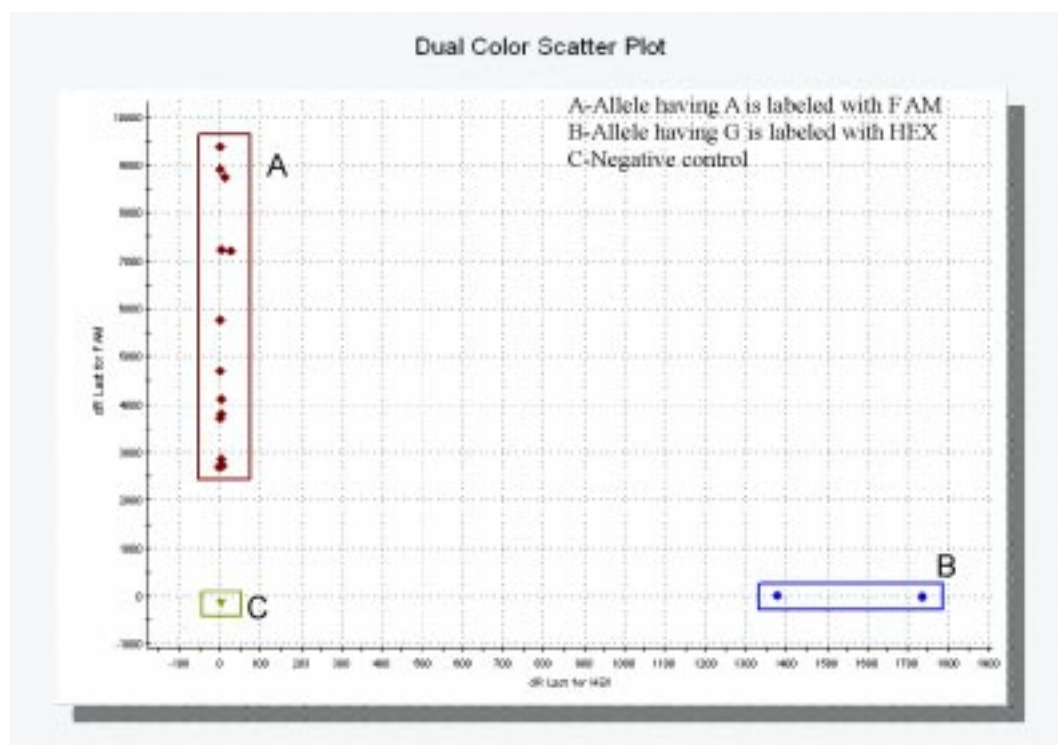
Fig. 1 : DNA polymorphism studies in control and solvent exposed population

DNA polymorphism studies in control and solvent exposed population

Studies were conducted to understand the polymorphic status of, GSTM1, GSTT1 and GSTP1 genes by PCR and RFLP protocols and CYP1A1 genes using Real Time



PCR for high throughput screening. A total of 220 control and 25 samples exposed to laundry solvents have been analyzed. Frequency of deleted/null genotypes for GSTM1, GSTT1 gene was determined by multiplex PCR whereas, GSTP1 genotype by PCR followed by restriction digestion (RFLP). The frequency of deleted/ null for either GSTM1, GSTT1 or both null genotype among the male and female subjects were found to be 40.93%, 41.35%; 21.47%, 22.45% and 12.0%, 13.42% respectively. The frequencies of GSTP1 isoforms having ile/ile, ile/val and val/val were 53.7%, 54.4%; 45.6% 44.9%, and 6.7% , 5.7%, in male and female respectively. Similarly, the CYP1A1 polymorphism is detected for codon 462 using Real Time PCR (Taq Man chemistry). The three isoforms follows Hardy-Weinberg Equilibrium. These genes have role in metabolizing and excretion of foreign compounds. The null genotype and val/val of GSTP1 will be having low enzyme activity. Once the deleted/null frequency of these genes are known, then it might pave the way towards understanding the susceptibility of an individual to the hazardous effects of foreign compounds to which he/she may be exposed accidentally or at the work place.



A to G transition leads to change in genotype which alters the enzyme activity “A” represents allele with ile/ile genotype at codon 462, “B” represents allele with val/val genotype at same position

Toxicogenomics of genetic polymorphism in CYP1A1 gene and susceptibility of individuals towards chemicals/diseases

Toxicogenomics explores the effect of toxicants on transcription and translation patterns that influence the susceptibility of an individual for toxic responses. In continuation of proteomics component of this program, analysis of plasma/serum proteome of arsenic exposed and unexposed human population was carried out. The differentially displayed



proteins were identified using MALDI-TOF/LC-MS. Proteomics based studies were also performed in animals exposed to varying doses of benzo(a)pyrene. Certain proteins were found to be differentially expressed.

Another study was undertaken to investigate the presence of SNPs in p53 and CYP1A1 genes in Indian women. Genomic DNAs were isolated from peripheral blood samples using rapid salting out procedure from 100 healthy control women and 100 breast cancer patients. Exon-4, 5 and 6 of p53 gene were PCR amplified with specific primers. DNA sequencing indicated involvement of 72-codon polymorphism in exon-4 which is responsible for onset of breast cancer even in Indian women. Additionally, insertions at several locations in exon 5 of p53 genes were also found in breast cancer patients. Further, four commonly occurring SNPs reported in CYP1A1 viz. isoleucine to valine substitution at 462 codon in heme binding region in exon 7 (M2), threonine to asparagine substitution at codon 461 (M4), T to C transition at 3801 position (M1) and T to C transition at position 3205 (M3) in 3' non-coding region were analyzed in Indian women. Association of M1, M2, M3 and M4 polymorphisms in premenopausal and postmenopausal women with breast cancer risk in north Indian women using PCR-RFLP was investigated. Polymorphism at M1 and M4 alleles was not found significantly associated with breast cancer risk and only wild type genotype was found in case controls and breast cancer patients for M3 allele in north Indian women. Lack of protective association between CYP1A1 M2 genotype was also observed, however, in postmenopausal women a significant protective association with breast cancer risk was found. Significant alteration in CYP1A1 expression and catalytic activity was neither observed in wild type nor in variant genotypes both in pre- and post-menopausal patients as compared with their respective controls.

Transcriptome profiles in the tissues of toxicant exposed and unexposed animals using microarrays/RT-PCR was performed. Involvement of inducible nitric oxide synthase (iNOS) and toxicant responsive gene CYP1A1 in benzo(a)pyrene induced cellular toxicity was also assessed. A significant augmentation was observed in the expressions of iNOS and CYP1A1 in PMNs of benzo(a)pyrene treated rats as compared to respective controls. NOS inhibitors resulted in a significant attenuation in iNOS expression; however, no significant alteration was observed in CYP1A1 expression. CYP1A1 inhibitor alpha-naphthoflavone inhibited the expression of iNOS. The study suggests that CYP1A1 induces iNOS expression and could be responsible for the augmentation of benzo(a)pyrene-induced injury in PMNs. Differential expression profiling to assess the differential expression of toxicant responsive genes in the tissues of unexposed and pyrogallol and/or rifampicin exposed animals and effect of sylimarin on pyrogallol and/or rifampicin-induced hepatotoxicity was also initiated during this year. Upregulation in the expression and activity of some toxicant responsive genes (as observed by RT-PCR) were observed following treatment with hepatotoxins, however, sylimarin attenuated hepatotoxin induced toxicant responsive gene expression and activity.



Project: Predictive medicine using repeat and single nucleotide polymorphisms

Single Nucleotide polymorphisms (SNPs) in the genes involved in toxication-detoxication

Studies were carried out to identify SNPs in the genes (Cytochrome P450B1-CYP1B1, CYP1A2, arylhydrocarbon receptor-Ahr, arylhydro-carbon nuclear translocator-Arnt) which are involved in the metabolic activation of procarcinogens and promutagens in the Indian population. PCR and sequencing reactions were standardized for each of the genes with the primers designed to identify novel SNPs in the regions in which functionally important polymorphisms have been reported in other populations. Sequence analysis for CYP1B1 gene, a constitutive CYP isoenzyme involved in the metabolic activation of the carcinogens, in the 38 representative samples of contrasting Indian population revealed 10 polymorphic sites (C903G, G1116T in exon 2 and C5090G, T5143C, A5154G, A5160T, G6123T, T6165G, A6403G, C7299T in exon 3) in CYP1B1 gene. Two of these SNPs (A5160T and T6165G in exon 2) could be novel as they have not been reported in the literature or in the database (dbSNP of National Center of Biotechnology Information, NIH, Washington, U.S.A). Likewise sequence analysis of CYP1A2, a constitutive CYP belonging to CYP1A family, involved in the metabolic activation of procarcinogens and promutagens, in these DNA samples revealed 8 SNP positions (-G3859A, -2466 Tdeletion, -C993A in promoter region; -T739G, -C161A in intron 1; C42T in exon 2; G2158A, G2320C in intron 4) in CYP1A2. Two of these SNPs (-C993A, C42T) could be novel.

SNPs were also found in AHR and Arnt genes to which carcinogens and mutagens bind and are important in initiating carcinogenesis. SNP analysis revealed 7 polymorphic sites in the regions studied (T10737C in exon 2; T11033C in intron 2; A35831G, T36013C and T36127C in intron 8; G40221A and G40268A in exon 10), of which SNP (T11033C) found in intron 2 was novel. Likewise, sequence analysis revealed 5 positions of SNPs which were earlier reported in other populations also.

Further studies are in progress to validate these SNP positions in these genes in a larger sample size. However, our preliminary data have indicated that functionally important SNPs reported in Caucasian and Asian populations and which predisposes individuals to the carcinogenic effects of environmental chemicals are also found to be present in the Indian population. Validation of these SNPs will further provide the necessary information that will help in understanding the role of genetic differences and variations in susceptibility to environment induced diseases.



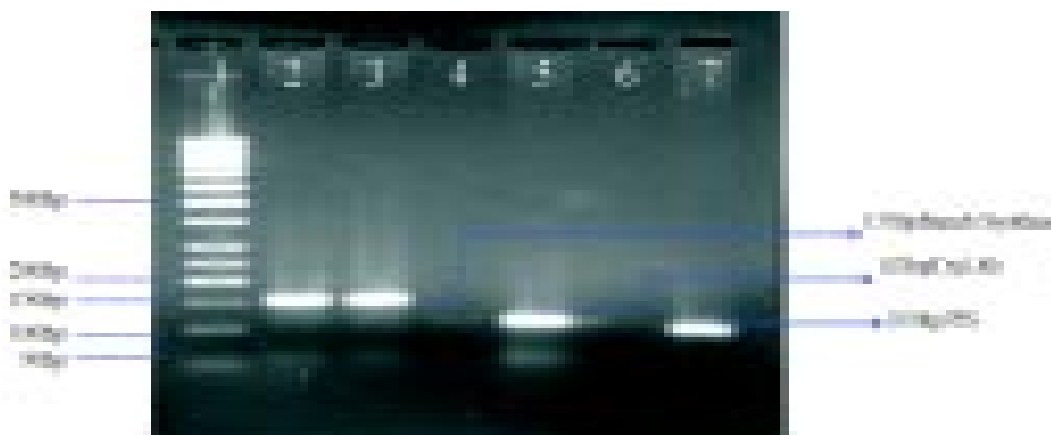
Project: Establishment of genetically modified food referral facility (GMFRF)

Detection of GM Foods using PCR technique

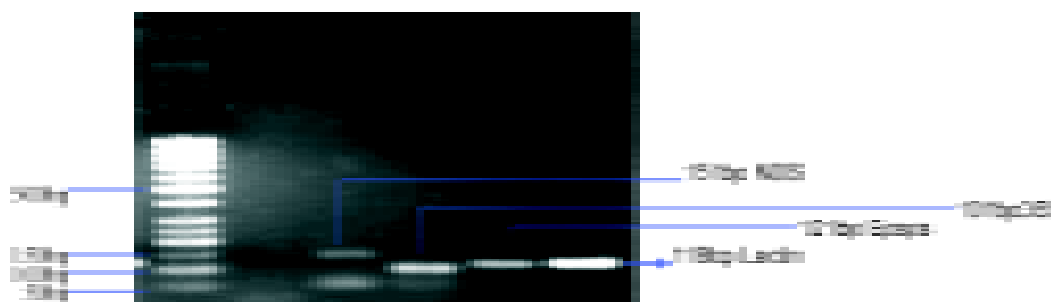
To meet the increasing demand for food, new varieties of GM crops are being produced and likely to be imported soon in India. However, at present no GM crop is approved to be marketed in India except Bt-Cotton, which is grown in six states in the country. The idea is to develop such GM crops which possess inherent capacity to cope with adverse environmental conditions. However, to ensure the safety of GM crops from the view point of human consumption, risk assessment studies are warranted. Strategically, quick and efficient detection of transgenes introduced in GM crops are the need of the hour to ensure the safety of crops before marketing.

ITRC has developed for detection methods of two GM crops RR Soybean and Maize MON810. PCR and Real time PCR (SYBR Green Chemistry) based detection of 35S promoter, Nopaline synthase terminator, Epsps and Cry 1Ab genes has been developed. As low as 0.1% GM could be detected using PCR Technique which is in compliance with International Labelling norms.

GMFRF

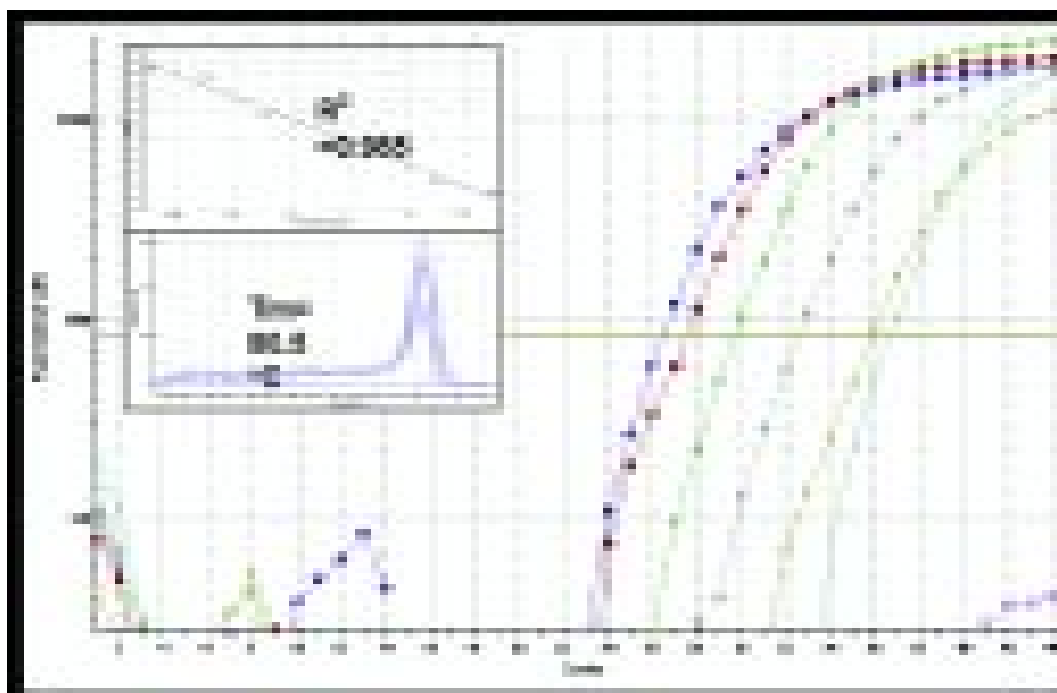


Detection of genetically modified maize (MON810)



RR soybean genes using a single PCR programme





Amplification plots for CAMV 35S promoter gene detection and confirmation of product formation with distinct melting peak

Assessment of in-silico tools for predicting potential allergenicity of novel proteins in transgenic crops

Genetically modified crops with pest or herbicide resistance character have been commercially exploited around the globe. Using an approach of bioinformatics, available on several online databases, comparison of a protein to a known allergen can be carried out. A sequence alignment programme known as FASTA was utilized here to compare the peptide sequences inserted in transgenic crops to the sequences of known allergens. According to the currently accepted criteria, a novel protein can be classified to be an allergen if any of the 80 amino acid peptide protein fragments of the same protein shares at least 35% homology with a known allergen. The studies were performed taking positive allergenic sequences (10), negative allergenic sequences (12) and also sequences (10) that have been inserted in transgenic crops to produce a native crop. In case of positive allergenic sequences, the FASTA search displays an expected correlation i.e. 6-, 7-, 8-mers showed exact matches and 80-mer searches showed more than 35% homology with known allergens. Negative sequences, as expected showed no match in case of 7- and 8-mers and not more than 35% homology to 80mers, but certain 6-mer matches were found as compared to sequences existing on the online database. Sequences, which have been used as an introduced trait in crop modification, have not shown exact matches for 7-, 8-, and 80-mers. However, when 6 contiguous amino acid matches were performed,



certain exact matches with known allergens were found. Thus, it is quite likely that 6-mer matches may generate unacceptable levels of false positives. Hence, the previous recommendation of WHO/FAO 2001 needs to be revived from 6-mer to 8-mer homology, since the former involves several dubious results. Further, the results indicate that positive sequences need to be theoretically allergenic and negative to be non-allergenic. The importance of bioinformatics in performing pre-laboratory testing of the probable inserted sequences has been put forth, since it requires limited resources and less tedious to perform such searches. The sequences, which were found to be allergenic by such a database search needs to be put under laboratory testing for validation of bioinformatics results.

Studies on simulated gastric fluid digestibility of proteins of different legumes: A possible indicator of allergenic potential

In vitro simulated gastric fluid (SGF) digestion assay has been recommended as one of the battery of tests to evaluate the allergenic potential of a new protein inserted into Genetically Modified (GM) crops. Under substantial equivalence, individual characteristics of both GM and non-GM crops have to be compared. Hence, digestibility of crude protein extract (CPE) of native legumes was envisaged. CPE from green gram, white kidney bean, black gram and soybean were digested in SGF digestion protocol at different time intervals followed by identification of protein bands by electrophoresis. An optimum concentration of 0.96% pepsin was found for digestibility of CPE. In White kidney bean CPE, the proteins having molecular weight of 17, 45 and 50 kDa were found undigested after 8 minutes of incubation. In Black gram CPE, 48 kDa protein was not fully digested after 8 minutes after digestion. In Soybean CPE, two bands (6.5 and 53 kDa) were found to be stable up to 8 minutes. In case of Green gram as many as five proteins bands having molecular weight of 8, 16, 20, 24 and 52 kDa were stable to digestion up to 8 minutes. The studies may be useful in identifying of non-digestible proteins in different crops and may find applicability in defining the allergenic potential of various proteins in crops.

GMFRF



Project: Establishing advanced facility for the safety evaluation of genetically modified/engineered drugs

A state-of-the art advanced pre-clinical toxicity evaluation facility for genetically modified/engineered drugs has been established at ITRC-Gheru Campus. The facility is equipped with sophisticated equipments like Fluorescence-assisted cell sorter (FACS), ELISA, Bright-field, fluorescence, and inverted microscopes with CCD camera and image-analyzing software, 2D-gel-electrophoresis, CO₂-incubators, bio-safety cabinets, deep-freezers, refrigerated centrifuge, water purification system, and accessory tools and apparatus. The facility is designed and furnished to provide optimum environmental conditions and separation of activities to establish cell/tissue cultures and *in-vitro* models suited for non-clinical safety/toxicity studies of diverse molecules and products as per GLP norms.

Applicable guidelines, open literature on protocols and SOPs for safety testing, and available databases from the published literature and regulatory submissions have been compiled towards creation of a “Referral Centre” for toxicity evaluation of chemicals, drugs, bio-products, etc.

The commitment towards development of human resource has been met through training more than 450 scientists, students, test facility personnel, regulatory personnel and prospective GLP-inspectors, in India and abroad, on OECD Principles of GLP and its implementation and monitoring towards global acceptability of data from non-clinical safety/toxicity studies.

Current efforts are directed towards generating essential pre-clinical toxicity evaluation data as per GLP norms for currently marketed genetically modified/engineered drugs as model/reference substance to validate the established protocols and SOPs, and those referred by the pharmaceutical industry to render services. Attempts are also being made to develop human resource in non-clinical safety/toxicity screening of molecules and products through technical training in laboratory operations using established protocols and SOPs.



Project : Newer scientific herbal preparations for global positioning

Studies were carried out for the development of a scientifically validated health promoter, based on traditional knowledge. The selected medicinal plants were subjected to contaminant testing for presence of Pb, Cd, Cr, Ni, Hg and arsenic. Presence of residual organochlorine pesticides such as isoforms of HCH, DDT and their metabolites and endosulfan was also evaluated. Extracts of contaminant free medicinal plants were prepared for evaluation of bioactivity. Altogether 31 selected plant extracts were screened for antioxidant potential using five semi-automated 96 well microplate assays for SOD mimetic activity, LPO inhibitory capacity, total thiol content, trolox equivalent antioxidant capacity and NO quenching capacity. The extracts received for bioactivity evaluation were also subjected to evaluation for their anti-Parkinsonian, anti-dementia, anti-depressant and anti-anxiety potential using receptor-radioligand binding assays. Out of the 31 extracts screened so far, 8 have been selected for antioxidant properties and 5 were found to have neuroactive potential as evident from more than 60% inhibition of receptor binding. Two extracts were found to have anti-anxiety activity as evident from inhibition of benzodiazepine receptor binding. These extracts were also found to be strong antioxidants as they showed considerable radical quenching capacity and activity on all the five screens for antioxidant testing. All the 31 extracts were tested for their toxic potential using OECD guideline 420 for acute toxicity. None of the extracts was found to have any toxic potential and their LD₅₀ was found to be >2000mg/kg. These extracts were classified as category 5 as per Globally Harmonised System of OECD. Based on the results obtained during the studies, 3 Positive Health Promoter (PHP) formulations are now being developed under GMP norms by Nicholas Piramal. These formulations are health promoters for aged population and have also anti-cancer and anti-diabetic properties. These formulations will now be subjected to detailed *in vivo* exploratory studies along with long term toxicity studies. The final product will be patented for global positioning after systematic clinical trials at hospitals selected by the task force.

Screening of antioxidant potential of selected barks of Indian medicinal plants using multiple *in vitro* assays.

Barks of five therapeutically important medicinal plants native to India i.e. *Crataeva nurvala* Buch.–Ham., *Buchanania lanzan* Spreng., *Aegle marmelos* Corr., *Dalbergia sissoo* Roxb. ex DC. and *Cedrela toona* Roxb. were evaluated for their antioxidant capacity using multiple *in vitro* assays. Standardised aqueous alcoholic extracts of the selected barks were prepared and screened using multiple assays targeting superoxide radical, peroxidative decomposition of phospholipids, nitric oxide and ABTS radical. These extracts were also tested for total phenolic content and tannin content which was found to be highest in *C. nurvala* i.e. 195 GAE mg/g and 218.3 mg/g CE. SOD mimetic activity was found to be highest in *Crataeva nurvala*, although all barks showed activity more than 100 units/mg extract. Lipid peroxidation inhibitory potential was found to be highest in *Crataeva nurvala* (83.4 % inhibition of MDA formation/10µg extract), which also



showed comparatively high NO quenching capacity i.e. 45.5% per 10 μ g extract. The highest NO quenching potential was found in *Aegle marmelos* i.e. 47.3% per 10 μ g extract. *Cedrela toona* showed lowest LPO inhibitory and NO quenching capacity i.e. 50.5% and 30.5% respectively. *Buchanania lanzan*, a medicinal plant extensively used for inflammatory disorders and *Dalbergia sissoo* also showed 72.5% and 69.1% LPO inhibitory potential/10 μ g extract. Trolox equivalent antioxidant capacity ranged between 0.24 to 0.39 mM TEAC/mg extract indicating all the barks tested had ABTS⁺ radical quenching capacity. On comparison, bark of *Crataeva nurvula* was found to have highest antioxidant capacity as evident from screening on multiple *in vitro* assays targeting different radical species, and a positive correlation between antioxidant activity and phenolic content was found.

Anti-microbial, antioxidant activity and chemical fingerprint profile of *Zingiber officinale* from different ecological zones of India.

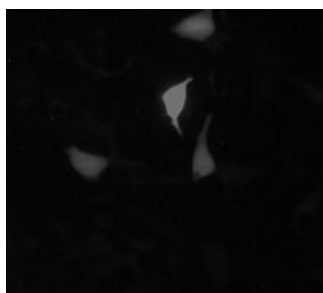
Zingiber officinale (Zingiberaceae) is one of the most utilized herbal drugs in traditional system of medicine. Its therapeutic uses include protection against throat ailments, bronchitis, dyspepsia, colic and as a stimulant. Samples of rhizomes were collected from different ecological zones of India to study any variation in their chemical fingerprint profile and biological activity. Aqueous alcoholic extracts of *Z. officinale* representing 9 locations across the country were analysed using TLC and HPLC. Camphene and Geraniol, two important constituents of the drug were found to be maximum i.e. 98% & 40% respectively in the sample from Madurai representing southern region. All the samples showed strong antioxidant potential on screen for SOD mimetic activity, LPO inhibitory potential & ABTS (2,2 Azino-bis(3-ethylebenythiozoline-6-sulphonic acid) radical scavenging assay. Madurai sample was again found to have highest superoxide scavenging capacity. Antimicrobial activity of these extracts was tested against seven gram +ve and gram -ve test bacteria. All the extracts showed strong to moderate antimicrobial activities against *B. cereus*, *B. subtilis*, *S. typhi*, *S. flexneri*, *S. sonnei*, *S. auerus*, *P. aeruginosa* and *E. coli*. The MIC values of *B. cereus* and *P. aeruginosa* ranged from 0.01 mg/ml to 10 mg/ml indicating strong activity against these bacteria, which was again highest in Madurai sample. The results obtained here using semi automated microassays and modern biological tools confirm that *Z. officinale* obtained from the southern region of India has higher antioxidant, antimicrobial activities and bioactive constituents. The information can be useful while procuring the raw material for preparation of therapeutic formulations.

6-Gingerol promotes apoptosis in prostate as evident from the loss of mitochondrial potential, caspases activation and DNA fragmentation

Ginger has been used as a spice in traditional oriental medicine. The rhizome of ginger contains pungent vanillyl ketones, including 6-gingerol and 6-paradol, which are credited for its therapeutic/preventive properties. Prostate cancer (PCA) is an attractive target for chemoprevention because of its ubiquity, treatment-related morbidity, long latency between premalignant to clinically evident cancers. The modulatory effects of 6-gingerol have been observed on testosterone-induced alteration of cell growth regulatory genes in mouse prostate and in LNCaP cells. *In vivo* studies showed that 6-gingerol treatment leads to restoration



of enlarged prostate and levels of serum prostate specific antigen, wild-type and mutant p53 levels in mouse prostate and LNCaP cells. Also, resulted in upregulation of testosterone-depleted, pro-apoptotic proteins Bax, Caspase-3 and Caspase-9 expression. This resulted in down-regulation of anti-apoptotic protein Bcl2 and survivin both *in vivo* in mouse prostate and *in vitro* in LNCaP cells. Flow cytometric analysis revealed dose dependent increase in the sub-G1 cells upto 20% by 50mM and 50% by 75mM of 6-gingerol in LNCaP cells at 48h. administration. Further studies revealed that 6-gingerol induced cell death of LNCaP cells was a result of apoptosis, as indicated by depolarization of mitochondrial membrane potential and the appearance of DNA laddering pattern in agarose gel electrophoresis. It was concluded that 6-gingerol can modulate cell-growth regulatory genes expression, which play vital role in progression of the PCA. Thus, 6-gingerol can act as an effective chemopreventive and therapeutic agent for prostate cancer.



A

B

C

6-gingerol induces apoptosis in prostate cancer line LNCaP as assessed by fluorescence microscopy.(A) No treatment (B) LNCaP Cells after low dose treatment with 6-gingerol (C) LNCaP Cells after high dose treatment with 6-gingerol.

Chemopreventive effects of lupeol and mango pulp extract in prostate cancer

Prostate cancer is one of the most invasive malignancy and second leading cause of cancer related deaths in United States. Long latency period makes prostate cancer an ideal disease for chemoprevention. Lupeol, a triterpene, present in mango and other fruits have been shown recently to possess chemopreventive properties. *In vivo* studies in mouse prostate and *in vitro* in human lymph node carcinoma of prostate cell line LNCaP were conducted to understand the apoptogenic potential of Lupeol and mango pulp extract (MPE). Subcutaneous injections of testosterone (5 mg/kg body weight) were given to Swiss albino mice for 14 consecutive days. In the experimental groups lupeol/MPE was given 1 hr prior to testosterone administration. Results showed that lupeol/MPE treatment prevents the enlargement of prostate and decreases levels of serum prostate specific antigen induced by testosterone as evident from an increase in apoptotic cell population in hypodiploid region of prostate cells as was recorded in lupeol and MPE supplemented groups of animals. Loss of mitochondrial transmembrane potential and DNA fragmentation was also recorded along with induction of apoptosis. In prostate of testosterone treated animals, upregulation of antiapoptotic protein Bcl-2 and downregulation of proapoptotic Bax and Caspase 3 were observed. These alterations were restored by lupeol/MPE,



indicating their apoptogenic potential. Under *in vitro* conditions, lupeol induced apoptosis in LNCaP cells can be summarized as early increase of ROS, followed by induction of mitochondrial pathway leading to death of cells. The observations demonstrated that lupeol/MPE were effective in combating benign hyperplasia of prostate and induction of apoptosis of LNCaP by modulating cell-growth regulators. Mango and its constituents therefore, deserve to be credited as potential chemopreventive/chemotherapeutic agents against prostate cancer.

Decline in antioxidant capacity of Indian herbal teas during storage and its relation to phenolic content

The changes in the stability of antioxidant capacity with time and its relation to the phenolic content were evaluated in eight Indian herbal teas. These herbal teas are claimed to have multiple bioactivities from antistress to antihypertensive and memory enhancer. Antioxidant capacity was determined over a period of 15 months from the date of their procurement using assays for SOD mimetic activity, LPO inhibitory capacity and total thiol content, which decreased positively with time. The SOD mimetic activity values in control samples (at the time of procurement) were seen to be in the range of 54.63–93.64 units/min/mg of extract which after 15 months of storage decreased upto 7.4-folds in some samples. LPO inhibitory capacity was observed upto 96.75% in herbal tea E at the time of procurement which dropped to 63.85% inhibition of MDA formation/5ml of extract after 15 months. In case of total thiol, the values were seen in the range of 0.55–1.71 mg/g and after 15 months it was from 0.12 to 0.21 mg/g. In all these cases high antioxidant activity was seen in the samples with higher phenolic content which also showed comparatively less decline in antioxidant capacity after considerable storage time. The results have significance, as most of the herbal teas available in the local markets in India do not carry any information regarding the period of use without decline in its beneficial effects.

Toxicity studies of herbal preparations

Herbal extracts were evaluated for their acute toxicity. Sighting study followed by main study as per OECD guidelines was performed. The test substances did not produce any toxicological symptoms and mortality at the limit test dose level of 2000 mg/kg body weight. Therefore, the acute oral medial lethal dose LD₅₀ of substances in female rats was evaluated to be more than 2000 mg/kg body weight.



Project : Discovery, development and commercialization of new bioactive and traditional preparations

A total of 3868 herbal preparations/extracts were screened *in vitro* for their activity on dopamine-D2, cholinergic, muscarinic, serotonin-2A and benzodiazepine receptors to assess their psychoactive potential. Based on the *in vitro* screening of extracts on different receptor targets, 182 extracts were found active – (Dopamine –D2 receptors- 50, Cholinergic-muscarinic receptors – 49, serotonin-2A receptors –35, benzodiazepine receptors – 48). The extracts/samples found active on *in vitro* dopamine-D2 receptors have been recommended for *in vitro* screening on mouse model of Parkinson’s disease to IICB, Kolkata. Extracts found active on cholinergic, muscarinic, serotonin – 2A and benzodiazepine receptors have been recommended to CDRI, Lucknow to assess their anti-dementia, anti-depressant and anti- anxiety activity respectively on animal models.

Anti-psychotic activity of extracts was also assessed on rat model. A total of 48 samples were screened out of which 5 were found active. These samples are in different stages of drug discovery.

In another set of study, 78 coded extracts from plants, Ayurvedic, Unani and Siddha sources were subjected to secondary screening for identification of strong antioxidants. 5 Unani extracts and 17 Siddha extracts have been selected for further studies. Six lead molecules found to have neuroactivity in repeat experiments were tested for antioxidant capacity and 2 were reported to be strong antioxidants after testing on multiple screens.



96-well plate microassay for ABTS⁺ radical quenching capacity

New bioactive & traditional preparations



Project : Comprehensive traditional knowledge, digital documentation & library

Conventional wisdom and experience is the essence of traditional knowledge. Since India has a rich knowledge base of traditional system of medicine and the vast biodiversity has been conducive in providing cures to ailments including poisonings, the existing information on medicinal plants is stored in ancient literature and among local people in the form of traditions and local folklore preserved for many many years. Collection and collation of these information systematically must be preserved in an electronic format for emergent retrieval so as to make it easily accessible to users and also to mitigate the risk of bio-piracy by patenting the interest of the knowledge holders.

ITRC is participating in this programme of value addition and will provide toxicological information and antidote potential of medicinal plants used in Ayurveda. A Digital Library has been created here replete with 8 computers and 131 referral books.

Out of the 1400 plants used in Ayurveda, information on toxicology parameters, active constituents, and antidote potential of 700 plants has been compiled and is being validated. Digital documentation of this information is being carried out on the software provided by the nodal lab, whereas information of 340 plants has already been added to the database.

CTKDL



Dr. C.M. Gupta, Director, CDRI and Prof. Y.K. Gupta, Director, ITRC during the inauguration of the TKDL facility at ITRC - June, 2005



Project: Asthmatic and allergic disorder mitigation mission

Prediction of acute oral toxicity (LD₅₀) in rodent from IC₅₀ by performing in vitro BALB/c 3T3 Neutral red Uptake (NRU) cytotoxicity test

Based on the 3T3 NRU regression model, $\log(LD_{50}) = 0.506 \times \log(IC_{50}) + 0.475$, we predicted acute oral toxicity of 12 new drugs provided by Indian Institute of Chemical Biology, Kolkata and Indian Institute Chemical Technology, Hyderabad was predicted. This model of toxicity testing helps in reducing usage of animals for generation of initial toxic indications. Some of the coded samples tested using this *in vitro* method are listed below :

IICB-D6	IICT-TA-45
IICT-TA-57	IICT-TA-62
IICT-TA67	IICT-TA78
IICT-TA52	IICT-TA55
IICT-TA71	IICT-TA83

Role of STAT3 in murine airways in response to IL-6, TNF- α and IL-13

The gene STAT3 is a transcription factor activated by a wide range of cytokines and may play a role in lung development and asthma pathogenesis. Recently STAT3 has been implicated in inflammatory and allergic airways asthma pathogenesis. This study was conducted to examine the role of STAT3 in murine airways in response to IL-6, TNF-, IL-13, which play a major role during asthma pathogenesis. Airway STAT3 activation and over-expression in mouse asthma models which was significantly correlated with airway inflammation, suggesting that STAT3 may play an important role in airway inflammation and asthma treatment. Heightened expression of IL-6, IL-13 and eotaxin was demonstrated in the trachea and lung of induced mouse model of asthma. Also intra nasal delivery of STAT3 siRNA could inhibit STAT3 gene expression and further exhibits global effect on inflammation-associated cytokines. Silencing of STAT3 gene in 3T3 cells suppressed the IL-6 mediated expression of TNF- α mRNA significantly. Collectively, these results demonstrate that transfection of STAT3 siRNA can regulate the expression of inflammation associated cytokines and may be of use in therapy.



Project: Animal models and animal substitute technologies

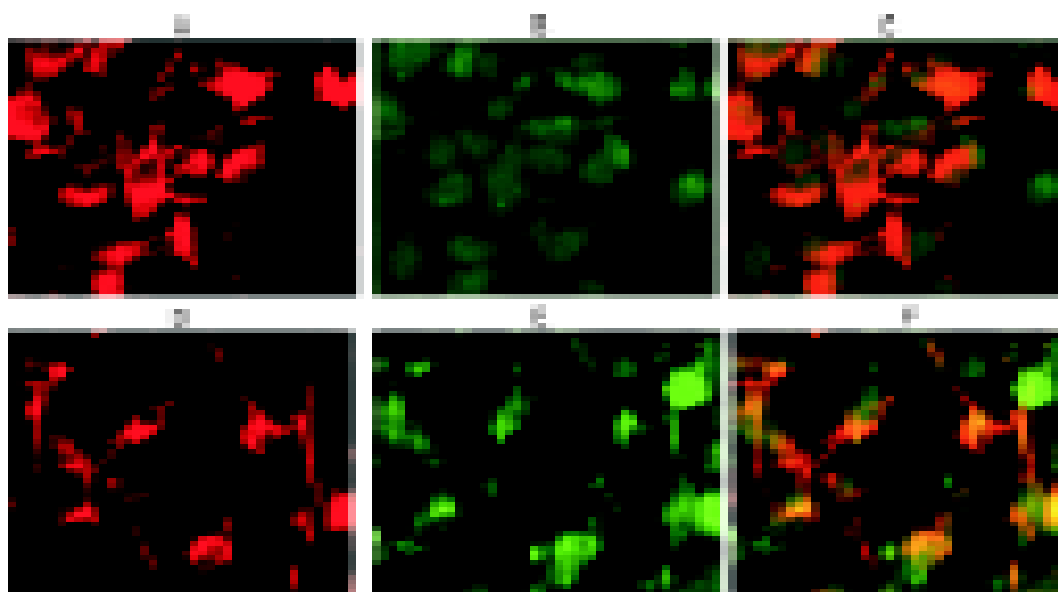
***In vitro* receptor binding screen for efficacy and toxicity of candidate psychoactive drugs and environmental chemicals**

Dopamine DA-D2 receptor binding in SHY-SY-5Y human neuroblastoma cell line was used as a model for the assessment of neurotoxicity of environmental chemicals. Studies with non-cytotoxic doses of cypermethrin (10^{-6} M), a pyrethroid pesticide and a known neurotoxicant, showed time dependent dopamine mediated changes comparable to that observed in brain. These changes were also found to be temperature and protein dependent. The results are indicative that the receptors for DA-D2 are expressed and physiologically functional in human neuroblastoma cell line, SHY-SY-5Y and could be used as an *in vitro* model for the assessment of neurotoxicity of environmental chemicals.

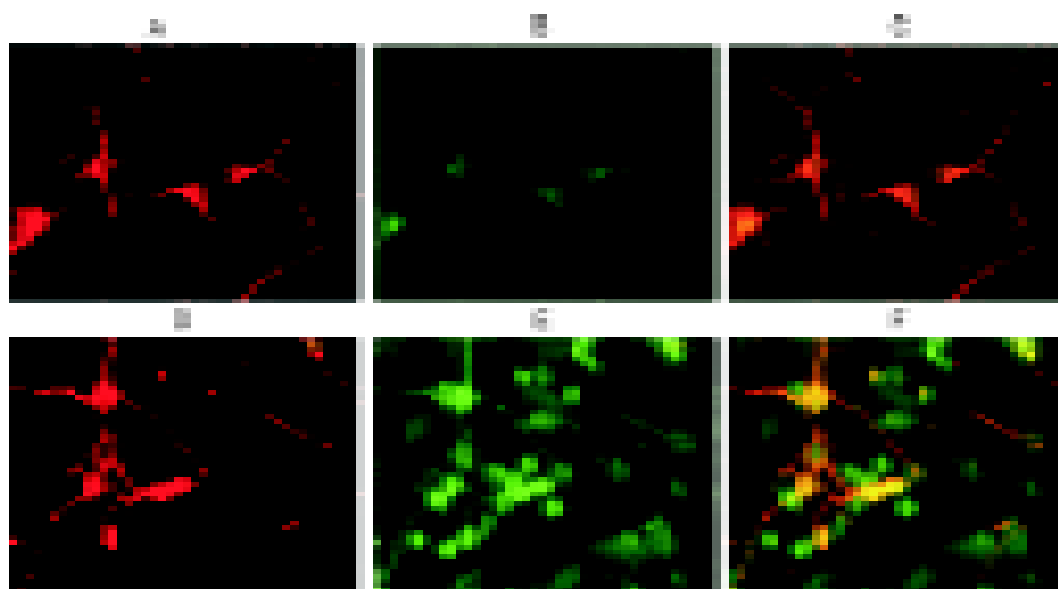
Establishment and validation of primary cultures of brain cells as *in vitro* model for neurotoxicity assessment

A correlation in the induction of specific expressions of CYP1A1, CYP2B1/2B2 and CYP2E1 at both transcriptional and translational levels following exposure to known inducers like methylcholanthrene, phenobarbital and ethanol respectively in both neuronal and glial cells was reported earlier. In order to establish the suitability of cultured neuronal and glial cells *in vitro*, the validation studies were conducted with deltamethrin (DM), a pyrethroid insecticide, keeping in view the cell specific effects of neurotoxicants. The studies were carried out to see the treatment-induced changes in CYP2E1 dependent NDMA-d, CYP1A1/1A2 dependent EROD activity and CYP2B1 dependent PROD activity in cultured rat brain neuronal and glial cells. Non-cytotoxic doses of DM were ascertained first by MTT and LDH assays under *in vitro* condition, prior to start of induction studies. DM demonstrated a dose and time dependent increase in EROD, PROD and NDMA-d activity in both the cultured cells. Neuronal cells in general, exhibited higher enzymatic activities than the glial cells. Expression (CYP2E1) studies with DM were also carried out in cultured neuronal and glial cells using immunocytochemical dual staining technique. Both neuronal and glial cells cultured with DMEM medium alone or treated with deltamethrin grown on PLL coated glass slides, immuno stained with isoform specific CYP or β III tubulin or GFAP antibodies followed by secondary antibodies labeled with FITC or TRITC showed positive staining for CYP2E1. The neuronal cells exhibiting staining with β III tubulin antibody also expressed CYP2E1 as evidenced by staining with CYP2E1 antibody. Likewise, glial cells exhibiting staining with GFAP antibody also expressed CYP2E1. The study revealed that treatment with deltamethrin resulted in an increase in the intensity of FITC fluorescence. These *in vitro* results showed consistency with the *in vivo* studies conducted in rat model following exposure to deltamethrin. The data suggests the utility of cultured neuronal and glial cells as *in vitro* tool assess neurotoxicity.





Immunocytochemical detection of CYP2E in cultured rat brain glial cells. A, B and C represent primary cultures of glial cells in DMEM. D, E and F represent cultures of glial cells in DMEM+deltamethrin. A and D show cells in culture that are positive for GFAP antibody (red-TRITC), a glial marker. B and E show immunoreactivity in the same glial cells with CYP2E antibody (green-FITC). C and F represent an overlay of the two images of control and deltamethrin treated cells respectively demonstrating that the intensity of fluorescence for CYP2E is more in treated cells as compared to the control. Original magnification x 400, scale 20m m.



Immunocytochemical detection of CYP2E in cultured rat brain neuronal cells. A, B and C represent primary cultures of neuronal cells in DMEM. D, E and F represent cultures of neuronal cells in DMEM+deltamethrin. A and D show cells in culture that are positive for β -III tubulin (red TRITC), a neuronal marker. B and E show immunoreactivity in the same neuronal cells with CYP2E antibody (green-FITC). C and F represent an overlay of the two images of control and deltamethrin treated cells as compared to the control. Original magnification x 400, scale 20mm.



Establishment and validation of *in vitro* model system for cytotoxicity assessment.

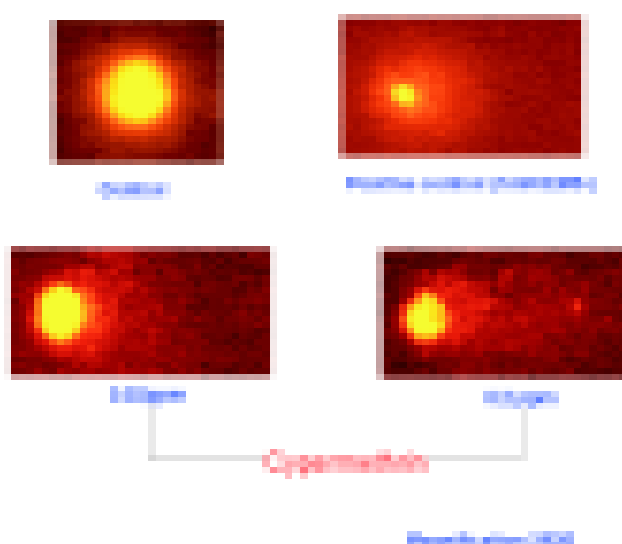
In continuation to earlier studies, validation of L929, a mouse fibroblast cell line was carried out with the leachates of plastic and polymeric finished products following the recommendations of ISO 10993-Part-5 and USP-23 guidelines. The same has also been used to assess the safety of various ready to use plastic products for industries.

Another USP recognized and validated *in vitro* test system for bacterial endotoxin detection has been utilized to detect endotoxin of various industrial products.

DNA damage by cypermethrin in *Drosophila melanogaster*: A mechanistic approach

Cypermethrin, a widely used type II pyrethroid pesticide has been shown to induce genotoxicity in target as well as non-target species. However, its molecular mechanism is yet to be properly elucidated. The study was undertaken to examine the mechanism of DNA damage by cypermethrin using different DNA repair deficient strains of *D. melanogaster* viz. *mus101^{D1}* (post replication repair), *rad201* (cell cycle control), *mei-9^a mei-41^{D1}* (the incision step in nucleotide excision repair, cell-cycle checkpoint) with respect to the wild type strain Oregon R⁺. Third instar larvae (74 ± 2 h) of *D. melanogaster* were exposed to 0.002-0.2 ppm cypermethrin mixed standard *Drosophila* food for 48h. Brain ganglia from control and treated larvae were dissected out, single-cell suspensions were prepared and Comet assay was performed. A concentration dependent increase in the DNA damage was observed in the wild type as well as mutant strains of *D. melanogaster* as evident by the Olive tail moment (OTM). The exposed larvae of *mei-9^a mei-41^{D1}* strain showed a significant DNA damage at the lowest dietary concentration of the chemical. At this concentration, no significant DNA damage was evident in the wild

Figure 1: DNA damage in brain ganglia cells of *Drosophila melanogaster* exposed to 0.002 ppm cypermethrin mixed standard *Drosophila* food for 48h.



type suggesting that cypermethrin induces single strand breaks probably by adding bulky group to DNA which does not get repaired by nucleotide excision repair pathway (NER) in *mei-9^a mei-41^{DI}*. The DNA damage induced in *mus101^{DI}* is comparable to that observed in the wild type indicating that post replication repair does not have any significant effect on cypermethrin mediated genotoxicity. Interestingly, DNA damage observed in *rad201* (radiation sensitive strain) suggests that cypermethrin may be producing DNA double strand breaks. Further studies are in progress to elucidate the mechanism of cypermethrin induced DNA damage.

Thiamine ameliorates lead induced genotoxicity *in vivo*

Lead has long been a concern for both environmental and human health. It is a potential carcinogen and adversely affects the central nervous system, cardiovascular system and kidneys. The genotoxicity of lead salts is attributed to its interference with DNA repair and also clastogenicity. Various chelating agents e.g. thiamine, calcium salt of EDTA etc, have been used to reduce the body burden of lead and may thereby reduce its long term toxicity. The study was undertaken to examine genotoxicity of lead as well as its amelioration by thiamine (Vitamin B1). Lead nitrate induced genotoxicity in blood and bone marrow cells of mice and the prophylactic as well as therapeutic effect of thiamine (Vitamin B1) was investigated using alkaline Comet assay. Male Swiss albino mice were administered lead nitrate intraperitoneally (i.p.) alone (3.25-15mg/kg body weight) for 24 hours, and a pre- or post- treatment with thiamine hydrochloride (25mg/kg body weight, i.p.) for 24 hours each. Comet assay was performed on the blood lymphocytes and bone marrow cells. The results revealed a dose dependent increase in the DNA damage in both cell types at all doses of lead nitrate tested when compared to the untreated controls. This was evident by a statistically significant ($p < 0.01$) increase in the comet parameters (OTM, arbitrary units: tail DNA (%) and tail length (μm)). Thiamine treatment significantly ($p < 0.05$) decreased lead induced DNA damage in both cell types, however, the reduction in bone marrow was more significant as compared to blood lymphocytes. The data demonstrates that pre-treatments with thiamine significantly ameliorates lead nitrate induced genotoxicity compared to post-treatment. The study assumes significance in view of implementing the human health management system in lead based industries.

Stress genes as bio-indicator against exposure to environmental chemicals

Environmental chemicals such as pesticides have been reported to elicit oxidative stress and stress gene expression in the exposed organism. Role of primary protective responses against various stresses suggesting a possible correlation among them warrants investigation. This hypothesis was tested with dichlorvos and chlorpyrifos (organophosphate insecticides), using *Drosophila melanogaster* as a model and quercetin (200 μM), diethyl dithiocarbamate (1 mM) and 3-Amino-1, 2, 4-triazole (1.5 mM) as selective inhibitors of *hsp70*, superoxide dismutase (SOD) and catalase (CAT) respectively. The test chemicals of 0.015 to 150 ppb with or without inhibitors mixed in food were fed to the third instar larvae of transgenic *D. melanogaster* to observe induction for *hsp70* (*hsp70-lacZ*) for 2-48 hrs. Expression of *hsp70*, activities of acetylcholinesterase (AChE) for organophosphate



induced neurotoxicity, SOD, CAT, malondialdehyde (MDA for lipid peroxidation; LPO), protein carbonyl (PC) content and glutathione content were performed as end points.

A time dependent induction of both *hsp70* and antioxidant enzymes as compared to the control was observed in the exposed organism. A comparison of Hsp70 expression with SOD, CAT activities, LPO product and PC and glutathione contents under similar experimental conditions revealed that induction of *hsp70* precedes the oxidative stress markers in the exposed organism. Concomitant with a significant inhibition of AchE activity, significant induction of *hsp70* was observed following chemicals exposure. An inhibition of Hsp70 expression was concurrent with a significant increase in the activities of antioxidant enzymes and a decreased LPO as compared to control with a decrease in exposure time. Inhibition of antioxidant enzymes resulted in a significant induction of *hsp70* and LPO.

The study suggests that dichlorvos is more hazardous as compared to chlorpyrifos and *hsp70* and anti-oxidant enzymes work together for cellular defense against xenobiotic hazard in *D. melanogaster*. Also, free radicals generated following organophosphates exposure may contribute to the induction of *hsp70* in *Drosophila*.

Assessment of estrogenic potential of chemicals of dietary sources (Plant origin) using *in vitro* models

In recent years, it has been reported that a number of chemicals possess properties that can mimic the endogenous activity of estrogen thereby causing reproductive health hazard. In continuation to our earlier studies, estrogenic potential of dietary sources especially of plant origin (bengal gram, soybean, cabbage and rajma) was evaluated using MCF-7 cell line. The study using E-assay suggests that soybean has the maximum and rajma the least estrogenic potential.

Further, the possibility of using different cell lines was explored (L929, 3T3 and A431) along with MCF-7 cell line to ascertain if the same can be used for detecting estrogenic potential of the chemicals using 17- β -estradiol as a marker of estrogenic surge. Preliminary observations suggests that only L929 cell line showing a doubling time close to MCF-7 cells has the potential to be used for the detection of estrogenic potential of chemicals.

Aquatic test model for ecotoxicological studies

Studies were conducted to assess the adverse effects of environmental chemicals during embryonic development of 3-day old trochophore larva till hatching stage following exposure to copper. Further, development of embryos after copper exposure, normally or abnormally, was regarded as survivors. The EC₅₀ values, confidence limits (95%), and percentage mortality at different concentrations of copper and mercury during 24 to 36 hours were determined. The developing embryos were adversely affected with the increase in metal concentration.



Effects of mercury and copper at various stages of embryonic development of a freshwater cladoceran, *Daphnia magna* were also studied. Embryos were incubated at 20 °C with or without metal. The development time was recorded for every hatched young animal. In addition, gross morphological abnormalities in the formation carapace, first and second antennae, eye, digestive caecum, heart, intestine, brood chamber, shell spine and pigmentation in the body of hatched animals were observed in mercury and copper treated embryos. No obvious morphological abnormalities were observed in eyes, digestive caecum, heart, intestine and brood chamber. The developed time of hatched embryos was within two days in control and 2-3 days in mercury and copper treated conditions, respectively.

Validation of Indian earthworms for acute toxicity testing

Earthworm *Eisenia foetida* is approved by regulatory agencies. However, suitability studies are needed to validate Indian strains of earthworms for acute toxicity testing of environmental pollutants in order to assess the sensitivity of the animals towards ecotoxicological risk assessment in Indian conditions. Acute toxicity in earthworm was conducted as per OECD guidelines using Indian earthworm, *Metaphire posthuma* and in *E. foetida* using carbofuran (1.0-32.0ppm) as a test chemical. LC_{50} at 72 hr. was found to be 1.5 ppm for *M. posthuma* and the same for *E. foetida* as 9.9 ppm respectively. Morphological changes like midsegmental swellings and bleeding sores were also observed. The study suggests that *M. posthuma* is more sensitive than *E. foetida*.

Validation of *Allium sativum* for genotoxicity testing

Studies were conducted to validate *Allium sativum* as a sensitive model for genotoxicity. Clean healthy garlic cloves were exposed to 2.0-32.0 ppm cypermethrin for 5 days. EC_{50} was determined at 8.0 ppm in *A. sativum* and 10.0 ppm in *Allium cepa* respectively. This observation indicates the better sensitivity of *A. sativum* as compared to *A. cepa*. For genotoxicity studies, roots of garlic cloves were exposed to the above concentrations for 24 h. Root meristem cells were examined for chromosomal and mitotic aberrations. Cypermethrin was found to induce a significant frequency of aberrations in *A. sativum* even at its lowest concentration. All other concentrations of the test chemical induced higher frequency of chromosomal and mitotic aberrations in *A. sativum* as compared to *A. cepa*. The study suggests that *A. sativum* is more sensitive as compared to *A. cepa* and more suitable for genotoxicological risk assessment.

A similar study to validate the above was carried out using carbofuran as a test chemical. The study reaffirms the utility of using *A. sativum* for assessment of genotoxicity of environmental chemicals.



Project: Exploration, assessment and management of ground water in hard rock areas

Development of techniques and methodologies for exploitation, assessment and management of groundwater in the hard rock area

Studies were conducted to understand the soil-water interaction in the alluvium geo-environment so as to develop geo-chemical mass transport model by assessing the anthropogenic pollution in the region and associated health risk due to groundwater contamination.

The study area of Unnao district of Uttar Pradesh lies in the northern Indo-Gangetic alluvial plains. In this region groundwater is used for domestic, agricultural and industrial purposes. The compositional variations and anthropogenic influence in the region have been considered as important problem.



Study area and sampling sites in alluvial watershed (Unnao district, UP)

The soil, surface and groundwater (post-monsoon) data set of the study region was analyzed.

Chemometric analysis of groundwater quality data of alluvial aquifer of Gangetic plain, north India

Water quality data set from the alluvial region in the Gangetic plain of northern India is influenced by high fluoride levels in soil and groundwater. It has been analysed by



chemometric technique to investigate the compositional differences between surface and groundwater samples, spatial variations in groundwater composition and influence of natural and anthropogenic factors. The groundwater in this region is mainly of Na/K-bicarbonate type. A visible differentiation between the water samples pertaining to two watersheds (Khar and Loni) was obtained. Six discriminating variables between surface and groundwater and also between different types of samples (dug well, hand pump and surface water) could be identified. Distinct grouping of the surface and groundwater samples was achieved using the PLS technique. Also, the groundwater sources have been found to be contaminated with various industrial contaminants in the region.

Persistent organochlorine pesticide residues in alluvial ground water aquifers of Gangetic plains, India

Samples of groundwater (42 from dug wells and 54 from bore wells) were collected and analysed for aldrin, dieldrin, endrin, HCB, HCH isomers, DDT isomers/metabolites, endosulfan isomers (*a* and *b*), endosulfan sulfate, heptachlor and its metabolites, *a*-chlordane, *g*-chlordane and methoxychlor. The aldrin residues were higher than dieldrin and residue of endrin ranged from BDL to 1355.2 ngL⁻¹. Mean concentration of HCB was higher in borewell water as compared to the dugwells. Among the chlordane isomers, *g*-chlordane dominated over the *a*-chlordane both in terms of frequency of detection and residue levels. *a*-endosulfan predominated among the isomers/metabolites of endosulfan (*a*-endosulfan, *b*-endosulfan and endosulfan sulfate) in both the shallow and deeper ground water aquifers. The residues of *a*-endosulfan, *b*-endosulfan and endosulfan sulfate ranged between BDL-81.6, BDL-28.4 and BDL-33.7 ngL⁻¹, respectively. Relatively higher residue levels of *a*- and *b*-endosulfan and absence of endosulfan sulfate suggest for fresh input of the pesticide, while, relatively lower levels of endosulfan isomers and presence of endosulfan sulfate indicates the earlier use of endosulfan in the studied region. Total heptachlor residue (sum of heptachlor and heptachlor epoxides) in dugwell and borewell water ranged between BDL-303.6 and BDL-138.1 ngL⁻¹, respectively. Among the HCH isomers *b*- and *d*-HCH were detected most frequently. *pp*-DDE was predominant among the isomers/metabolites of DDT, followed by *op*-DDT, both in the dugwells and borewells. Total OCPs residues were found higher in the dugwell water (285.7 ngL⁻¹) as compared to the borewell waters (191.2 ngL⁻¹). It was also observed that residues of POP pesticides viz. aldrin, chlordane, DDT, dieldrin, endrin, heptachlor and HCB, except aldrin and DDT, are higher in the deeper aquifers (borewells) than shallow aquifers (dugwells).

The present study suggests that the residues of the OCPs, that are banned for last several years for manufacture/use in the country, are still present in the groundwater in this region. Their presence along with residues of pesticides still used poses health risk to the local population using these water sources.



Persistent Organochlorine Pesticide Residues in Soil and Surface Water of Northern Indo-Gangetic Alluvial Plains

This study reports the concentration levels and distribution pattern of the organochlorine pesticide (OCPs) residues in the soil and surface water samples collected from the northern Indo-Gangetic alluvial plains. Soil and surface water samples (54) were collected from the study region in Unnao district covering an area of 2150 km² and analyzed for aldrin, dieldrin, endrin, HCB, HCH isomers, DDT isomers/metabolites, endosulfan isomers (α and β), endosulfan sulfate, heptachlor and its metabolites, α -chlordane, γ -chlordane and methoxychlor. In both the soil and surface water samples β - and δ -isomers of HCH were detected most frequently, whereas, methoxychlor was the least detected pesticide. The total OCPs level ranged from 0.36-104.50 ng g⁻¹ and 2.63-3.72 μ g L⁻¹ in soil and surface water samples respectively.

Decontamination of water

Low cost adsorbents derived from waste material (coconut shell, coconut fibers) characterized for their physical and chemical properties were studied for removal of phenols (phenol, 2,4-dichlorophenol) from water under various set of conditions (pH, temperature, contact time, etc.). Major sources of phenols include coal based activities, gasoline, plastic, rubber proofing, pharmaceuticals, steel industries, disinfectant, domestic wastewater, agricultural run-offs, and chemical spills. The adsorption data were subjected to non-linear and linear Langmuir modeling to evaluate the monolayer adsorption capacities of the adsorbents.

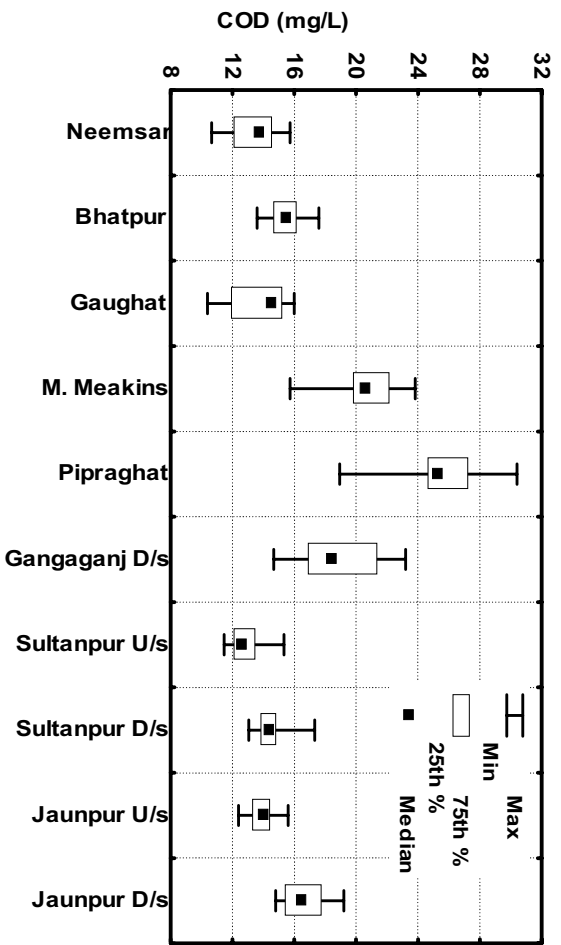
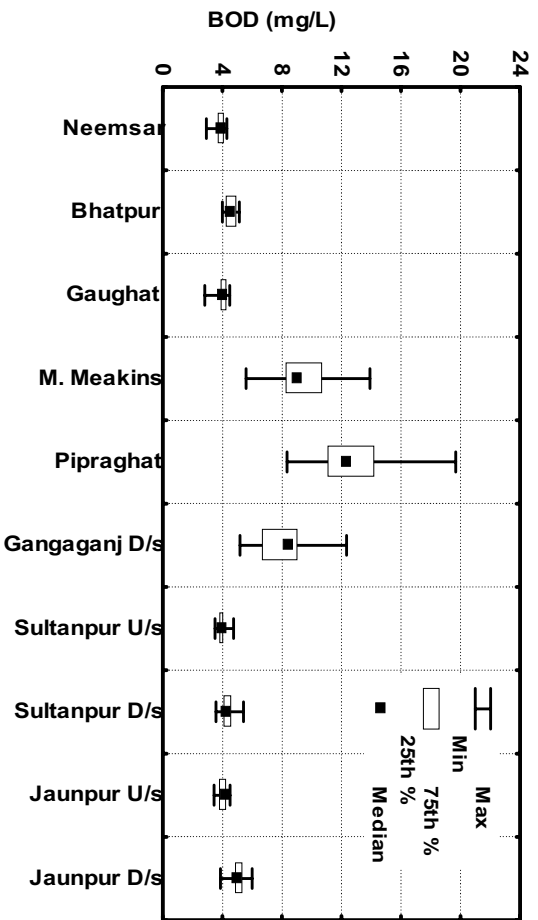
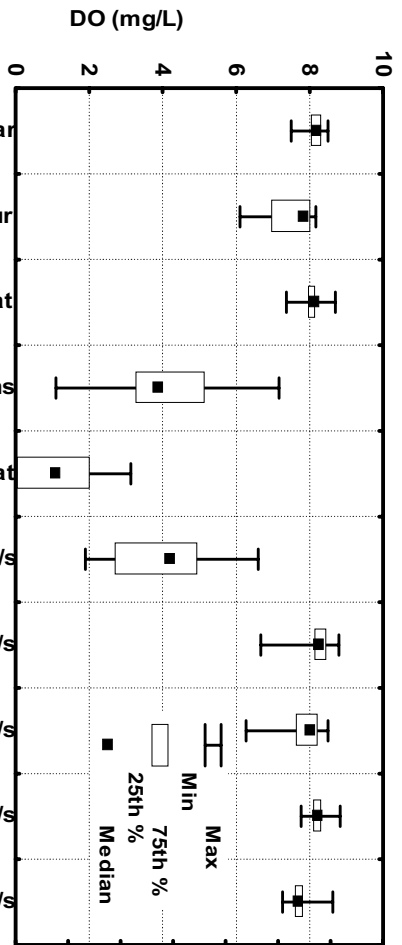
The developed low cost adsorbents (shell activated carbons-SAC; acid treated shell activated carbon-ATSAC) exhibited good adsorption capacities for both the phenols from water/wastewater.

Assessment of the Gomti River Quality

In an ongoing study, to establish the baseline database for developing river pollution control strategies, water and sediments quality of the Gomti River were monitored at ten different locations between Neemsar and Jaunpur. The river meets about half of the total drinking water demand of Lucknow city.

The river water quality data generated during the period Jan. 2005-March 2006 revealed that river water quality deteriorates after Gaughat, the site for intake of water for domestic supplies of Lucknow. The spatial variation plots of biochemical oxygen demand (BOD), chemical oxygen demand (COD) and dissolved oxygen (DO) in river water indicated that water quality remains deteriorated up to Gangaganj, where two major tributaries empty into Gomti river. However, the river water quality improves through natural processes at upstream of Sultanpur. In the river stretch of about 40-50 kms, between Gaughat and Gangaganj, the river water quality is worst in terms of high biochemical oxygen demand, and chemical oxygen demand, bacterial counts (MPN/100ml) and low dissolved oxygen (DO) as it receives huge untreated wastewater through drains and tributaries.



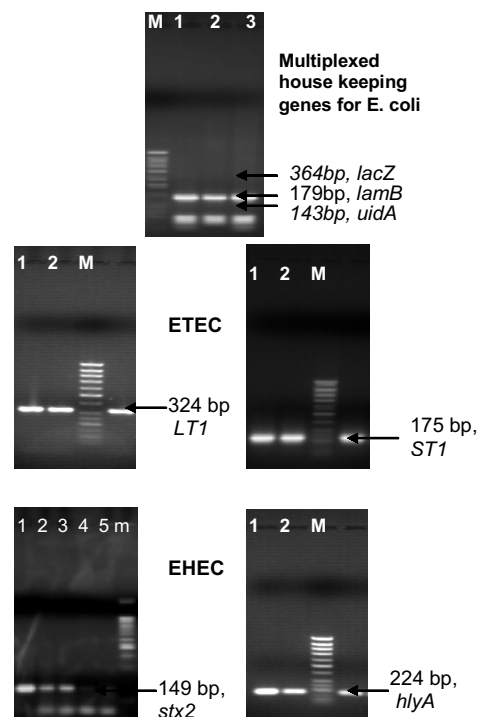


Ground water assessment



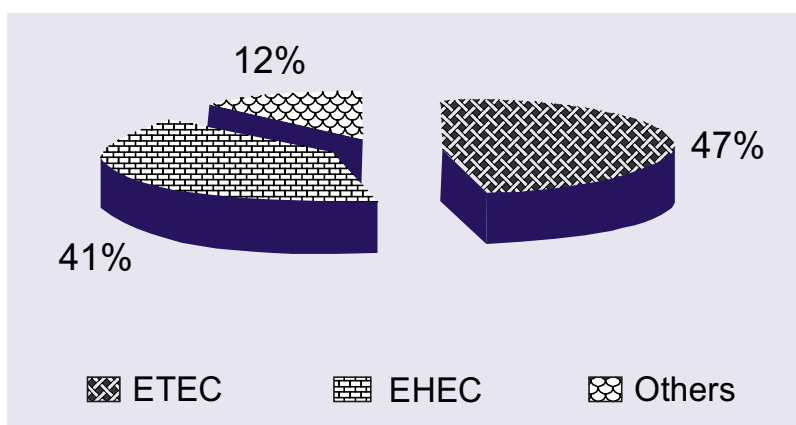
Project : Pollution monitoring, mitigation systems and devices

A large population in developing countries mostly depends on untreated water from rivers, lakes and wells for drinking, laundry, recreation and other domestic purposes. Unsafe water is responsible for diarrhoeal diseases and related mortality, particularly among children. The major source of water supply in northern India, river Ganga and its tributaries are overburdened due to rapid urbanization and population growth. Also, feecal pollution and the indiscriminate use of antibiotics is responsible for emergence of drug resistant bacteria. Hence, there is an urgent need to identify pathogens in over stressed water resources to minimize health risks. The bacterial indicators of water quality, *Escherichia coli* and Enterococci, have pathogenic variants that cause disease. There is paucity of data on environmental *E. coli* and Enterococci in surface waters of urban environment. Hence, the present study has focused on determination of anti-microbial drug resistance profiles and virulence gene signatures of environmental isolates of *E. coli* and Enterococci from surface waters of river Ganga.



PCR amplification products of certain genes present in *E. coli* isolates

m : 100 bp + 1.5 bp Ladder (Bioenzyme)
M : 50 bp Ladder (MBI Fermentos)

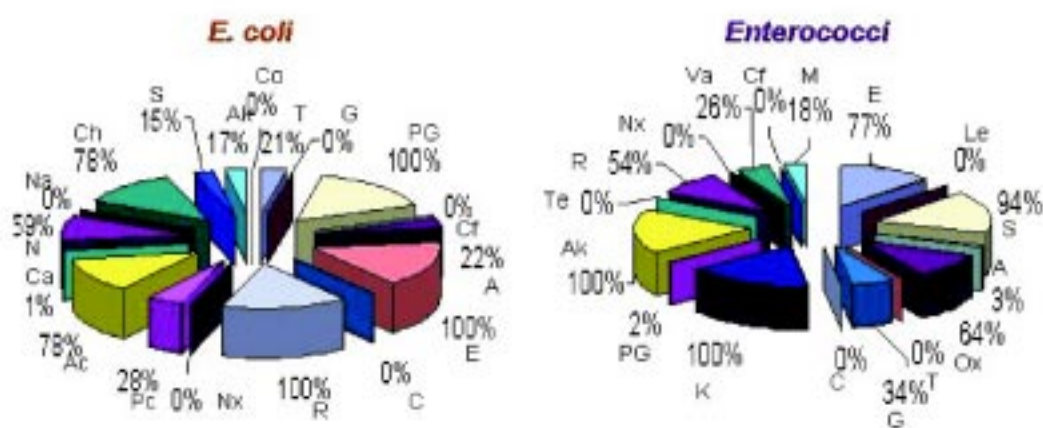


Occurrence of Enterotoxigenic *E. coli* (ETEC) and Enterohemorrhagic *E. coli* (EHEC) isolates in River Ganga



E. coli and Enterococci were isolated from five sites of river Ganga in Kanpur city. The sites were selected based on human activity including domestic and recreational use. *E. coli* and Enterococci isolates exhibited multiple drug resistance. *E. coli* isolates were sensitive to norfloxacin, ciprofloxacin and gentamicin while Enterococci isolates were observed to be sensitive to levofloxacin, teicoplanin, norfloxacin and ciprofloxacin.

Polymerase chain reaction based virulence gene fingerprinting of *E. coli* isolates revealed presence of *stx1* (shiga like toxin typeI), *stx2* (shiga like toxin typeII), *eae* (intimin), *hlyA* (enterohemolysin), *chuA* (heme transport system), LT1 (heat labile toxin I) and STI (heat stable toxin I) genes in isolates. The virulence gene profiles indicated presence of Enterohemorrhagic and Enterotoxigenic *E. coli* in water. The presence of multiple drug resistant *E. coli* and Enterococci in surface waters demands remedial measures as these organisms have low infectious doses.



Antimicrobial drug resistance profile of *E. coli* and Enterococci isolates from river Ganga

Numbers indicate percent isolates exhibiting resistance to the drug tested using disk diffusion technique

Cf: Ciprofloxacin, A: Ampicillin, E: Erythromycin, C: Chloramphenicol, R: Rifampicin, Nx: Norfloxacin, Pc: Piperacillin, Ac: Amoxicillin, Ca: Ceftazidime, N: Neomycin, Na: Nalidixic Acid, Ch: Cephalothin, S: Streptomycin, Ak: Amikacin, Co: Co-Trimoxazole, T: Tetracycline, G: Gentamicin, PG: Penicillin G, M: Methicillin, Le: Levofloxacin, S: Streptomycin, Ox: Oxacillin, K: Kanamycin, Te: Teicoplanin, Va: Vancomycin



Project: Industrial waste minimization and clean up

Immobilization of heavy metals in contaminated soil using non-humus and humus soil and hydroxyapatite

Contamination of soil with heavy metals is a world-wide problem mostly prevalent in industrial, mining and waste disposal sites. Techniques for immobilization of heavy metals at contaminated sites by using chemical additives, such as lime, phosphate fertilizers (e.g. apatite rocks) and alkaline waste materials are feasible options. The reduction of the solubility of heavy metals in contaminated soils can be an inexpensive *in situ* remediation method. Column experiments were conducted to evaluate the ability of non-humus/humus soil and hydroxyapatite to reduce the solubility of metals. Leachability was taken as an index for immobilization. A progressive increase in the concentration of metals immobilized was observed on increasing the concentration of hydroxyapatite from 0.5% to 5%. The concentrations of metals in the matrix were Pb (92.8%)>Cu (91.2%)>Cr (90.4%)>Cd (88.2%) > Fe (78.6%) > Ni (75.8%) > Zn (75.2%), Mn (74.8%). Apart from this, a reasonable amount of the input Mn (20.5%), Zn (18.5%), Ni (17.5%), Fe (6.5%), Cd (6%), Cr (5.5%), Cu (4.5%), Pb (3%) was leached out in the collected fractions. The findings suggest that amendment of non-humus soil with humus soil and hydroxyapatite can immobilize and reduce bioavailable metals more than 90% in soil.

Optimization of decolourisation of distillery effluent in constructed wetland system after bacterial pre-treatment

The decolourisation of anaerobically digested coloured effluent (3000 Copt) was achieved at pilot scale (500 L capacity) upto 60% at pH 7.0±0.2 and temperature 36±1°C using a consortium of *Bacillus sp.*



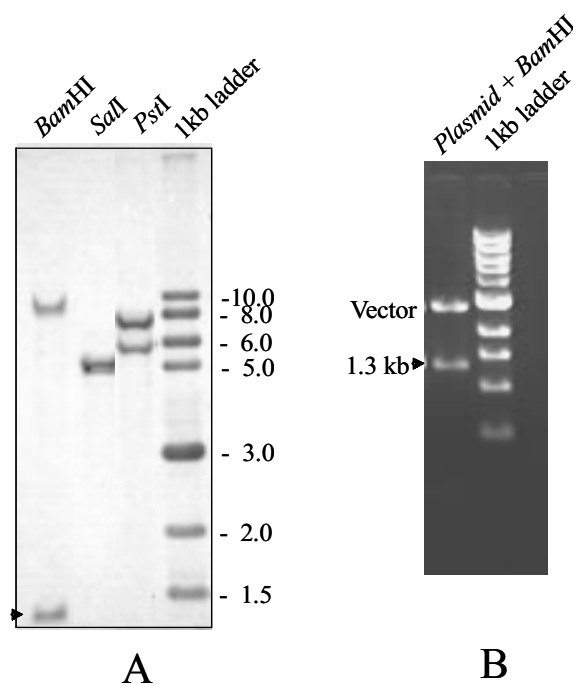
Pilot plant for bacterial decolourisation of distillery effluent

An enhancement of bacterial decolourisation of effluent was observed on treatment of the bacterial pre-treated distillery effluent in the constructed surface flow wetland system (CSFWS). There was decrease in BOD (~95%), COD (~96%), phenol (~97%), sulphate (~93%), phosphate (~35%) and nitrogen (~80%) along with reduction of colour upto 92% within seven days.



Development of bioreactors and genetic engineering tools for cleanup of lindane based wastes

In the present study, characterization of the plasmids and location of *lin* genes involved in γ -HCH degradation was carried out. A bacterium, *Pseudomonas aeruginosa* ITRC-5, isolated and characterized earlier, was found to degrade the four major isomers of the chlorinated pesticide, hexachlorocyclohexane. In the bacterium *Pseudomonas aeruginosa* (ITRC-5), the genes *linA*, *linB* and *linC* that encode the first three enzymes of the pathway for γ -hexachlorocyclohexane-degradation are distributed on multiple plasmids. Copies of the gene *linA* were present on plasmids pHCH-1 and pHCH-4, and both *linB* and *linC* were present together on plasmids pHCH-2 and pHCH-3.



(A) Southern blot analysis of ITRC-5 genomic DNA using gene *linA* as probe, and (B) cloning of 1.3 kb Bam H1 fragment in *E. coli* DH5a using the vector pUC 19

The genes *linA*, *linB* and *linC* have earlier been reported to encode the first three enzymes of the degradative pathway for gamma-hexachlorocyclohexane in *Sphingomonas paucimobilis* UT26 and B90 strains. Southern blot analysis of the genomic DNA of ITRC-5, after restriction digestion with *Hind*III, *Pst*I, *Bam*H1 and *Sal*I, revealed the presence of two or more DNA fragments that were cross-reactive with *linA*, *linB* or *linC* probes. The observations suggest that two copies of each of these genes might be present in ITRC-5, and is in agreement with earlier studies wherein two copies of *linA* and *linC* have been reported. The genes were lost, when ITRC-5 cells were grown in non-selective LB-medium suggesting them to be present on plasmids.

Another strain was screened for the degradation of all four HCH isomers. The *lin* genes namely *linA*, *linB*, *linC*, *linD*, and *linE* were amplified using the genomic DNA as template from the *Sphingomonas* sp. The nucleotide sequences obtained from these amplified products revealed 95-98 % similarity to the reported *lin* genes. The amplification of 16S rRNA gene from this isolated strain resulted in its identification as a *Sphingomonas* sp. The 1403-bp nucleotide has been deposited in the NCBI-Gen Bank and bears the accession no. DQ231244.



Project: Physico-mechanical and electrical & electronic standards

This project was initiated to upgrade SI Base Units and National Standards of Measurements and Apex Calibration Facilities as well as creation of high quality network of testing and calibration laboratories and preparation and dissemination of certified reference materials. During the period, 58 instruments/devices were calibrated for the NABL accredited laboratories of ITRC and 12 equipments were calibrated for the outside parties. In addition, new Reference Standards have been acquired, installed and used for calibration of AC/DC voltage and current, resistance, temperature, revolution per minute, pressure, weights & wavelengths of spectrophotometers.



Research Council meeting in progress. Seated (L-R) Prof. M.S. Valiathan, Dr. C.M. Gupta, Dr. D.K. Saxena and Dr. H.N. Saiyed



R & D Programmes

Prevention of neurodegeneration in experimental animal model of Parkinson's and dementia diseases using cultured neuronal and non-neuronal cells

It was demonstrated earlier that glial cell line-derived neurotrophic factor (GDNF) has ability to increase the cell viability of the remaining host dopaminergic neurons in substantia nigra region in animal model of Parkinson's disease (PD), which shortened the functional restoration of transplanted cells for a short period of time. In order to increase the functional viability of transplanted cells for a longer period, the idea of giving continuous neurotropic support using paraneural tissues was visualized for restorative medical studies. With this idea, studies were conducted to validate the role of Zuckerkandl's organ (ZK) cells co-transplantation with fetal VMC on long-term functional restoration and viability of transplanted VMC in 6-OHDA lesioned rat model of PD, as ZK organ, (an extra adrenal paraganglionic tissue) lies near the bifurcation of abdominal aorta and has ability to endogenously secrete GDNF and catecholamines including dopamine and norepinephrine. Four weeks post transplantation, functional restoration was assessed using neurobehavioral and immunohistochemical parameters. A significant restoration in d-amphetamine induced rotations and spontaneous locomotor activity in rats co-transplanted with VMC and ZK cells was observed as compared to VMC alone transplanted rats. The functional viability of transplanted VMC was confirmed by tyrosine hydroxylase (TH) expression in the striatum and a significant restoration in TH-IR fibers density in co-transplanted animals compared to VMC transplanted animals.

Effect of prenatal exposure to deltamethrin on the ontogeny of xenobiotic metabolizing cytochrome P450s in the brain and liver of offsprings

Prenatal exposure to low doses (0.25 or 0.5 or 1.0 mg/kg, p.o.) of deltamethrin, a type II pyrethroid insecticide, to pregnant dams from gestation day 5 to 21 (GD5-21) produced dose dependent alterations in the ontogeny of xenobiotic metabolizing cytochrome P450 (CYP) isoforms in brain and liver of the offsprings. RT-PCR analysis revealed dose-dependent increase in the mRNA expression of cerebral and hepatic CYP1A1, 1A2, 2B1, 2B2 and 2E1 isoenzymes in the offsprings exposed prenatally to deltamethrin. Similar increase in the activity of the marker enzymes of these CYP isoforms have indicated that placental transfer of the pyrethroid, a mixed type of CYP inducer, even at these low doses may be sufficient to induce the CYPs in brain and liver of the offsprings. Our data have further revealed persistence in the increase in expression of xenobiotics metabolizing CYPs upto adulthood in brain and liver of the exposed offsprings suggesting the potential of deltamethrin to imprint the expression of CYPs in brain and liver of the offsprings following its *in utero* exposure. Furthermore, though the levels of CYPs were several folds lower in brain, almost equal magnitude of induction in cerebral and hepatic CYPs have further suggested that brain CYPs are responsive to the induction by environmental chemicals. The present data indicating alterations in the expression of xenobiotic metabolizing CYPs during development following prenatal exposure to deltamethrin may be of significance as



these CYP enzymes are not only involved in the expression of neurobehavioural toxicity of deltamethrin, but have a role in regulating the levels of ligands that modulate growth, differentiation and neuroendocrine functions.

Effect of immobilization stress on neurobehavioral toxicity of deltamethrin

Effect of simultaneous exposure to deltamethrin (3 mg/kg/day, p.o.) and immobilization stress (rats placed in rat restrainer for 1 hour/day) for 10 days on certain behavioral parameters in rats was studied. No significant change was observed in locomotor activity (distance travelled, resting time, stereotypic time, ambulatory time, number of stereotypic movements) in rats exposed to deltamethrin or those subjected to immobilization stress compared to controls. No significant change in the time of fall from the rotating rod, tested for motor coordination using Rotomax and learning acquisition tested using shuttle box was observed in these rats in comparison to controls. Also, no significant change in any of these parameters was observed in rats co-exposed to deltamethrin and immobilization stress as compared to control, deltamethrin treated and stress group of rats.

In continuation to this, effect of simultaneous exposure to deltamethrin (3 mg/kg/day, p.o.) and immobilization stress was studied on neurotransmitter receptors to understand the role of immobilization stress on the neurotoxicity of deltamethrin. Rats subjected to immobilization stress or those exposed to deltamethrin alone for 10 days did not exhibit significant change in the binding of 3^H -Spiperone to striatal membrane, known to label dopamine (DA)-D2 receptors as compared to controls. Interestingly, simultaneous exposure to deltamethrin and immobilization stress significantly decreased the binding of striatal DA-D2 receptors (40%) as compared to controls. A significant decrease in the binding of 3^H -Flunitrazepam to frontocortical membranes, known to label benzodiazepine receptors was observed in rats subjected to immobilization stress (18%) or those simultaneously exposed to deltamethrin and immobilization stress (20%) as compared to controls. Binding of 3^H -Quinuclidinyl benzilate (QNB) to frontocortical membranes, known to label cholinergic-muscarinic receptors was significantly decreased in rats subjected to immobilization stress (45%) while no such effect was observed in rats treated with deltamethrin alone. Simultaneous exposure to immobilization stress and deltamethrin in rats also did not cause significant change in the binding of cholinergic-muscarinic receptors as compared to controls however, the binding remained increased as compared to rats treated with deltamethrin alone.

Simultaneous exposure to deltamethrin and immobilization stress in rats had no significant effect on behavioral parameters. However, changes in dopamine and benzodiazepine receptors suggest that stress is an important contributor to enhance the neurotoxicity of deltamethrin.

***In Vitro* Models of Cerebral Stroke: Tool for Evaluation of Neuroprotective Potential of Herbal Drugs**

Acute ischemic stroke is the third largest cause of mortality and the cause of long-lasting disability in adults, leading to 1.2% of total deaths in India. The treatment is not



experimentally conclusive and largely trial and experienced based because of poorly understood complex pathophysiological phenomenon. Experiments have been initiated to develop the rapid and reliable *in vitro* pharmacological model systems for assessing cerebral ischemic strokes using PC-12 cells, a rat pheochromocytoma cell line, and primary cultures of rat brain neuronal and glial cells. PC-12 cells (1×10^4 cells/well) were seeded in poly-L-lysine pre-coated 96 well plates and allowed to adhere to the bottom under 5% CO₂-95% air at 37°C for 24 h. Then the cells were exposed to ischemic insult {(Oxygen-glucose deprivation, (OGD))} for a period of 1-8 hr in a medium having no glucose, followed by re-oxygenation period of 6-96 hr in complete medium having glucose concentrations between 0-11 mg/ml. Cells were assessed for cell viability using trypan blue dye exclusion and tetrazolium bromide salt MTT assays. Parallel sets of cells were also run in identical conditions in normoxia and served as control. A continuous decrease in cell viability (16-96%) was observed with increase in OGD insult i.e., 1-8 hr respectively, when compared to normoxia control. In general, reoxygenation period of 24hr was found to restore the maximum cell viability for batches exposed to OGD insult for different time periods within the available concentrations of glucose used in the study. However, best restoration was observed in the cells which were allowed to re-oxygenate in culture medium supplemented with 4-6mg/ml glucose. The data indicates that PC-12 cells can surrogate as an *in vitro* model of cerebral ischemic stroke, if provided an OGD insult for 6hr and reoxygenation of 24 hr in medium containing 4-6mg/ml glucose.

Effect of cadmium exposure on blastogenesis and apoptosis-study on murine lymphocytes

Studies were conducted to evaluate the immunotoxicity by cadmium and to ascertain the relationship of apoptosis and immune function in murine lymphocytes. The effect of Cd on blastogenesis i.e. proliferative response to mitogens at various time intervals was studied. Thymocytes were stimulated with plant lactins-concanabalin A (Con A) while splenocytes with Con A and Plant lectin-Lipopolysaccharites(LPS) for proliferation. The proliferation capacity was estimated by [³H] thymidine incorporation into cellular DNA.

It was observed that mitogen stimulated proliferation occurred at least 24 hr later, while apoptosis both in thymocytes and splenocytes occurred much earlier. Apoptotic cell death by cadmium seems to delay the proliferative response to mitogens.

Evaluation of *in vitro* effect of antibiotics on isolated intestinal bacteria and IEC-6 cell line.

Gastrointestinal (GI) cell lining is the prime target site of interaction for any chemical following oral administration. Different groups of antibiotics used for curing various diseases caused by microorganisms exert specific effects on gut bacteria. The large number of bacteria and gut microflora found in intestinal habitat is known to play a significant role in the host cell homeostasis. A breakdown in the relationship between intestinal epithelial cells and bacteria results in manifestation of GI-disorders. Simultaneously, antibiotics may also cause cellular toxicity to the functional intestinal epithelial cells leading to GI-disorders/toxicity. Since specific cell lines are considered to be suitable for toxicity screening and



testing of chemicals, the present study was designed to evaluate and compare the *in vitro* toxicity of antibiotics on rat intestinal epithelial cells, isolated intestinal bacteria and IEC-6 cell line.

In vitro interaction of Ampicillin (0.5–2.0 mg/ml), Amphotericin-B (25-200 mg/ml) and Ciprofloxacin (50-500 ng/ml) with four isolated intestinal resident bacteria viz. *Escherichia coli*, *Pseudomonas* sp. (gram –ve); *Lactobacillus* sp. and *Staphylococcus* sp. (gram +ve) were studied. *In vitro* exposure to Ciprofloxacin showed significant dose-dependent inhibition throughout the growth phase in both gram –ve and gram +ve bacteria. The inhibition was more prominent (60-65%) in *E.coli* and *Pseudomonas* sp. Growth phase studies of gram –ve bacteria with Amphotericin-B revealed a 15-20% inhibition at late log phase with 50 mg/ml concentration. A dose-dependent decline in dehydrogenase (DHA) and esterase (EA) activity tests (ranging from 15-60%) was observed in both gram (-ve) and gram (+ve) bacteria. The antibiotic effects were in the order of Amphotericin-B < Ampicillin < Ciprofloxacin. Lower doses of Amphotericin-B did not show significant alterations in DHA and EA. These findings suggest a dose-dependent inhibition of the respiratory and energy producing processes, and general heterotrophic activity of bacterial cells, which were similar to that of rat intestinal epithelial cells as observed earlier.

In order to evaluate and validate the cellular toxicity of antibiotics in rat intestinal epithelial cells, intestinal loops were filled with different concentrations of three antibiotics and incubated for 30 min. *in situ*. Results revealed significant decrease in epithelial cell membrane alkaline phosphatase (37%) and Ca^{2+} - Mg^{2+} -ATPase (21%) at highest tested concentration of Ampicillin. Whereas, a concentration-dependent decrease (up to 50%) was observed in two enzyme activities with Ciprofloxacin and Amphotericin-B with an exception of Ca^{2+} - Mg^{2+} -ATPase showing dose-dependent increase in case of Ciprofloxacin. Significant dose-dependent decline (ranging from 17-68%) in membrane structural constituents viz. hexose, sialic acid and cholesterol contents were also evident. Similar findings were observed earlier with intestinal bacteria.

To evaluate the effect of antibiotics in rat intestinal epithelial cell line (IEC-6), cultures were incubated without or with the different concentrations of three antibiotics at 37° C for 24h. Findings similar to the *in situ* studies on rat intestinal epithelial cells were evident. Overall findings suggest that isolated intestinal bacteria and IEC-6 cell line can be used for preliminary *in vitro* screening of GI-cellular toxicity caused by antibiotics.

Studies on use of indigenous minerals/natural products for the removal of heavy metals from drinking water

A study was conducted for removal of hexavalent chromium from drinking water by using indigenous minerals and natural products, in order to purify the water. Certain adsorbents were screened and used for the purification. Silver impregnated sand and ground nut husk carbon were assessed for the removal of hexavalent chromium. The maximum removal of hexavalent chromium (95%) was noticed at optimum condition.



Drinking water disinfection by silver ionization

Technology based on silver ionization has been evaluated by estimating its bactericidal activity for disinfection of drinking water supply in order to provide safe drinking water to community. Pre- and post-treated samples were evaluated at different periods for their disinfection efficacy under standard laboratory conditions. Simultaneously, these samples were also analysed for their physico-chemical characteristics and persistent silver ions with post-treated samples. 10-20 ppb silver ion exhibited 100% disinfection of water containing approx. 4800 *Escherchia coli* /ml even after 51 hrs of treatment.

Disinfection by silver ionization may be considered as a suitable alternative technique to chlorination for disinfection of drinking water at community level because the concentration of persistent silver ions were found below WHO/ EPA prescribed limits (80-100 ppb).

In vivo DNA damaging potential of sanguinarine alkaloid, isolated from argemone oil, using alkaline Comet assay in mice

Our earlier studies have shown that argemone oil produces genotoxic effects in mice. Since, sanguinarine alkaloid is the major component of argemone oil, the *in vivo* DNA damaging potential of the isolated alkaloid was investigated in blood and bone marrow cells of mice using alkaline Comet assay. Swiss albino male mice were given single intraperitoneal administration of 1.35-21.60 mg sanguinarine. These results indicate that single exposure to sanguinarine alkaloid causes DNA damage in blood and bone marrow cells of mice, which could be responsible for the genotoxicity of argemone oil.

Oxidative damage to plasma proteins and lipids in epidemic dropsy patients: Alterations in antioxidant status

The present study was aimed to evaluate the development of oxidative stress in terms of oxidation of plasma proteins and lipids and its correlation to enzymatic and non-enzymatic antioxidants in epidemic dropsy patients. Total plasma protein and globulin contents were found to be significantly ($P<0.05$) enhanced with a concomitant decrease in albumin/globulin ratio in dropsy patients when compared to controls. Total cholesterol, triglycerides, low density lipoprotein cholesterol and very low density lipoprotein cholesterol were found to be significantly increased with a simultaneous decrease (51%) in high density lipoprotein cholesterol in dropsy patients. The oxidation of plasma proteins and lipid were substantially enhanced (162-175%) in dropsy patients when compared to controls. Further, significant decrease in superoxide dismutase, catalase, glutathione reductase and glutathione-s-transferase with a concomitant increase in glutathione peroxidase (69%) activity was noticed in dropsy patients. A significant reduction in plasma total antioxidant capacity, α -tocopherol, glutathione, retinol and retinyl esters content was observed in dropsy patients. The results suggest that there exists an unproportionate equilibrium between free radicals formation and enzymatic and non-enzymatic antioxidant scavengers, which may cause oxidative damage to proteins and lipids in dropsy patients.



Correlation of DNA damage in epidemic dropsy patients to carcinogenic potential of argemone oil and isolated sanguinarine alkaloid in mice

Sanguinarine, an active alkaloid of argemone oil (AO), has been shown to intercalate DNA. Therefore, a possible correlation of DNA damage in epidemic dropsy patients to tumorigenic potential of AO and isolated sanguinarine alkaloid in mice was investigated. Single topical application of AO (0.15-0.3ml) or sanguinarine (4.5-18 mmol) followed by twice-weekly application of tetradecanoylphorbolmyristate acetate (TPA) for 25 weeks resulted in the formation of tumors. Histopathologically these tumors were of squamous cell carcinoma type and the activities of cutaneous g-glutamyl transpeptidase and glutathione-S-transferase P, marker enzymes of tumorigenesis, were found to exhibit higher expression in AO or sanguinarine/TPA treated groups. The higher expression of p53 and p21WAF1 in skin after single topical application of AO or sanguinarine further confirms the tumorigenic response. The DNA damage in the blood of dropsy patients was found to be significantly higher as compared to normal population, indicating the genotoxic effects of AO exposure. Although the genotoxic lesions may be repaired to some extent on withdrawal of consumption of AO contaminated mustard oil, the residual genotoxic effects caused by AO may not be expressed as signs of carcinogenesis. Environmental factors or hormonal changes during aging process may lead to stimulate/promote the genetically altered latent cells to form neoplastic lesions and can act as one of the etiological factors responsible for higher incidence of gall bladder carcinoma in the population of Indo-Gangetic basin.

***In vitro* cytotoxicity of polycyclic aromatic hydrocarbon residues arising through repeated use of fish fried oil in human hepatoma Hep G2 cell line**

In order to understand the mechanism of toxicity of repeated use of fish fried oil (RFFO) extracts containing a mixture of polycyclic aromatic hydrocarbons (PAHs), the *in vitro* cytotoxicity assays in human hepatoma cell line, HepG2 was undertaken. In addition to RFFO extract, benzo(a)pyrene (BP) and chrysene were used as prototype compounds for heavy and light PAHs, respectively. Out of total content of PAHs (1240.4 mg/kg) in RFFO, major composition is of light PAHs (854.8 mg/kg) while heavy PAHs showed the concentration of 385.7 mg/kg. Treatment of cells with 1 mg/ml RFFO extract for 48 h showed significant induction in ethoxyresorufin-O-deethylase (EROD) activity. Exposure of cells to higher doses of RFFO extract (10–100 mg/ml) for 24, 48 and 72 h caused 3.5–5.2, 4.3–8.5 and 1.8–2.3-fold enhancement in EROD activity, respectively. Further, RFFO extract caused a dose dependent increase (2.1–3.5-fold) in aryl hydrocarbon hydroxylase (AHH) activity at 48 h. Induction of EROD and AHH activity in HepG2 cells was found to be relatively more following BP or chrysene treatment as compared to RFFO extract. RFFO extract did not cause any significant effect on cell viability at 1 µg/ml and 10 mg/ml. However, 100 mg/ml RFFO extract significantly decreased the cell viability at 24, 48 and 72 h. Exposure to 10 mg/ml RFFO extract reduced the colony forming ability (CFA) of HepG2 cells with maximum decrease of 33.5% at 72 h. However, exposure of cells to RFFO extract at highest concentration of assay (100 mg/ml) reduced CFA (35–52%) at 24, 48 and 72 h. RFFO extract (1–100 mg/ml) had no significant effect on growth inhibition of cell up to 48 h of exposure. However, exposure of RFFO extract at all doses showed



significant growth inhibition (20–25%) at 72 h. The results suggest that RFFO extract has cytotoxic potential through the metabolic activation process of PAHs generated *per se*.

Exposure risk to contaminants in pharmaceutical and cosmetic powders

There are different types of cosmetic powders such as body powder, baby powder, face powder, eye shadow and powdered blush as well as pharmaceutical powders available in the market. Both the sexes of all age groups are using these powders. These are talc-based. Talc is a mineral product and often contaminated with asbestos fibres. The aim of the study was to investigate the safety of such powders being sold in the market, initially by analyzing the asbestos content. Five branded samples of talcum powder were analysed and all were found contaminated with asbestos fibres. Asbestos fibre contamination in these powders ranged from 10.3 – 15.4%. Fibre length study on two samples revealed that asbestos fibres were 22.8 – 34.7%, 48.2 – 55.1% and 17.1 – 22.1% in the range of <10µm, 10 – 20µm, and > 20µm, respectively. The study indicates risk of human exposure to asbestos through the use of naturally contaminated talcum powder. It is noteworthy that asbestos takes many years to cause asbestosis and carcinogenic malignancies which are irreversible. It also necessitates a regular monitoring and surveillance on all the cosmetic and pharmaceutical powders being marketed for asbestos contamination.

Genotoxicity of indigenous asbestos

Asbestos is an established carcinogen and very little is known about the genotoxicity of indigenous asbestos. Therefore, indigenous samples of asbestos were collected from Rajasthan to conduct genotoxicity studies. The samples analysed showed presence of tremolite, an amphibole variety, more toxic than chrysotile, the commercial variety. Genotoxicity of tremolite asbestos was assessed and enhanced formation of micronuclei and aberrant metaphases was observed. The most common observed cytogenetic abnormalities were chromatid gaps and breaks and chromosome gaps and breaks. Chrysotile-exposed human lymphocytes showed significantly enhanced micronuclei and chromosomal aberration in a concentration dependent manner suggesting genotoxicity of tremolite asbestos.

Cancer chemopreventive properties of black tea and its constituents

In continuation of our earlier studies now we showed that black tea inhibit initiation of tumorigenic events as evidenced by decrease in N-nitrosomethylbenzylamine (NMBA) (0.25 mg/kg subcutaneously once per week for 15 weeks) induced esophageal tumor incidence and multiplicity, reduced proliferative indices, and inhibition of preneoplastic lesion formation in Wistar rats. Administration of 0.5-1.5% BTE before, during and after NMBA treatment significantly reduced tumors multiplicity. Total number of tumor decreased from 45.4-69.7% following 0.5-1.5% BTE treatment respectively, compared to NMBA-treated controls. Non-NMBA-treated animals did not show esophageal tumors.

In addition, we observed that administration of BTE before, during and after DMBA treatment (orally single dose, 20mg/kg.b.wt.) significantly reduced tumor multiplicity in Wistar rat mammary carcinogenesis model. The total number of tumors decreased by 46-



75.7% with administration of 0.5-1.5% BTE respectively compared to DMBA-treated controls. Furthermore, BTE appears to have its primary effect on tumor formation. These data indicate that BTE may be useful in the chemoprevention of breast cancer.

Tumor suppressive effects of resveratrol on mouse skin carcinogenesis

Protective effects of resveratrol were studied in DMBA induced mouse skin complete carcinogenesis assay as well as in 2-stage (DMBA-TPA) mouse skin carcinogenesis bioassay. A significant delay in tumorigenesis could be seen in the complete carcinogenesis model in terms of total number of tumors, delay in onset of tumorigenesis as well as reduction in tumor volume. Results of the present investigation revealed a significant delay in the onset of tumorigenesis in the animals pretreated with resveratrol for antitumor initiating activity as well as of antitumor promoting activity. About 40% to 60% of animals remained tumor free till. At the termination of the experiment. Results of the western blot analysis of skin/tumor lysates showed that there was a marked increase in the expression of wild type tumor suppressor p53 by topical treatment of DMBA. However, this was further enhanced by the application of resveratrol both prior and post to DMBA treatment. No effect on the expression of the protein could be seen in resveratrol alone treated group. An opposite trend could be observed in case of mutant p53 expression. Expression was enhanced significantly over untreated control in DMBA treated group. However, resveratrol supplementation resulted in restoration of mutant type p53 expression up to the normal levels in both given prior and post to DMBA treatment. Further, DMBA treatment alone resulted in marked increase in the expression of proapoptotic Bax, Caspase 3 and Caspase 9 with concomitant increase in the expression of anti-apoptotic proteins Bcl-2 and Survivin. Resveratrol treatment both given prior and post to DMBA treatment resulted in significant enhancement in the expression of proapoptotic proteins Bax, Caspase 3 and 9 with concomitant restoration of antiapoptotic proteins Bcl-2 and Survivin.

Results of the flowcytometric analysis of skin/tumor showed a marked increase in the subG1 population of DMBA treated mouse skin tumor. However, significant increase could be seen in the sub G1 cells population in resveratrol supplemented groups. It was upto 40% of total population. Results of the DNA gel electrophoresis further supported the results obtained by flowcytometric analysis. A significant DNA damage in case of resveratrol supplemented mouse skin tumors in comparison to DMBA treated mouse skin tumors indicative of induction of apoptosis by resveratrol both prior and post to DMBA treatment was observed.

Flow cytometric analysis of cervix cancer

A flow-cytometry analysis of DNA ploidy was carried out in cytological diagnosed cases of mild (79), moderate (36) and severe (12) dysplasia and “atypical squamous cells of unknown significance” (57) along with controls (69), in order to understand its importance in malignant progression of disease in women. Cytologically diagnosed dysplasia, which were employed for DNA ploidy studies, 39 mild, 28 moderate and 11 severe dysplasia cases were found to be aneuploid. Out of the 69 control subjects, 6 cases showed aneuploidy pattern and rest 63 subjects were diploid. An aneuploidy pattern was observed



in 8 out of 57 cases of cytologically evaluated 'atypical squamous cells of unknown significance'.

Follow up study was conducted, altogether, with all aneuploidy and cytologically evaluated cases of dysplasia within a year of registration. The results of follow up studies show that aberrant DNA content reliably predicts the occurrence of squamous cell carcinoma in cervical smear that otherwise would be regarded as at very low risk in gynecological malignancies.

Prevention of occupational respiratory disorders by functional food-jaggery

Unhygienic environment and uncontrolled exposure from the exhaust of automobiles on human leads to the severe adverse health effects. In developing countries, fairly large portion of the population is dependent on biomass fuels, wood, charcoal, agriculture residue and animal waste. Suspended Particulate Matter (SPM) below 2.5 micron ($PM_{2.5}$) is one of the major pollutants in this outdoor and indoor air pollution. It has been demonstrated that jaggery is effective in the reduction of the deleterious effects induced by fine and ultrafine particles in rural and urban environment.

Organochlorine pesticides exposure and risk of childhood aplastic anemia

Aplastic anemia is a rare hematological disorder in which all cellular components of bone marrow origin are deficient. Relatively little is known about its possible etiologies and risk factors. A hospital based case control study for the first time in India was conducted to determine the incidence of childhood aplastic anemia in and around Lucknow keeping in view the presence of organochlorine levels in the blood in order to establish co-relation, if any, between the disease and pesticides exposure. A total of 25 cases of childhood aplastic anemia were identified as per established criteria during the study period of one year. The levels of organochlorine pesticides in the blood were determined using a gas liquid chromatograph equipped with an electron capture detector. The annual incidence of childhood aplastic anemia in and around Lucknow was found to be 7 cases per million which is on the higher side as compared to many other countries (e.g. France, Brazil, U.K. and United States). However, it was lower than those reported in Sweden, China and Europe. In an Israeli collaborative study, blood levels of α -HCH, γ -HCH, δ -HCH, total-HCH and p,p -DDE were higher in children with aplastic anemia as compared to controls, except, α -HCH which differed significantly ($p < 0.05$). Although, this pilot study with limited statistical power did not support any association between exposure to organochlorines and risk of childhood aplastic anemia but a possible association between the two could not be ruled out in view of the cases so far studied.

Microarrays and proteomics based approaches to assess the modulation of multiple genes and proteins involved in maneb and paraquat induced Parkinson's disease phenotype in mouse

Parkinson's disease (PD) is a progressive multi-factorial neuro-degenerative disorder, wherein combination of age, genetic and environmental factors plays an important role in the onset of the disease. Degeneration of dopaminergic neurons leads to biochemical and molecular changes in striatum. Combined exposures of maneb+paraquat enhance sensitivity



of nigrostriatal dopaminergic neurons, leading to irreversible and progressive neurodegeneration. Despite the neurotoxic potential of maneb and paraquat, their combined treatment inducing neuronal damage at genome and proteome level, is not clearly understood. The present study was undertaken to investigate the differential gene and protein expression patterns in striatum of control and maneb + paraquat-induced Parkinson's disease phenotype in mouse using microarray and proteomics based approaches. The differential display of proteins expressed in the *striatum* region of the brain in normal and maneb + paraquat treated mice (time dependent) were performed using two-dimensional polyacrylamide gel electrophoresis (2-D PAGE). Some differentially expressed spots were identified by mass spectrometry. Three proteins significantly down regulated in maneb + paraquat treated mouse *striatum* as compared to respective controls, were identified as α -enolase, glia maturation factor-b (GMF-b) and complexin-I. Results obtained from the present investigation clearly suggested the involvement of α -enolase, glia maturation factor-b (GMF-b) and complexin-I in maneb + paraquat induced PD phenotype in mouse and also provide a platform for potential use of proteomics in understanding the pathogenesis of PD.

Proteomics based approaches for the development of peripheral protein biomarker(s) and assessment of contribution of selected environmental chemicals in the onset of Parkinson's disease

Studies were conducted to develop a simple laboratory test procedure in order to diagnose a patient of Parkinson's disease even at an early stage of development by identifying peripheral/cerebrospinal protein biomarker(s) in human population. The study was aimed to delineate the mechanism of involvement of peripheral or cerebrospinal proteins in the onset and progression of Parkinson's disease by comparing the presence of total proteins in the serum/plasma, isolated blood cells and cerebrospinal fluid of normal individuals among the PD patients using modern tools of proteomics. Few differentially expressed proteins were seen in 2D gels of blood samples. The study is expected to open an insight for understanding the phenomenon of developing peripheral/cerebrospinal protein biomarker(s) leading to development of test procedure to diagnose PD patients by using small amounts of blood/cerebrospinal fluid.

Molecular mechanism of caffeine and nicotine mediated neuroprotection in MPTP induced Parkinson's disease phenotype in mouse

Caffeine and nicotine are being hypothesized as protective agents, however, the underlying mechanism explaining the involvement of caffeine or nicotine inducing protection in the onset of Parkinson's disease at genomic level has not yet been clearly understood. Therefore, the studies were conducted to delineate the mechanism involved in nicotine and caffeine induced changes at genome level in *striatum* of MPTP induced PD in mouse. Alteration in the expression of detoxification genes in *striatum* region of animals in presence or absence of nicotine and/or caffeine is being studied. Expression of VMAT2 in the *striatum* of control and MPTP induced PD phenotype and alteration in its expression due to nicotine and caffeine exposure is also being investigated.



Artificial evolution of genes for the improved degradation of persistent pollutants

Earlier studies from the laboratory showed the presence of homologous genes in the bacterium *Pseudomonas aeruginosa* ITRC-5, isolated for the degradation of HCH-isomers. Briefly, the genomic DNA of ITRC-5 was digested with restriction enzymes *Hind*III, *Pst*I, *Bam*HI and *Sal*I. Southern blot analysis by probing with the gene *linA*, revealed the presence of two or more cross-reactive fragments in all the digests, suggesting that two copies of this gene might be present in ITRC-5 (Fig 3A). One copy of *linA* (1.3kb *Bam*HI fragment) gene was cloned in *E. coli* by using the vector pUC19 (Fig 3B).

Similarly, Southern blot analysis with gene *linB* revealed the presence of two or more cross-reactive fragments in all the digests (Fig 4A). One copy of *linB* (1.2 kb *Bam*HI fragment) gene was cloned in *E. coli* as above.

Nucleotide sequencing of both the cloned *linA* and *linB* genes was determined. Other copies of both the genes are also being cloned and sequenced. These will be subjected to 'artificial evolution' for the generation of 'variant forms' towards the improved degradation of the persistent α - and β -isomers of HCH.

Biotechnological approaches for the detection and amelioration of pollutants

Total DNA from a pesticide contaminated soil was isolated in order to construct metagenomic library and selection of genes for HCH degradation. PCR amplification and sequencing of *lin* genes using the soil DNA suggested the presence of early genes like *linA* and *linB* which were involved in α -HCH biotransformations. After digestion of the DNA into large sizes \sim 10 kb, DNA have been planned to be ligated into vector (cosmid, fosmid or BAC libraries) so as to transform packaged libraries into *E. coli* host cells. The colonies harboring activity to convert β -HCH or showing increased activity towards other HCH isomers would be selected. Thus, through this metagenomic approach an efficient degradation of persistent HCH-isomers may be achieved leading to eco-friendly bioremediation of pollutants.

Genome-wide detection of microbial communities involved in pollutants biodegradation using DNA microarray technology

The detection and monitoring of catabolic gene expression in the environment has become integral aspects of bioremediation and microbial ecology. Microarray analysis offers the potential to monitor and compare the expression patterns of thousands of mRNA species simultaneously. Microarray also provides a vehicle for exploring a genome in a way that is both comprehensive and systematic.

In order to screen effectively and monitor the biodegradative microorganisms, a 50-mer based oligonucleotide microarray comprising genes are being constructed involved in biodegradation and metal resistance. This array will have around 250 unique and group specific target probes with each 50-nucleotide length. The array is being developed through AquaBioChip LLC, Michigan, USA. Further, environmental samples from geographically



diverse sites contaminated with varieties of chemicals such as pesticides, solvents, agrochemicals and metals were collected. Total RNA was extracted from these samples were run through reverse transcription reaction to cDNA. The DNA templates will be labeled with Cy3 and or Cy5 fluorescent dyes to assess presence of degradative genes and their expression from environmental samples.

Neurogenotoxicity assessment of lead and ethanol: an *in vitro* study

Occupational and agricultural exposure to pesticides is one of the primary concerns in most of the developing countries. The metabolism and toxicity of pesticides may be influenced by factors such as protein malnutrition, essential metal deficiencies or alcoholism. It is well documented that ethanol could enhance the absorption efficiency of pesticides and alcoholic persons may be more susceptible to pesticide intoxication. However, the modulatory effect of ethanol on pesticide intoxication is poorly understood to arrive at a conclusion. Therefore studies were carried out to understand the modulatory effect of ethanol on genotoxicity of rotenone, in cultured human peripheral blood lymphocytes. Rotenone, a widely used pyrethroid pesticide, is known to cause detrimental effects in brain, central nervous system and many other vital organs. Cytotoxicity studies were carried out using various concentrations of ethanol (50mM-600mM) and rotenone (10^{-3} M - 10^{-9} M) for 24-72 hours. For genotoxicity studies, cells were exposed to non-cytotoxic doses of ethanol (50mM, 100mM, 200mM, 250mM, 300mM) and rotenone (10^{-6} M). Parallel sets of cells were also run under identical condition without the test compound and ethyl methane sulphonate (EMS) serves negative and positive controls respectively. Automated software guided karyotyping, micronucleus assay and kinetochore analysis were selected as end points. Individual exposure to either ethanol (7MN/1000, CA 0.02%, 50mM, 5MN/1000, CA 0.01%, 100mM, CA 0.02%-200mM, 4MN/1000, 0.01%-250mM, 7MN/1000, 0.03%-300mM) or rotenone (10- M 9MN/1000, CA 0.04%) showed no genotoxic effects in PBL cells, whereas, positive control (EMS 3mM) caused a significant induction in MN (28 MN/1000, CA 7%). Interestingly, co exposure to rotenone (10^{-6} M) and ethanol at 200mM and 250 mM caused a dose dependent ($P < 0.001$) induction in MN (27 MN/1000, 32 MN/1000) and chromosomal aberrations, as compared to control. Aneugenic effects were observed in kinetochore study following treatment of both rotenone and ethanol. Data indicates that independent exposure to either rotenone or ethanol does not cause any genotoxic damage in cultured PBL cells. However, co exposure to ethanol and rotenone even at non-cytotoxic doses leads to a synergistic effect and makes genetic system more vulnerable under the experimental condition.

Imprinting of cerebral and hepatic cytochrome P450s in rat offspring following prenatal exposure to lindane

Oral administration of low doses of lindane (0.0625- or 0.125- or 0.25 mg/kg b. wt., p. o., corresponding to 1/1000th or 1/480th or 1/240th of LD₅₀ of lindane) to the pregnant rats from gestation day 5 (GD5) to the GD21 was found to produce a dose dependent increase in the cerebral and hepatic cytochrome P450 (CYP) dependent monooxygenases in the brain and liver microsomes isolated from rat offsprings at postnatal day (pnd) 21. The increase was found to be statistically significant only at relatively higher doses of 0.125



and 0.25 mg/kg. Interestingly, the increase in the activity of CYP1A1/1A2 dependent 7-ethoxyresorufin-O-deethylase (EROD), CYP2B1/2B2 dependent 7-pentoxyresorufin-O-dealkylase (PROD) and CYP2E1 dependent N-Nitrosodemethylamine demethylase (NDMA-d) were found to persist upto pnd 45 in liver and brain microsomes from the offsprings, though the magnitude of induction was less as compared to that observed at pnd 21. This increase in the activity of the CYP enzymes indicates the placental transfer of the insecticide even at these low doses and this may be sufficient to induce the CYPs in brain and liver of the offsprings. Further studies are required to investigate the effect of lindane on the ontogeny of cerebral CYPs.

Study of functionally important Single Nucleotide Polymorphisms (SNPs) in cytochrome P450 2E1 gene in Indian population

Studies were conducted to identify the role of SNPs in cytochrome P450 2E1 gene in liver cirrhosis. Genomic DNA was extracted from blood samples of 40 patients suffering from alcoholic liver cirrhosis registered at Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow and equal number of age matched controls. PCR based Restriction Fragment Length Polymorphism (RFLP) methods were standardized to detect the Rsa I and Dra I polymorphisms, present in 5' flanking region and intron 6 region of CYP2E1 gene respectively. The case control study data in 40 cases showed that individuals for Rsa I polymorphism, were higher in the patients suffering from alcoholic liver cirrhosis as compared to the controls. However, no significant difference was observed in Dra I. Further studies are warranted with larger sample size for detection of homozygous variant form for both Rsa I and Dra I.

Safety evaluation of selected herbs used in Ayurveda and Siddha medicine

A facility has been created for safety evaluation of herbal products and contaminants testing in terms of heavy metals, persistent pesticides and microbial load. This facility has been sponsored by Department of AYUSH. The studies carried out are:

Estimation of heavy metals such as Pb, Cd, Cr, Ni, As and Hg and persistent organochlorine pesticides has been carried out in 130 samples of therapeutically important medicinal plants supplied by different units of Department of AYUSH.

Microbial load in terms of total bacterial and fungal count has been carried out in 125 samples which were also tested for presence of *E. coli*, *Salmonella*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* as per WHO guidelines.

Heavy metal estimation was carried out in coded samples of Ayurvedic drugs randomly selected and procured from market for Department of AYUSH, Ministry of Health & Family Welfare.

Heavy metals and persistent pesticide analysis in selected Indian medicinal plants-Phase II

In the phase II of the project sponsored by ICMR, about 180 medicinal plants extensively used by manufacturers of Ayurvedic medicines have been selected and samples



are being supplied by five laboratories involved in the Task Force Project. Heavy metals like Pb, Cd, Cr, Ni, As and Hg have been estimated in 213 medicinal plant samples. Organochlorine pesticides such as isoforms of HCH, DDT, its metabolites and endosulfan have also been estimated in 190 samples during the report period. The data is being uploaded in the QAMP database developed during the first phase of the project.

Safety evaluation of Ayurvedic Bhasmas

Two herbo-mineral Ayurvedic drugs (bhasmas) with heavy metals as an ingredient are being tested for their safety as per the protocol developed by Department of AYUSH. Acute toxicity studies and 28 days sub-acute toxicity studies have been completed for both the bhasmas in rats and mice including hematological/clinical parameters and histopathological studies. 90 days long term studies are in progress. Locomoter activity of these animals is being periodically monitored using Optivarimax and heavy metals in blood is being estimated as an R & D exercise.

DNA damage and micronucleus induction by benzene and its metabolites in mice

Benzene and other aromatics are constantly released in the environment from automobiles as well as from industry, resulting in human exposure. In the present study, benzene (BZ) and its metabolites [hydroquinone (HQ), p-benzoquinone (BQ)] were assessed for *in vivo* genotoxicity using alkaline Comet assay and micronucleus test. Swiss albino mice (22 ± 2 g) were administered 10%, 5% and 2% of LD_{50} of each compound intraperitoneally for 10 consecutive days. Normal saline and ethyl methanesulphonate (EMS, 100mg/kg b.w. for 24 hr) served as vehicle and positive controls respectively.

Comet assay was conducted in bone marrow and blood lymphocytes while the micronucleus assay was done in bone marrow erythrocyte cells. The data demonstrated that benzene and its metabolites induced both DNA strand breaks and micronucleated polychromatic erythrocytes (MNPCE) in a significant ($P < 0.01$) and dose dependent manner at all the doses studied. The comet assay results demonstrated that benzoquinone (BQ) had the higher genotoxic potential in blood lymphocytes followed by $BZ > HQ$ while in bone marrow DNA damage was in the order $BQ > HQ > BZ$. However, micronucleus induction was observed maximum with BQ followed by $BZ > HQ$.

The study demonstrates the utility of Comet assay and support from MN assay to quantify *in vivo* genotoxicity of benzene and its metabolites in mammalian cells even at lower doses. The study also suggests that these effects may be long term and may cause adverse health effects in benzene exposed human population.

Evaluation of restorative potential of cryopreserved/ cultured fetal dopaminergic neurons in rat model of Parkinson's disease: Effect of co-graft with trophic factors

In view of the work reported earlier showing viability of VMC cryopreserved in presence of GDNF in culture conditions, further, studies were conducted to assess the



functional viability of cryopreserved VMC by transplantation in rat model of Parkinson's disease. Functional restoration was assessed in 6-OHDA lesioned rats, transplanted with hibernated ventral mesencephalic cells in presence and absence of glial cell line derived neurotrophic factor (GDNF). Rats transplanted with upto 96 hrs cryopreserved VMC along with GDNF exhibits a significant restoration in locomotor activity and amphetamine induced rotations as compared to rats transplanted with VMC cryopreserved in absence of GDNF. Further, significant high expression of rate limiting enzyme for dopamine biosynthesis, tyrosine hydroxylase (TH) was evident in striatum region of rats, transplanted with cryopreserved VMC+GDNF as compared to cryopreserved VMC transplanted alone. Results suggest that cryopreserved VMC could remain viable following transplantation as GDNF helps to increase the viability of transplanted VMC leading to long-term functional restoration. The observations give new insight into understanding the phenomenon that cryopreserved fetal dopaminergic cells under the influence of neurotrophic factor may be a viable approach in neural transplantation studies.

Paraneural cell transplantation in restoring the functional deficits in rat model of Parkinson's disease

In continuation with the earlier studies of co-transplantation of VMC and CB, long term functional restoration (24 weeks) was assessed in 6-OHDA lesioned rat model of PD. Primary culture of CB cells was done as described in the 3rd Report. Significant neurobehavioral impairment ($p < 0.001$) was observed in the 6-OHDA lesioned groups, when compared to the sham group. VMC and CB alone transplanted group exhibited no significant recovery. However, VMC+CB co-transplanted animals exhibited more pronounced ($p < 0.001$) neurobehavioral recovery as compared to the lesioned animals. Similar to above findings, 6-OHDA lesioned group demonstrated significant ($p < 0.001$) neurochemical deficits. VMC and CB alone transplanted group exhibited no significant recovery. However, VMC+CB co-transplanted animals exhibited more significant restoration ($p < 0.001$) of neurochemical deficits persisting upto 24 weeks post transplantation. Functional recovery was accompanied by significantly high ($p < 0.001$) TH expression in the co-transplanted group, when compared to the lesioned group as well as VMC alone transplanted group. Quantification of TH positive cells by image analysis revealed a significant restoration in TH-IR fiber density in striatum as well as TH-IR neurons in SNpc in co-transplanted animals as compared to VMC alone transplanted animals. Our results exhibiting significant attenuation of neurobehavioral and neurochemical deficits in co-transplanted group suggests that co-transplantation of CB cells along with VMC provide better and long-term functional restoration in rat model of PD possibly by supporting the survival of newly grafted cells as well as remaining host DA neurons.

Identification of functionally important Single Nucleotide Polymorphisms (SNPs) in PAH responsive cytochrome P450 genes

Studies were conducted to identify the SNPs in cytochrome P4501A1 and CYP1B1 genes in order to understand the role of these genes in the susceptibility to head and neck cancer. Genomic DNA was isolated from blood samples from 100 patients suffering from



head and neck cancer registered at King George's Medical University, Lucknow and an equal number of age matched controls. PCR based Restriction Fragment Length Polymorphism (RFLP) methods were used to detect the functionally important polymorphisms CYP1A1 and CYP1B1 genes. The case control study data in 100 cases showed that the frequencies of MspI and Ile/val polymorphisms of CYP1A1 and Ala119Ser and Leu432Val polymorphisms of CYP1B1, were higher in the patients suffering from head and neck cancer as compared to the controls. However, no significant differences were observed in Arg48Gly and Asn453Ser polymorphisms. Studies are required to identify other functionally important polymorphisms in other PAH responsive genes.

Assessment of genetic and environmental factors in causation of Parkinson's disease

Studies were conducted to identify the susceptibility genes and the possible genotype combinations as one of the predisposing factors for Parkinson's disease. Single nucleotide polymorphisms (SNPs) in the candidate genes involved in dopamine metabolism and regulation such as dopamine receptor-D2 (DRD2), dopamine transporter (DAT), monoamine oxidase-B (MAO-B) were studied. Those involved in toxication-detoxication mechanisms such as cytochrome P450 2D6 (CYP2D6) and glutathione S-transferase (GSTs) were also studied. Genomic DNA was isolated from the blood samples, drawn from 50 patients suffering from Parkinson's disease and equal number of age and gender matched healthy controls. PCR based RFLP and allele-specific PCR methods were used to detect the polymorphisms in above said genes. The case control study data in 50 cases showed increased frequency of CYP2D6 (G1934A), GST-T1 (null), DAT (A1215G) and MAO-B (intron-13A/G) polymorphisms in patients as compared to controls. Further analysis is required to identify the causative genes as well as genotype combinations for pathogenesis of Parkinson's disease.

Assessment of genetic susceptibility to environmental chemicals using molecular markers

In vitro and *in vivo* studies were conducted to assess the genotoxicity of lead (Pb) and its amelioration by thiamine (Vitamin B1) using Comet assay and micronucleus assay. Isolated human peripheral blood lymphocytes were treated *in vitro* with varying concentrations (0.01-100 μ M) of lead acetate and lead nitrate with pre- or post-coexposure to thiamine (5 and 10 μ g/ml). Both compounds caused significant ($p < 0.05$) DNA damage at 0.1-10 μ M, as was observed from the increased values of Comet assay parameters viz Olive tail moment and tail % DNA. Thiamine (5 and 10 μ g/ml) caused significant ($p < 0.05$) reduction in the lead-induced genotoxicity.

Swiss albino mice were treated intraperitoneally with lead nitrate alone (5%, 10% and 20% of LD50) and pre- or post- treatments with thiamine (25mg/kg b. wt.) for 24 hours. The data revealed that Pb caused significant ($p < 0.001$) increase in DNA damage in mouse blood and bone marrow cells as evident from Comet parameters and elevated frequency of micronucleated erythrocytes. Pre- and post treatments with thiamine significantly ($p < 0.05$)



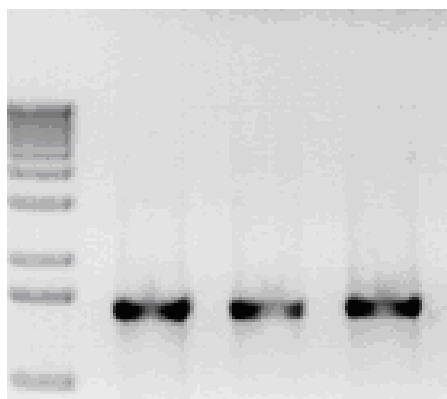
ameliorated Pb-induced genotoxicity as reduction in DNA damage (in blood and bone marrow cells) as well as frequency of micronuclei (in bone marrow) was observed.

Cellular and molecular toxicity studies with organochlorine and pyrethroid pesticides

In vitro studies were conducted to assess the genotoxic potential of cypermethrin, (a broad spectrum, non-cumulative synthetic Type II pyrethroid pesticide) by assessing the induction in the frequency of micronucleus formation using flow cytometry. CHO cells were exposed to cypermethrin at different concentrations (0.01- 5mM) for 3hr and 6mM ethyl methanesulfonate was taken up as positive control. A significant induction in the frequency of micronucleus formation at higher concentrations (1mM, 5mM) was observed.

Characterization of three novel potential aerobic bacterial strains for kraft lignin degradation from pulp paper mill waste

Three aerobic bacterial strains *Paenibacillus* sp (AY952466), *Aneurinibacillus aneurinilyticus* (AY856831) and *Bacillus* sp (AY952465) as new strains for lignin degradation which effectively decolorize/degrade kraft lignin, a by product of the major pulping process and main contributor to the colour and toxicity of paper industry waste were identified by biochemical tests and analysis using 16S-rRNA gene sequencing.



16S rDNA gel picture of three isolates: Lane 1: 1Kb ladder; Lane 2: ITRC S6, Lane 3: ITRC S7; Lane 4: ITRC S8

Growth of bacteria

Their phylogenetic relationship is shown in the above phylogenetic tree. In batch decolorization experiments *Bacillus* sp (AY952465), ITRC S₈ reduced the maximum colour of lignin amended mineral salt medium at pH 7.6 by 65% after 6 days and *Paenibacillus* (AY952466) ITRC S₆ by 43%. The High performance Liquid Chromatograph (HPLC) analysis revealed that under these conditions the three strains degraded the kraft lignin by 37, 33 and 30% respectively. However, the mixed culture of its three species reduced colour by 69%, lignin by 40% and total substrate by 50% under these conditions.



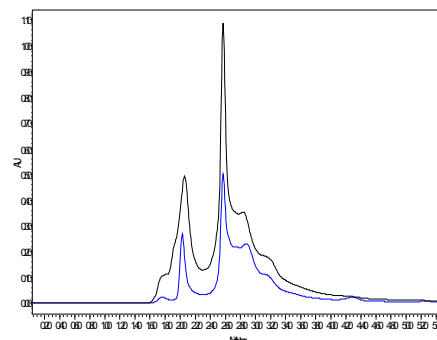
Phylogenetic tree of the isolates and their related genera has been linked based on 16 S rDNA sequence comparisons. Their names and respective accession numbers are given in tree.

The sharp decrease in dissolved oxygen was found initially due to the rapid utilization of primary growth substrate by bacteria, which established that minimum dissolved oxygen was used during the biodegradation. Likewise, initial decolourisation was triggered with decreased pH and simultaneously increasing culture OD, the pH of medium exceeded the initial level on subsequent incubation. The lignin analysis from medium with HPLC indicated degradation with biotransformation.

The kraft lignin from pulp paper mill waste was extracted with ethyl acetate (50:50 v/v) and further it was derivatised with trimethyl silyl (TMS) before GC-MS analysis. The structural analysis of biotransformed lignin by GC-MC (Make Perkin Elmer auto system

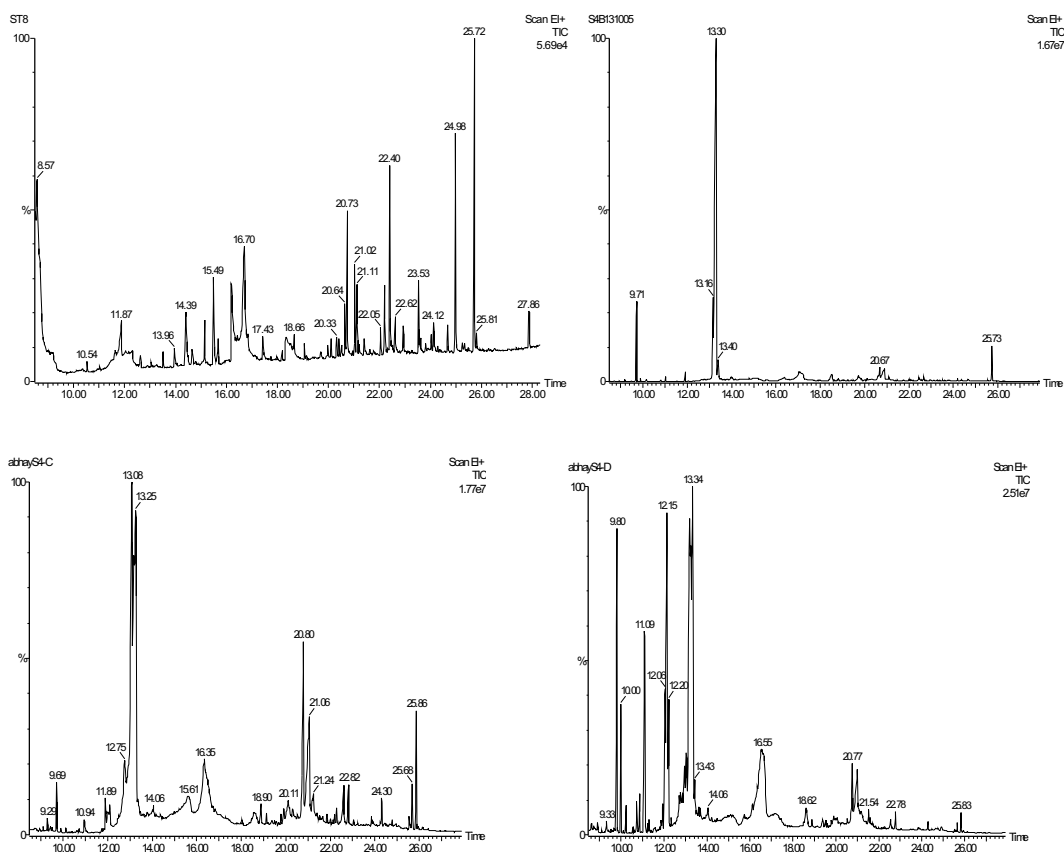


Kraft Lignin Control and decolourized sample



HPLC Data of decolourised & control

XL gas chromatograph with tubular mass spectrometer) revealed the generation of lignin monomer structure. The total ion chromatograph (TIC) corresponding to the compound of ethyl acetate extractable from acidic supernatants (treated) with respect to the strain showed maximum production of lignin monomer by *Bacillus sp.* ITRC S8 (AY952465) which showed decolourisation of effluent up to 65% followed by *A. aneurinibacillus* ITRC S7 (AY856831) while the *Paenibacillus sp.* ITRC S6 (AY952466) showed least change in lignin polymer structure. The prominent lignin monomers were Vanillic acid (RT 16.90) guaiacol (RT 11.90), acetoguanone (RT 15.6), vanillic acid (RT 16.9) and 3,4,5-trimethoxybenzaldehyde (G units); gallic acid (RT 21.2), ferulic acid (RT 22.6), sinafylic acid and coniferylic acid. These products are expected to have various biotechnological applications.



TIC of standard kraft lignin (a) inoculated with bacterial strains; *Paenibacillus sp.* (ITRC0-S₆) (b) *A. aneurinilyticus* (ITRC-S₇) (c) and *Bacillus sp.* (ITRC-S₈) (d) after six days.



Survey studies/Societal programmes

Assessment of environmental quality of Lucknow city, during pre-monsoon (May–June 2005) and post-monsoon (October–November, 2005)

Survey of air pollution in the Lucknow city was conducted during May- June 2005 and October–November – 2005 representing pre-monsoon period and post-monsoon period. The basic objective of these surveys is to create awareness amongst masses about the increasing trend of urban pollution and help the administrative agency to take remedial measures for the improvement of environmental conditions. The findings of the surveys were compiled in the form of reports and were released on 5th June, 2005 i.e. World Environment Day and 4th November, 2005, ITRC Foundation Day. The surveys included study of air pollutants (SPM, RSPM, SO₂, NO_x, HCHO and Pb) and noise levels at twelve locations, comprising 4 residential, 5 commercial cum traffic and 1 industrial area. Sampling locations near traffic junctions have shown higher concentration of pollutants as compared to other areas. SPM and RSPM levels were found to be higher than the National Ambient Air Quality Standards (NAAQS) at residential and commercial areas. Since the removal of diesel operated tempos from the trunk roads and introduction of CNG tempos; significant reduction in the concentration of the SPM and RSPM was observed.

Assessment of asbestos fibre counts in work zone area

An industry in Patiala, manufacturing asbestos Cement (AC) sheets was surveyed to assess the “Asbestos fibre counts in work zone area”. Asbestos fibre counts were determined in different locations of work zone-godown, ingredient mixing, AC sheets production and the main gate. Fibre counts in these locations ranged from 0.04 – 0.07 fibre/cc, which were below the standard value. Sludge sample was also analyzed for asbestos content and was found to have 0.14 % asbestos. Asbestos content in two powder and from two solid samples ranged 11.18% -11.27% whereas solid samples manifested 40.89 – 46.55%.

Association of body composition and cardiovascular risk factors among active and sedentary population of Lucknow using Bioelectric Impedance (BI) method

A study was undertaken to assess the Body fat %, BMR (Basal Metabolic Rate), visceral fat level and other anthropometric measurements based on bioelectric impedance analysis and their association with cardiovascular risk factors among active and sedentary population of Lucknow with special reference to their age and sex. The study was conducted on 1000 policemen of different police stations of Lucknow for active population and comparative study was undertaken on 113 Government officers for sedentary population of Lucknow. Extensive data generated is under analysis and more police personnel are being assessed.



Justifying the need to prescribe limits for toxic metal contaminants in food-grade silver foils

The use of silver foils in various food preparations is a common practice in Middle Eastern and South East Asian countries. The FAO/WHO Joint Expert Committee on Food Additives (JECFA) has included silver in the list of food additives, but specifications were not prepared. Indian food legislation has included food-grade silver foil and laid down a purity requirement of 99.9%. This leaves an unspecified margin of 0.1% or 1000 mg/g for contaminants. Therefore, a study to investigate the levels of metallic contaminants in food-grade silver foil was undertaken. Of the 178 foils analysed, 161 (90%) contained silver, whilst 10% were fraudulently made up of aluminium. In the case of silver foils, 46% of the samples adhered to the desired purity requirement of 99.9%, while 54% had a lower silver content. Copper was present in 86.3% of the silver foils, while chromium, nickel and lead contamination was found in over 54% of samples. Cadmium was detected in 28% while manganese in 6.8% of the samples. In silver foils showing metal contaminants, average levels were found for nickel (487mg/g), lead (301 mg/g), copper (324 mg/g), chromium (83 mg/g), cadmium (97 mg/g) and manganese (43mg/g), which being appreciable justify the need to prescribe limits for some metals in food-grade silver foil.

Drinking water quality surveillance in Lucknow City

Bacteriological quality of drinking water in residential, commercial and industrial areas of Lucknow city was assessed under the drinking water quality surveillance programme, 2005. During pre-monsoon surveillance, bacteriological contamination in drinking water samples was 15%, 33% and 20% in residential, commercial and industrial areas respectively. In post-monsoon the bacteriological quality of drinking water sample was 22%, 43% and 13% in residential, commercial and industrial areas respectively. Thus, 24% of the water samples collected in pre-monsoon and 27% in post monsoon seasons from Lucknow city were found to be bacteriologically unsafe for drinking purposes.

Awareness programme for school children and teachers

Environmental Awareness programme for school children was continued this year also. Popular lectures were held on May 13, 2005 for students. About 80 students and 10 teachers of Municipal Girls' Inter College & Playway High School participated in the programme. Two senior scientists of the Institute, Dr P Kakkar and Er. A H Khan addressed the issues of water pollution and noise pollution respectively.

Poster painting and elocution competitions for school children on the occasion of World Environment Day, 5th June, 2005 were held. Children from class V-XII participated in both the contests.

An awareness programme was coordinated with police personnel and medical experts, specifically for teachers of local schools, in order to apprise them about the harmful effects of firecrackers used during Diwali. This was organized a week prior to Diwali.

A collaborative programme for science teachers was organized along with Institute of Career Studies (ICS) on Jan. 9 & 10, 2006. Twenty teachers from local schools visited ITRC labs where several techniques, such as HPLC, AAS, microassays, etc were demonstrated to them in the Analytical Section and Herbal Research Lab.



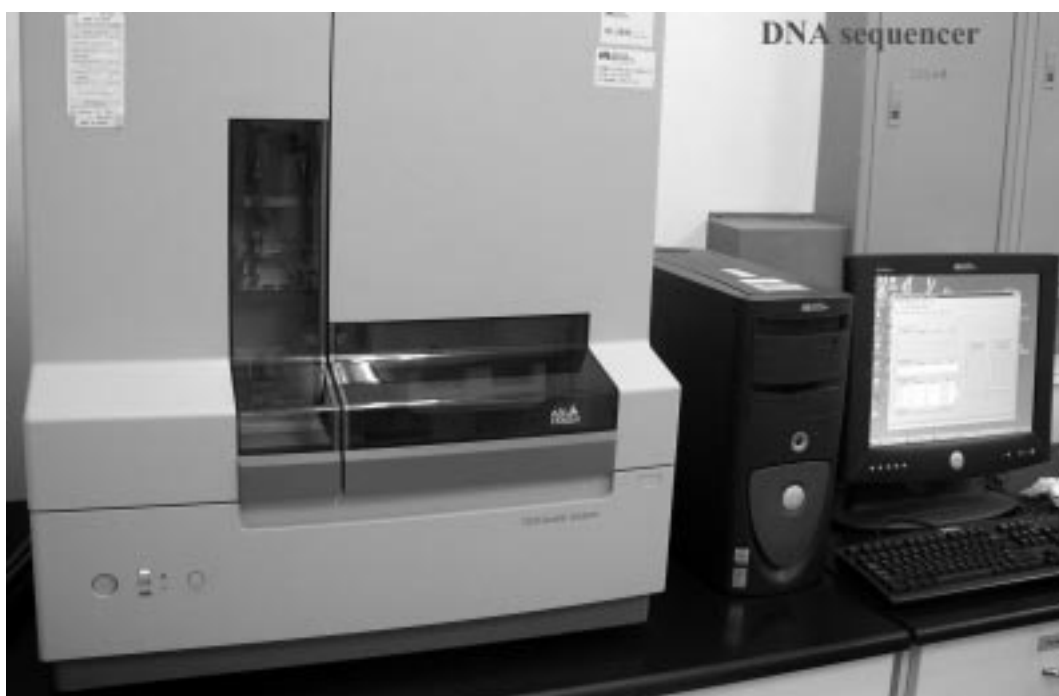
New Facilities

DNA Sequencer:

A state-of-the-art facility for DNA sequencing has been established at the centre. Process of DNA sequencing has been upgraded with the help of advanced computer technology. The discovery has allowed more access to the secrets of DNA. An automated DNA sequencer, “ABI Prism 3100 genetic analyzer” is used for determining DNA sequencers. This is a 16-capillary automated sequencer which can sequence 16 samples simultaneously in a single run.

DNA sequencing techniques represent a major breakthrough in biological research. Two most popular methods are : (i) base specific chemical cleavage method of Maxam and Gilbert and (ii) enzymatic di-deoxy terminator method also called Sanger’s method. The automated capillary sequencer utilizes the principle of Sanger’s method.

New Facilities



The sequencing machines are capable of reading and storing the data and result in data with lower percentage of errors.



Denaturing High Performance Liquid Chromatography (dHPLC)

It is the robotic method to screen the variations/mutations from its wild type. dHPLC analysis is based on the principle that from a column, partially denatured hetroduplexes will elute earlier than non-denatured homoduplexes.

Hybridization of wild type DNA with polymorphic DNA, after denaturation and cooling, will yield hetroduplexes. The specific nucleotide mismatch and the melting characteristics of the surrounding bases, influences the manner in which a hetroduplex peak resolves.



Elution profiles that differ from the wild type or reference DNA indicate the presence of mutations or polymorphisms.

New Facilities



Capabilities and Expertise

- A battery of toxicity studies as per the approved National and International guidelines.
- *In vitro* and *in vivo* test systems such as rat intestinal microorganisms, cell cultures, transgenic *Drosophila melanogaster* and *Bacopa monneri* for the evaluation of genotoxic, carcinogenic and mutagenic potential of xenobiotics and mechanistic studies.
- Semi automated system using 96 well microplate for testing total antioxidant capacity of test sample using ABTS radical quenching.
- Comparative antioxidant potential of medicinal plants using multiple semiautomated microassays.
- Identification of specific herbal tea ingredients using marker compounds by HPLC and HPTLC methods.
- Receptor binding microassays by high throughput screens for neurological disorders.
- Analysis of polyaromatic hydrocarbons, dopamine, 3,4-dihydroxyphenylacetic acid, homovallenic acid, aldehydes and aromatic hydrocarbons in biological samples and different environmental matrices like air, water, river sediment and soil.
- Analysis of herbo-mineral and drugs of poisonous plant origin including their anatomical features and chromatographic finger print profile.
- Flow cytometry for mechanistic studies.
- HPLC analysis of carcinogenic dyes.
- Assay of benzene, toluene and xylene in blood, air and smoke samples by GC-MS.
- Monitoring of emission from biomedical incinerators.
- Oligomer designing for PCR and real time PCR to detect water and food borne pathogens, genetically modified crops.
- Morphotomeric analysis of the bronchoalveolar lavage fluid cells.
- Carcinogen risk assessment capability using *in vitro* experimental model.
- *In vitro* assessment of xenobiotic metabolizing P450s in cultured rat brain neuronals and glial cells.
- *In vivo* genotoxicity assessment in multiple organs and tissues of mouse using alkaline comet assay.
- Expertise in the area of “Multivariate Statistical Modeling” and “measurements uncertainty in chemical analysis”.
- Expertise for calibration of pressure gauges, balances and spectrophotometers.
- Capability has been developed to standardize Alloxan induced diabetes model in rats.
- Expertise on development of a database on “Traditional Plants as antidotes: Snakes and Scorpions”.



Services Offered/Rendered

Health and Environmental Monitoring

- Epidemiological surveys on occupational diseases in industrial workers with suggestion for remedial measures.
- Surveys for adulteration and contamination of food material.
- Environmental monitoring at selected sites.
- Monitoring of noise level in industrial, commercial and residential areas.
- Environmental and ecotoxicological impact assessment studies.
- Analysis of serum samples of protein malnourished children for their antioxidant status.

Safety Evaluation

- Drinking and packaged water.
- Agrochemicals, dyes, food additives, plastics and polymers, petrochemicals, detergents, fibres and particulate matter.
- Herbal products and pesticides.

Toxicity Studies

- Long term toxicity studies for neurological, reproductive, teratogenic, mutagenic, carcinogenic and phototoxic evaluation of environmental chemicals/NCEs.
- Gastrointestinal toxicity evaluation of petroleum products (multifunctional additives) following oral and dermal exposure.
- GI-toxicity evaluation of extract of plastics in water/simulant.

Analysis of Pollutants and Quality Assurance

- Quality assurance for purity of herbal raw drugs and presence of contaminants.
- Analysis of residues of pesticides and metals in biological and environmental samples.
- Analysis of waste water from industries.

Disposal of Wastes

- Biodegradation of persistent pesticides and bioremediation of contaminated sites.

Information Services

- Electronic information database: Chembank, Poltox, Poisonsdex, IPCS-INTOX, ILO encyclopedia, CHEMWATCH
- Updated database (DABTOX) on toxicity profile of industrial chemicals/agrochemicals; food additives and cosmetics used in India.



Technical and support services

Library and Information Centre

A well established set up of library attracts and encourages the scientists and research scholars of an institution to devote excitingly towards R&D activities. ITRC library tried to become a model library through collection of rich literature encompassing state-of-the-art information in the area of industrial and environmental toxicology. Presently, the library is enriched with 30,000 different categories of information materials such as books, bound periodicals, databases, reports and specific reference material on print and electronic format. In addition, during the period library acquired 103 periodicals, four online journals, three international databases on CDROM-220 books, 590 bound volumes, 88 ITRC research papers this year and annual reports of different institutions. Full text access of 3095 periodicals of nine biomedical publishers is available to all scientist on their desk top computer under CSIR E-journals consortium. The abstracting services, in house bulletin and other current awareness services are also brought out. The staff of the library also imparted training to two students of Diploma in Library and Information Science under apprenticeship act 1961.

Research, Planning and Business Development

Research, Planning and Business Development Division (RPBD) is the central point to govern and project the overall activities of the centre by planning, monitoring and evaluating the inhouse, networked and externally funded projects activities. It also explores the possibilities of business development by establishing liaison with industries, private and public sector undertakings, government organizations, research institutions and universities. Further, it interacts with International Scientific and Technology Affairs Directorate of CSIR and other International and National agencies to organize the visits/ deputation of scientists under various bilateral exchange programmes. Preparation of annual scientific reports, five year plan, proper management of intellectual material by coordination with the scientists for identification of patentable content of the material and sending it to the Intellectual Property Management Division of CSIR for execution, are some of the important activities of the division. The R&D output of six major areas namely: Preventive Toxicology, Health Risk Assessment, Predictive Toxicology, Environmental Toxicology, Analytical Toxicology and Inhalation Toxicology are compiled, collated and published yearly in the form of Annual Report to apprise the industry government and academia with the centre's current contribution towards science, economy, society and extramural human resource development. The division is also responsible to attend parliament questions, prepare audit replies and arrange the meetings of Research Council (RC), Management Council (MC) and various other scientific activities. In addition, the division facilitates the signing process of MOU/Agreements between the institute and outside parties related to project related activities and training. The division also arrange to impart training to postgraduate students of various universities and also to arrange training for officials of national and international organizations.



Further, the division interacts with media to highlight various institutional programmes and celebrations (National Technology Day, World Environment Day, CSIR/ITRC Foundation Day, Workshops, Seminars and Conferences) by making them accessible with the highlights of the programmes and day to day R&D activities of the institute for proper coverage and publicity.

Biomedical Illustration and Photography

The division is well equipped with modern tools for projection and photography viz. computers, digital interactive screen, multimedia slides and overhead projectors, SLR and digital cameras to facilitate various activities of the institute. It also prepares posters and other display materials required for presentations. Facilities exist for developing and printing of black and white photographs and of coloured slides required for publication. The division organizes projection and plays important role in exhibition of our achievements at various locations in the country.

A Distributed Information Centre on Toxic Chemicals

The main activities of the ENVIS Centre at ITRC have been constructing and developing a data base on toxic chemicals, publication of Newsletter; and answering of chemicals/environment related queries. The ENVIS website is being maintained Data entry of toxic chemicals is in progress and information on 42 chemicals related to dyes and solvents has been compiled whereas 35 Chemicals have been updated. In addition, online information available : (a) Newsletters up to Feb.2006 and archives since Feb 2000. (b) Abstracts of Current Literature in Toxicology, more than 2000 are available.

Information related to priority chemicals used in the country has been compiled and stored in the existing database. During the year, ENVIS Centre increased the list of data profiles of chemicals to 809 in the database. Updating of the existing information in the chemicals' database is also carried out regularly.

Abstracts of current literature in Toxicology, Vol. 16, No.3-4 (July-Dec) 2003 with 209 abstracts, Vol. 17 No. 1-2 (Jan-June) 2004, with 178 abstracts and No. 3-4 (July-Dec) 2004 with 180 abstracts pertaining to various environmental and toxicological topics have been printed this year.

Newsletter: A quarterly publication, ENVIS Newsletter is brought out regularly. Vol. 12, Nos. 3 & 4 and Vol. 13, Nos. 1 & 2 have been published. All publications have been uploaded on the website.

Further, attended a total of 68 technical queries related with chemical poisonings, toxicity and waste management, pollution aspects; from industries, govt. departments, researchers.

A database on "Traditional plants as antidotes: snakes and scorpions" has been developed and submitted for copyright.



Computer Centre

Computer Centre provides central computing facility to the staff of the Institute engaged in R&D and S&T activities. The facility includes development & maintenance of application softwares, web sites, databases and data analysis. Computer Centre maintains a Campus wide Local Area Network consisting of more than 100 nodes. It also manages a 512 kbps broadband Internet connectivity which has been provided to the scientists, technical staff and research students so as to assist them in their R&D and S&T work. The Centre maintains central internet services for the students and staff members of the institute. It houses a central DTP facility, which caters to the need of scientists for preparation of reports and presentations. This Centre also regularly provides in-house computer software training for human resource development.

Animal Facility

The Animal House facility at ITRC follows GLP norms where animals are being maintained under standard conditions. Breeding of animals is supervised in order to supply healthy animals to the scientists of the centre for R&D studies. In-bred colonies of animals viz mice, rats, guinea pigs, rabbits, fishes and sheep are being maintained. Professional veterinary services are provided to all animals as and when required during experimentation. The animal facility is recognized by the National Accreditation Board for Testing and Calibration Laboratories, India. The section organizes regular meetings of Institutional animal Ethics Committee to review proposed animal experiments along with their protocols before giving clearance for the use of animals for research projects. King George's Medical University, Lucknow, B.P. Institute, Lucknow and Sri Chitra Tirunal Institute of Medical Sciences, Trivendram are using animals for their research work from this facility.

Analytical Chemistry

The section continued its support to various R&D activities/sponsored projects of the institute. It is equipped with modern instruments, like, Luminescence and Spectrophotometers, AAS, GLC, HPLC and GC-MS which are used to conduct routine analysis of the referred samples of biological/environmental origin for the determination of chemical pollutants/toxicants as per NABL guidelines. Arsenic evaluation studies in water samples of hand pumps sponsored by U.P. Jal Nigam, Lucknow were successfully completed. Also, analysis of blood, urine and water samples for pesticides and metals received from PGI, Chandigarh and Remote Sensing Application Centre, Lucknow and heavy metals analysis in fish, medicine samples referred by ICMR, New Delhi as desired by Andhra Pradesh High Court were completed. Studies are going on for the analysis of pheromones '3 (air borne chemical substances that are secreted externally by animal urine, feces) in the samples of urine/cervical mucous of cows/buffaloes at different phases of estrous period in collaboration with IVRI, Izatnagar. In addition, samples of water and soil are also being analysed for pesticides including organochlorines and organophosphorous compounds as well as pyrethroids, mainly cypermethrin and fenvalerate, which are used as mosquito repellants.



Human Resource Development

Training programme on analysis of pesticides and other organics (SELA-2) (October 18-22, 2005)

A 5-day training programme on “Analysis of Pesticides and other Organics” (SELA-2) sponsored by Central Pollution Control Board (CPCB), Delhi was organized at ITRC, Lucknow from October 18-22, 2005. Twenty four chemists and analysts from State Pollution Control Boards, CPCB, Central Ground Water Board, Universities and scientific institutions participated in the programme.

Dr. Jai Raj Behari, the chairman, organizing committee emphasized on the need of correct analysis to combat the increasing trend of environmental pollution and associated health problems. The analysis of chemical pollutants/toxicants in various matrices is needed to arrive at a sound decision of controlling such pollutants. Dr. R.B. Raizada, Dy. Director, ITRC, gave the genesis of the programme and spoke on the importance of pesticide analysis in different matrices including, water, air, food, soil. A brief account of how pesticides and other organic chemicals like polycyclic aromatic hydrocarbons (PAH's) directly or indirectly affect human health was also given along with significance of setting permissible limits of these chemicals.

The course was designed in 5 modules which included Analytical laboratory management, national status of organic pollutants, chromatographic systems, quality assurance, compilation and reporting of data.

Dr. R.B. Raizada presented the national scenario and informed about permissible limits, the restricted use of some pesticides and those which have already been banned. Dr. Sushil Kumar delivered his lecture on safety measures in laboratory work and Dr. A.K. Srivastava delivered the lecture on health effects of pesticides and PAHs. Later, in the afternoon the participants were taken to Gomti river sites and a demonstration on collection of water samples was given. Dr.R.C.Murthy delivered a talk on Analytical laboratory management. Routine problems in analytical laboratory and their solutions were discussed with the participants. In the afternoon, the participants were taken to Water Analysis Laboratory at Gheru Campus of ITRC, where a demonstration on accelerated solvent extractor system was given.

Dr. M.K.J.Siddiqui, Director, Council of Science and Technology, Uttar Pradesh, Lucknow delivered a talk on biological monitoring of pesticides. Later Er.A..H.Khan demonstrated the sampling machine for monitoring of air. A session was devoted to processing of water samples, spiked water samples for pesticide and PAH analysis on GLC and HPLC respectively. The complete solvent extraction, concentration and cleanup of the samples were demonstrated to the participants, who interacted with zest during the session.

During the valedictory function, Dr.C.M.Gupta in his presidential address expressed his views on quality of analysis in relation to chemical pollutants especially pesticides which somehow find their way into the food chain. He also emphasised the need of



precise and accurate analysis of heavy metals as they are also organic contaminants in environment. Dr. M.Q. Ansari, Sr. Scientist, CPCB and Guest of Honour laid emphasis on the necessity of such courses in the present environmental scenario and informed the role of CPCB in training the manpower all over the country. Dr. L.P.Srivastava, Scientist EII, Pesticide Toxicology Division of ITRC and Organising secretary of the programme while proposing the vote of thanks, expressed his happiness over the success of the programme, which was mainly due to interest of the participants and the cooperation of ITRC team.

Indo-US workshop on public health and medical education (April 7-8, 2005)

A two-day Indo-US conference on Public Health and Medical Education was organized jointly by ITRC and King George's Medical University (KGMU), Lucknow from 7-8th April, 2005 at Scientific Convention Centre, Lucknow. Prof. YK Gupta, Director, ITRC, Lucknow welcomed the guests and participants. Prof. PK Dave, President, Indian Academy of Medical Sciences and Ex-Director, All India Institute of Medical Sciences (AIIMS), New Delhi was the chief guest. Dr E Cassimatis of USA highlighted the agenda of Indo-US program and Dr RK Maheshwari of US discussed the genesis and overview of the seminar. Prof. Dave spoke on "Problems in Health Care and Medical Education" and suggested the methods of revamping medical education in India and USA. Prof. Dave highlighted the 20-point programme of Government of India on Public Medical Health and the role of tertiary super-speciality hospitals in each state for providing medical benefits to each and every individual of this country. He further suggested that all the health centres of this country must be attached with a Medical College situated locally to avoid the unnecessary crowd in the big hospitals for easily curable diseases that can be cured even at Primary Health Centres. The inaugural session was presided over by Dr RC Srimal, Ex-Director, ITRC, Lucknow, Prof. Shally Awasthi of KGMU, Lucknow, delivered the vote of thanks.

Dr E Cassimatis presented an overview of the development in medical education and medicare in USA in the last three decades. Dr Richard Convan delivered a talk on "Pathology: introduction to clinical medicine" that addressed issues such as disease, diagnosis and clinical pathologic correlation. Prof. RK Maheshwari delivered a lecture on "Role of environmental pollutants and therapeutic agents in increased pathogenesis of viruses".

Dr Anoop K Singh of USUHS, USA in his talk "Cancer chemopreventive studies and its impact on public health" highlighted the fact that since India is growing from a developing country to a developed country, the incidence of cancer has increased. This is primarily due to the dietary habits and lifestyle. Dr JT Stocker, USUHS, during his lecture dwelled upon the congenital pulmonary alveolar malformation. Dr YK Gupta, Director, ITRC discussed "Rational use of antibiotics" and emphasized on the use, misuse and abuse of antibiotics.

Prof. Mahendra Bhandari, Vice-chancellor, KGMU, Lucknow, presented an overview of the challenges and the future of medical education in India. Dr M Turner of USA spoke



on the practice of global public healthcare and highlighted the importance of public health with reference to epidemiology in diverse population. Dr. P Pushpangadan, Director of NBRI, stressed on the need for revitalization of traditional remedies for primary healthcare.

Dr Shakti Gupta, AIIMS, New Delhi gave an overview on the changing role of hospitals for the future. Dr M Huynh of USA highlighted the major health challenges faced by USA for human welfare and security and emphasized the need of similar approaches worldwide. Dr R Lipnick discussed about communicable diseases and their surveillance under drastic conditions.

Prof. CP Govilla, Vice Chancellor KG Dental University, Lucknow, delivered the valedictory address. Dr Yogeshwer Shukla, Organising Secretary, presented the vote of thanks.



Prof. Y.K. Gupta speaking during the inauguration of Indo-US workshop on Public Health & Medical Education (April, 2005)

International conference on Toxicology, Environmental and Occupational Health (ICTEOH) (November 14-17, 2005)

Industrial Toxicology Research Centre, Lucknow and Society of Toxicology (STOX), India jointly organized the International Conference on Toxicology, Environmental and Occupational Health (ICTEOH-2005). On 14th November, the Continuing Education Courses on selected topics for deliberation were organized and these were: Toxicogenomics and Metabonomics; Good Laboratory Practices (GLP); Biomarkers of Toxicity and Disease Progression and *In Silico* methods in toxicology. Postgraduate and doctoral level attended the course. The courses emphasized the upcoming technologies in Toxicity and safety evaluation of consumer products, drugs, agrochemicals, industrial and environmental chemicals and pollutants for regulatory control and safety to human health and environment.

Professor Mahendra Bhandari, Vice Chancellor, K.G. Medical University, Lucknow presided over while Professor A. Wallace Hayes was the Chief Guest of the inaugural function. Dr. R. Ettl, Chief, Basel Operations, Novartis Pharma AG, Switzerland and Professor Tohru Inoue were Guests of Honour. Dr. C.R. Krishna Murthi Honour Lecture



was delivered by Dr. A. Wallace Hayes, Secretary General, International Union of Toxicology and Professor, Environmental Health, Harvard School of Public Health, USA, entitled "Corner-stones of Toxicology". He was of the opinion that three axioms are central to toxicology. These are people differ, dose matters and things change. The plenary lecture on "Benzene Induced Leukomogenesis between wild-type and P53 gene



Inaugural function of International Conference on Toxicology, Environmental and Occupational Health - Prof. B. Dev is being felicitated by Dr. P. Pushpangadan, Director, NBRI. Also on dais (L-R): Dr. A.P. Sahu, Prof. R.P. Singh, Dr. C.M. Gupta and Dr. Deepak Agarwal

knockout mice" was delivered by Dr. Tohru Inoue, Director, National Institute of Public Health Sciences, Tokyo, Japan and Vice President, International Union of Toxicology. Several Scientific Symposiums on Toxicogenomics; Risk Assessment of Biotechnology derived Products; Chemical disaster Management; Toxicity of Metals, Toxicity of Pesticides; Environmental Health; Occupational and Environmental Diseases and Asthma; Ecotoxicology; Preventive Toxicology and General Toxicology took place.

XXIX All India Cell Biology conference and symposium on Gene to genome: Environment and Chemical interaction (Jan 17-20, 2006)

The XXIV All India Cell Biology Conference was organized at ITRC. In the inaugural function held on January 17, 2006 at the Scientific Convention Centre, King George's Medical University, Dr. V.P. Kamboj, Former Director, Central Drug Research Institute, Lucknow and President National Academy of Sciences India, Allahabad graced the occasion as chief guest and Dr. P.K. Seth, Former Director, Industrial Toxicology Research Centre, Lucknow and CEO, Biotech Park, Lucknow presided over the function. Other dignitaries were Dr. C.M. Gupta, Director, Central Drug Research Institute and Industrial Toxicology Research Centre, Lucknow, Dr. D.K. Saxena, Vice Chairman Organizing Committee: Prof. J.K. Roy, Executive Secretary, ISCB and Dr. D. Kar Chowdhuri, Organizing Secretary, Industrial Toxicology Research Centre, Lucknow. More than 250 delegates attended the conference.

In summary, 6 plenary lectures, 21 invited talks, 22 selected oral presentations by students, 4 oral presentations by senior members, 123 poster presentations were held at the centre. The poster session saw extensive interaction among student presenters with experts of the field everyday for three hours.



Notable among the speakers were Prof. Rajiva Raman, BHU, Varanasi; Prof. Partha P. Majumder, Indian Statistical Institute, Kolkata; Prof. Lalji Singh, CCMB, Hyderabad; Dr. A. Kumar of MRDG, IISc, Bangalore; Prof. B.K. Thelma, Delhi University; Prof. Balraj Mittal, SGPGIMS, Lucknow; Prof. G.N. Pandey, University of Chicago, USA; Dr. Amitabh Mukhopadhyay, NII, New Delhi; Dr. Amitabha Chattapadhyay, CCMB, Hyderabad; Dr. G. Swarup,



Inaugural function of XXIX All India Cell Biology Conference and Symposium on Gene to Genome at Scientific Convention Centre, Lucknow on 17th January, 2006. Release of scientific abstract book by the dignitaries (L-F) Dr. D. Kar Chowdhari, Dr. C.M. Gupta, Dr. V.P. Kamboj, Dr. P.K. Seth and Prof. R. Raman

CCMB, Hyderabad; Prof. M.M. Godbole, SGPGIMS, Lucknow; Prof. M.R.S Rao, President, JNCASR; Prof. Anuradha Lohia, Bose Institute, Kolkata; Prof. Alok Bhattacharya, JNU, New Delhi; Dr. J. Gaurishankar, CDFD, Hyderabad; Dr. Ramesh Sonti, CCMB, Hyderabad and Dr. Imran Siddiqui, CCMB, Hyderabad. Other eminent scientists who delivered the lectures were Dr. Rishi Shanker, ITRC, Lucknow; Prof. K.P. Gopinathan, IISc, Bangalore; Dr. K. Subramaniam, BSBE, IIT, Kanpur; Dr. S. Ghaskadbi, ARI, Pune; Prof. J. K. Roy, BHU, Varanasi; Dr. David de Pomerai, Nottingham University, UK; Prof. Umesh Varshney, IISc, Bangalore; Dr. S. Laloraya, IISc, Bangalore; Dr. D. Parmar, ITRC, Lucknow and Dr. Satish Kumar, CCMB, Hyderabad.

A unique feature of this conference was an interactive one-to-one meet of students of local schools (convent and Government), colleges and Lucknow University with the leading scientists during all the three days. In the valedictory function on January 20, 2006, chief guest was Prof. S.S. Agarwal, Former Director, SGPGIMS, Lucknow while Dr. R.C. Srimal, Former Director, ITRC, Lucknow presided over the function. Both the distinguished guests in their address stressed the need to take the research programmes in Cell and Molecular Biology that can ultimately out reach to masses.

Workshop on Genomics and Proteomics (Jan 30 to Feb 4, 2006)

The above course was designed to achieve a state-of-art understanding of modern techniques of genomics and proteomics including a hands-on training. Eleven young investigators from academic institutions and research organizations like ICMR, ICAR, CSIR and postgraduate institutions attended the course. Eminent scientists from CCMB, ITRC, CDRI and SGPGI delivered lectures and also discussed the experimental methods relevant to the course. The major focus of the training was on the detection of SNPs by high throughput DNA sequencing and protein profiling by two dimensional (2-D) gel electrophoresis of samples that were exposed to various toxicants.



CSIR Programme on Youth for Leadership in Science (CPYLS) - January 24-25, 2006

On 24th and 25th of January, 2006, Industrial Toxicology Research Centre organized the CSIR Programme on Youth for Leadership in Science (CPYLS). Out of the ten students selected from the merit list of U.P. Board, CBSE and ICSE Boards' class X examination of 2005, the following participated in this programme: Akash Gandotra of St Mary's Convent Inter College, Lucknow; Gulrukh and Kanchan Verma of New Public Inter College, Lucknow; Shashank Tripathi of Jugal Devi Saraswati Vidya Mandir, Kanpur; Narendra Mukherjee and Raghav Bhatt of La Martiniere Boys' College, Lucknow and Vikas Prasad Verma of Maharani Laxmi Bai Memorial Inter College, Barabanki.

At the inauguration of the CPYLS programme, the chief guest Prof. S.S. Agarwal former Director, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, delivered a popular lecture. Incidentally, as all the participating students belonged to the PCM stream Prof. Agarwal gave them a glimpse into the interrelationship of physics and biology. Narrating examples of physics in modern medicine he said that science in itself is an ocean of knowledge and that anybody working diligently and patiently could achieve his dreams. He lauded the efforts of CSIR

Selected meritorious students under the CPYLS programme interacting with Dr. S.K. Bhargava during a laboratory demonstration

in popularizing science among the students through CPYLS programme and providing motivation at the right time by "catching them young". Before this, the Director of the Centre Dr. C.M.Gupta while welcoming the students, their parents and the chief guest, emphasized on the importance of scientific knowledge for the growth of the country. He also informed that though this is a century of biology, physics and mathematical sciences are integrated as could be seen in latest surgery and diagnostic techniques. Every child, he said, is a born scientist having an inquisitive temperament and that it is up to us elders to channelize and satiate his curiosity. Dr D.K.Saxena, Chairman HRDC while presenting the genesis of the programme said that this was basically meant to encourage class X students to continue their scientific pursuits and interest in science as they prepare for college. Dr Farhat Jaffery, Convener of the programme, proposed a vote of thanks.

Further, a programme was chalked out for the children to visit various institutional laboratories and facilities. The techniques for detecting and quantifying chemicals and toxicants were shown in the Dyes & Food Adulterants Lab, Developmental Toxicology, Petroleum Toxicology and the Analytical Toxicology labs. The application of DNA microarray and proteomics in toxicogenomics; Polymerase Chain Reaction (PCR) technique and its applicability in biological research; Comet assay for the qualitative and quantitative assessment of DNA damage and repair were demonstrated to the students. The first day



activities concluded with a talk on biotechnology by Dr Ashwani Kumar, Dy. Director, ITRC.

On the next day CPYLS students visited the Herbal Research Lab, Environmental Monitoring Lab and Cell Culture Facility. Assessment of the impact of chemicals on growing embryos; microassays for high throughput screening of antioxidant potential of natural products and protocols for assessing the impact of occupational hazards on workers was demonstrated to the children. This exercise was carried out so as to acquaint the students with the modern approaches to toxicology—at molecular and genetic levels and also the impact of toxicants and pollutants on human health with modern tools. Later, Dr. D.N.Kachru, a senior scientist at ITRC presented a talk on genetically modified food.

A valedictory function was held later in the evening where the students expressed their views on the experience of the two days' programme. The children were quite impressed by the working facilities available here; the instruments and techniques particularly in the Herbal Research, In vitro toxicology, and Environmental Monitoring laboratories fascinated them most. While airing their opinions, generally the students expressed their satisfaction and gratitude towards the CPYLS programme. One of the students who had plans of becoming an engineer is "giving it a second thought" now, that is after seeing the scope in integrating biology and physics. All the students marveled at the patience displayed by scientists in answering their queries.

The Director presented mementos and certificates to CPYLS participants and concluded the event with an open invitation to them to visit ITRC anytime they wished, interact with scientists here, and also participate in any activity organized by this Institute.

A Training Workshop on Need for innovative teaching in science under 'Faculty training and motivation & adoption of schools and colleges by CSIR Labs' - March 22-24,2006

Industrial Toxicology Research Centre (ITRC), Lucknow organized a training workshop for middle and senior school teachers, under the programme 'Faculty Training and Motivation & Adoption of Schools and Colleges' funded by Human Resource Development Group of CSIR. This three days' course was scheduled from 22-24th March 2006 for science teachers (chemistry, biology, environmental science, physics and mathematics) and was designed to emphasize the need for innovative methods of teaching that would enable them to motivate students and develop their interest in science. The intention has been that the course will result in teachers who are better informed about the new and emerging areas in science.

A total of 28 teachers from 13 schools and colleges partook training. Teachers from two schools that have been adopted by ITRC under the ongoing CSIR scheme also participated. Dr. Farhat N. Jaffery and Dr. Poonam Kakkar Scientists, ITRC, coordinated the programme.

Dr P.K.Seth, CEO, Biotechnology Park, Lucknow and Former Director of ITRC delivered the Keynote address. He highlighted the importance of introducing biotechnology in the curriculum of schools. There was a vast scope for the future entrepreneurs with increasing globalization, he informed.



Faculty training workshop on “Need for innovative teaching in science”, March – 2006
Sitting on the dias are L-R: Dr. P. Kakkar, Dr. P.K. Seth and Dr. F.N. Jaffery

Teachers attending the demonstration of techniques at Herbal Research Laboratory

The Workshop covered a wide range of topics—biotechnology, innovative methods of teaching science, good laboratory practices, total quality management, grooming of students to select the right and successful careers. The faculty included renowned scientists, Dr Nitya Anand, Former Director, CDRI and Prof. Bhumitra Dev, Former Vice Chancellor, Gorakhhpur and Bareilly Universities besides senior scientists from ITRC. They emphasized on innovative methods of teaching science and its application in daily life and also the value of science teaching in building students’ careers. It was explained how a scientific approach and temperament is important in developing creativity, interest and enthusiasm among students.

Importance of teaching intellectual property issues at school level; food safety—particularly the adulteration and contamination of popularly sold eatables were some other topics covered which were much appreciated by the participating teachers. Along with lectures, online science quiz, and tours of research labs were also organized. Ample time was allotted for interaction and discussion. The programme also included experimental techniques and methods for applying strategies in the classroom.

The participants visited several laboratories of the Institute: Analytical, Food Toxicology, Herbal Research and Developmental Toxicology labs. Here, the participants were shown various instruments, their functioning and certain indigenous methodologies were also displayed. Scientists imparted demonstrations and briefed the participants about the need for development and adoption of cost-effective and rapid methods of testing.

Later, teachers interacted with each other to create lessons from everyday objects. In this way, their contribution in implementing new ideas and methods in the teaching of science in their schools was judged. After two days of intensive deliberations, a panel discussion was held to sort out the problems faced by teachers in conveying the practical application of theoretical lessons and ways of improving it. The programme was evaluated through post-workshop questionnaires. These indicated a high degree of teacher satisfaction with the quality of the training, the use of hands-on learning, and the applicability of the material to their own classes.

A valedictory function was held at the end of the workshop where the teachers received certificates of participation from Dr Ashwani Kumar, Deputy Director, ITRC.



Annual Events

National Technology Day - May 11, 2005

On the occasion of National Technology Day, the institute was opened for students and general public. They visited the labs and interacted with scientists. A film show was held which showcased R & D activities being carried out at ITRC.

World Environment Day - 5th June, 2005

June 5, 2005 was a historical day for Industrial Toxicology Research Centre where luminaries from all walks of life, namely judicial and administrative services, academicians, researchers, NGO's, children, people from rural areas, social workers gathered to celebrate the occasion. While welcoming them, Prof. Y.K.Gupta, Director, ITRC expressed his happiness on the presence of the large gathering from diverse professions. He said that Lucknow, a city of culture, which transformed into a city of culture and science, will now be regarded as a city of culture, science and environment. Lucknow should become a role model for the city in caring for the environment. He further added that all those present on the occasion will sign the Science Environment Awareness Network (SEAN) roll and take an oath to save the environment. He was hopeful that the SEAN will enroll large number of members in the network by the year end.

Dr. C.M.Gupta, Director, CDRI inaugurated the roll of SEAN and administered the oath. Dr. Gupta also released the following publications on the occasion:



Children participating in a poster painting competition held on World Environment Day, 2005



- Industrial Toxicology Bulletin
- Report on “Environmental Status of Lucknow”
- Vish Vigyan Sandesh.

A few guests of honour namely, Mr. Bhaiyajee, Social Worker, Dr. Seema Javed, Journalist and Mr. Sul Khan Singh, Inspector General, Lucknow Zone expressed their concern about the environment.

Dr. S. C. Barman, Scientist, ITRC presented an overview of the ‘Environmental Status of Lucknow’ Dr. C. M. Gupta gave away the prizes to the winners of the painting and elocution contests. Mr. A. H. Khan, Scientist, ITRC proposed a vote of thanks.



World Environment Day celebration. Sitting on the dais (L-R) : Dr. S.K. Bhargava, Dr. C.M. Gupta, Prof. Y.K. Gupta and Er. A.H. Khan

A panel discussion was held in which school children posed a number of questions before a team of panelists comprising of Dr. Krishna Gopal, Scientist, ITRC, Dr. Abhiraj Singh, Regional Officer, Ministry of Environment & Forests, Govt. of India, Er. K.K. Sharma, U.P. Pollution Control Board, Mr. M.M. Lal, Ex-Scientist, ITRC, Prof. Y.K. Gupta, Director ITRC, Dr. R.C. Simal, ex-Director, ITRC, Dr. M.Z. Hasan, ex.Scientist, NEERI, Nagpur, Dr. S.K. Bhargava, Scientist, ITRC and Dr. P. Kakkar, scientist and moderator.

Dr. S.K. Bhargava presented the pre-monsoon environmental status report of Lucknow and informed average concentration of RSPM in residential area was found in the range of 118.7 (Aliganj) to 170.3 (Indira Nagar), in commercial area it was 128.8 (Chowk) to 198.9 (Aminabad). In industrial area at Amausi 103.3. The average concentration of SPM in residential area was found in the range of 297.3 (Gomti Nagar) to 402.6 (Vikas Nagar), in commercial area 378.0 (Alambagh) to 471.2 (Charbagh) and only industrial area Amausi was 273.5.

हिन्दी पखवाड़ा - सितम्बर 14-28, 2005

औद्योगिक विषविज्ञान अनुसंधान केन्द्र (आई.टी.आर.सी) में दिनांक 14.09.2005 को प्रातः 10:00 बजे हिन्दी पखवाड़ा 14 से 28 सितम्बर, 2005 के उद्घाटन समारोह का आयोजन किया गया। इस अवसर पर मुख्य अतिथि प्रोफेसर रूप रेखा वर्मा, भूतपूर्व कुलपति, लखनऊ विश्वविद्यालय थीं। उन्होंने कहा कि इस महत्वपूर्ण दिन के अवसर पर आमंत्रण के लिए आभारी हूँ। उन्होंने कहा कि इतने सालों से हिन्दी को राष्ट्रभाषा का दर्जा दिया गया किन्तु इसमें सूझबूझ के साथ कार्य किया जाना चाहिए। भाषा सिर्फ कागजों पर दर्ज करने वाली कोई लिपि नहीं होती है। भाषा के मर्म को समझना चाहिए। भाषा से हमारी ज़िन्दगी स्पंदित होती है। यह हमारी आशाओं और भावनाओं एवं कल्पनाओं की जीती-जागती तस्वीर है। भाषा के मूल अर्थ से ही अनुवाद नहीं कर सकते हैं। अनुवाद हास्यास्पद नहीं होने चाहिए। संस्कृतनिष्ठ अनुवाद से सरकारी कामकाज



की भाषा बोझिल हो जाती है। वैज्ञानिक लेख और सरकारी कामकाज के लिए नये शब्द गढ़ने पड़ेंगे। अपभ्रंश से भाषा विकसित होती है। वैज्ञानिक लेखन में आई.टी.आर.सी. का प्रयास काफी सराहनीय है। मुख्य अतिथि को प्रतीक चिन्ह भेंट करते हुए कार्यक्रम के अध्यक्ष और वरिष्ठतम वैज्ञानिक डॉ. अश्विनी कुमार ने कहा कि भाषा की शुद्धता की ओर ध्यान देना चाहिए। उसे बोझिल नहीं बनाना चाहिए। हमें हिन्दी का ज़्यादा से ज़्यादा प्रचार-प्रसार करना चाहिए। साथ ही हिन्दी के प्रकाशनों को ज़्यादा से ज़्यादा पढ़ना चाहिए। इससे पूर्व कार्यक्रम में डॉ. डी.के. सक्सेना, वैज्ञानिक ने मुख्य अतिथि का औपचारिक परिचय दिया। श्री तारिक कुतुबुद्दीन, प्रशासन नियंत्रक एवं प्रभारी राजभाषा तथा समारोह के आयोजन सचिव ने केन्द्र के सभी लोगों से अपील की इस पखवाड़े के दौरान आयोजित विभिन्न प्रतियोगिताओं में बढ़-चढ़ कर प्रतिभागिता करें। साथ ही उन्होंने सभी के प्रति आभार व्यक्त किया।

हिन्दी पखवाड़ा के दौरान दिनांक 23.9.2005 को प्रातः 11:00 बजे डॉ. आर.आर. खान, सलाहकार, पर्यावरण एवं वन मंत्रालय, नई दिल्ली का “रासायनिक दुर्घटनाएं - नियंत्रण एवं निवारण” पर व्याख्यान आयोजित हुआ। उन्होंने बताया कि रसायनों ने पूरे विश्व में मानव जाति की मूल जीवन पद्धति और तौर-तरीकों में एक क्रांति ला दी है। अनुमान है कि आज समाज 60,000 से भी अधिक किस्म के रसायनों का इस्तेमाल कर रहा है। भोपाल में हुई गैस दुर्घटना इस बात की साक्ष्य है तथा यह याद दिलाती है कि हमें अपनी प्रौद्योगिकीय प्रगति के साथ-साथ इसके दुष्परिणामों के प्रति सतर्क रहना चाहिए। पर्यावरण और वन मंत्रालय द्वारा पर्यावरण (सुरक्षा) अधिनियम 1986 के तहत परिसंकटमय रसायनों और रसायनिक अपशिष्टों के विनिर्माण, भण्डारण, आयात, निर्यात और परिवहन के दौरान होने वाली दुर्घटनाओं के नियंत्रण के तरीकों का विकास करने के लिए एक ढांचा तैयार किया गया है। बड़ी रासायनिक दुर्घटनाओं से निपटने के लिए पर्यावरण और वन मंत्रालय नोडल मंत्रालय है। रासायनिक आपात स्थिति से निपटने के लिए विस्तृत संकट प्रबंध योजनाएं तैयार करने हेतु राज्यों का सहयोग लिया जाता है। भारत सरकार ने 1991 में लोकदायिता बीमा अधिनियम बनाया है। भारत सरकार द्वारा हाल ही में लागू किए गए नियमों के कठोर कार्यान्वयन के बावजूद भी रासायनिक दुर्घटनाओं की संभावना से बचा नहीं जा सकता है। ऐसी दुर्घटनाओं से जीवन, सम्पत्ति तथा पर्यावरण को नुकसान होता है यह ज़रूरी है कि केन्द्र, राज्य तथा स्थानीय स्तर पर प्रशासन को दुर्घटनाओं के परिणामों से निपटने के लिए पूरी तरह से तैयार रखा जाए। परिसंकटमय उद्योगों को चलाने वाले व्यक्तियों को यह सुनिश्चित करने के लिए गतिविधियों का आकलन करना चाहिए।

मूल्यांकन के लिए पर्यावरण मंत्रालय द्वारा पर्यावरण संरक्षण तथा अपशिष्टों के द्वारा होने वाली हानि से बचाव के संबंध में अनेक अधिनियम बनाए गये हैं। इनमें से प्रमुख रासायनिक दुर्घटना (आपदा नियोजन) अधिनियम, 1996, परिसंकटमय रसायनों का विनिर्माण, भण्डारण और आयात (संशोधन) नियम, 2000, बैटरी (प्रबंधन एवं हथालन) नियम, 2001, जीव चिकित्सा अपशिष्ट (प्रबंध और हस्तन) नियम, 1998, पुनः चकित प्लास्टिक विनिर्माण और उपयोग



हिन्दी पखवाड़ा समारोह में मुख्य अतिथि प्रो. रूप रेखा वर्मा को स्मृति चिन्ह प्रदान करते हुये डा. अश्वनी कुमार साथ में डा. डी.के. सक्सेना एवं श्री तारिक कुतुबुद्दीन



नियम, 1999, फ्लाइऐश अधिसूचना, 1999, और परिसंकटमय अपशिष्ट (प्रबंधन और हथालन) नियम, 1989 है। यह सुनिश्चित करना राज्य सरकार का काम है कि प्रत्येक परिसंकटमय उद्योग, प्रचालन या प्रक्रम ने आन-साइट योजनाएं तैयार कर ली हैं। राज्य सरकार द्वारा किसी उद्योग, प्रचालन या प्रक्रम में जनता तथा पर्यावरण को प्रभावित करने वाली आपात स्थितियों के लिए एक आफ-साइट आपात योजना तैयार की जानी चाहिए। आन-साइट और आफ-साइट योजनाओं में इस प्रकार से सामंजस्य होना चाहिए कि आपात सेवाएं उपयुक्त समय पर अपनाई जा सकें। कार्यक्रम में डॉ. अश्विनी कुमार, उपनिदेशक ने डॉ. आर.आर. खान को प्रतीक चिन्ह भेंट किया। कार्यक्रम का आयोजन डॉ. जयरात बिहारी, वैज्ञानिक ने किया। उन्होंने एवं सभी के प्रति आभार प्रकट किया।

पुरस्कार वितरण एवं समापन समारोह का आयोजन दिनांक 28.09.2005 को अपराह्न 2:00 बजे केन्द्र के प्रेक्षागृह में आयोजित हुआ। इस अवसर पर मुख्य अतिथि श्री छेदा लाल, निदेशक, उत्तर प्रदेश हिन्दी संस्थान, लखनऊ थे। मुख्य अतिथि ने कहा कि अपने विचारों को व्यक्त करने की क्षमता सिर्फ मातृभाषा में है। वैज्ञानिक और तकनीकी क्षेत्र में अंग्रेजी में कार्य करने की मजबूरी है। कंप्यूटर की प्रगति में हिन्दी में कुछ साफ्टवेयर विकसित हुए हैं। भाषा का विकास तभी हो सकेगा जब वह रोजी-रोटी से जुड़ जाए। हिन्दी में ज्यादा से ज्यादा कार्य किया जाना चाहिए, तभी भाषा का विकास संभव है।

कार्यक्रम की अध्यक्षता करते हुए केन्द्र के वरिष्ठतम वैज्ञानिक डॉ. अश्विनी कुमार ने मुख्य अतिथि को प्रतीक चिन्ह भेंट किया। उन्होंने कहा कि मैं मुख्य अतिथि का संस्थान में स्वागत करता हूँ। जो भाषा जनजीवन से जुड़ी है उसके विकास में हमारा हित है। हिन्दी का प्रयोग ज्यादा से ज्यादा बढ़ रहा है। अपनी भाषा में ज्यादा से ज्यादा प्रकाशन उपलब्ध होने से देश ज्यादा विकास कर पाएगा। आशा है ऐसे कार्यक्रम हिन्दी की उन्नति में सहायक होंगे।

इस अवसर पर पखवाड़े में आयोजित विभिन्न प्रतियोगिताओं में विजयी प्रतिभागियों को मुख्य अतिथि ने पुरस्कार और प्रमाण पत्र प्रदान किया। डॉ. अश्विनी कुमार ने हिन्दी में कार्य करने की प्रोत्साहन योजना के नकद पुरस्कार के अन्तर्गत 18 कर्मचारियों को नकद पुरस्कार एवं प्रमाण पत्र प्रदान किया। साथ ही अन्तर्राष्ट्रीय वैज्ञानिक हिन्दी संगोष्ठी, वैज्ञानिक हिन्दी कार्यशाला और राजभाषा कार्यान्वयन के लिए भी प्रमाण पत्र प्रदान किया। समारोह के आयोजन सचिव श्री तारिक कुतबुद्दीन, प्रशासन नियंत्रक ने विशेष रूप से केन्द्र के निदेशक, डॉ. सी. एम. गुप्ता का आभार प्रकट किया जिनके कुशल नेतृत्व, मार्गदर्शन एवं प्रेरणास्वरूप इस पखवाड़े का सफल आयोजन संभव हुआ। उन्होंने इस कार्यक्रम के आयोजन हेतु सभी संबंधित के सहयोग हेतु हृदय से आभार प्रकट किया।

CSIR Foundation Day - 26th September 2005

CSIR Foundation Day was celebrated on September 26, 2005. An essay competition was held on environmental issues for children of CSIR staff. An exhibition showcasing major achievements of the four Lucknow based CSIR laboratories, the Industrial Toxicology Research Centre, Central Drug Research Institute, Central Institute of Medicinal and Aromatic Plants and National Botanical Research Institute was jointly organized at Central Institute of Medicinal and Aromatic Plants. The exhibition was inaugurated by Dr. Deepak Pental, Vice Chancellor, University of Delhi. The exhibition remained open for one week. Many dignitaries, farmers, students of various schools and general public visited the exhibition site and discussed their concern with the experts.



Industrial Toxicology Research Centre

All the four laboratories jointly organized the foundation day lecture at 3.00 p.m. at the Scientific Convention Centre, Shahmeena Road, Lucknow. Dr. Deepak Pental, Vice Chancellor, University of Delhi delivered a lecture entitled “Molecular biology and precision breeding of crops”.

Dr. P.L. Gautam, Vice Chancellor, GB Pant University of Agriculture and Technology, Pant Nagar presided over the function. Besides the scientific activities, prizes and cash awards were given to children for winning essay competition and securing meritorious positions in various examinations. Members of the staff, who had superannuated in the last one year were awarded certificates and shawls whereas staff members who completed 25 years of service were awarded wrist watches.

40th Foundation Day of ITRC

Industrial Toxicology Research Centre (ITRC) celebrated its 40th Foundation Day on 3rd November, 2005. Earlier in the day the 9th Prof. S.H. Zaidi oration was delivered by Prof. A.K. Tyagi, Deptt. of Biochemistry, University of Delhi South Campus. While delivering the lecture entitled “Mycobacterium tuberculosis: a pathogen that refuses to be tamed”, Prof. Tyagi said that tuberculosis claims between 2-3 million lives every year and one-third of the world’s population is latently infected with *Mycobacterium tuberculosis*. Dr. V.P. Kamboj,



CSIR Foundation Day celebration. Seated on the dais :
(L-R) Dr. D.K. Saxena, Prof. S.S. Agarwal;
Dr. Nitya Anand and Dr. C.M. Gupta



Prof. S.H. Zaidi oration : Sitting on the dais (L-R) :
Dr. Poonam Kakkar, Prof. A.K. Tyagi, Dr. C.M. Gupta and
Dr. GSD Gupta. Dr. V.P. Kamboj is addressing the audience

Former Director, Central Drug Research Institute (CDRI), Lucknow while presiding the function suggested that extracellular signaling studies which recognize the *Mycobacterium tuberculosis* in a human body may be elaborated. In the afternoon the Foundation Day was celebrated. Dr. C.M. Gupta, Director, ITRC welcomed the chief guest, Dr. S.S. Agarwal, Former Director SGPPI, Lucknow and Dr. Nitya Anand,



Former Director, CDRI, Lucknow and other dignitaries. Dr. Gupta focused on the ongoing R&D activities related to thirteen Networked projects and a few important major in-house programmes. He informed that ITRC is coordinating in one of the CSIR-Networked projects entitled “Toxicogenomics of genetic polymorphism in Indian population exposed to industrial chemicals for the development of biomarkers”. He stated that proteomics approach for identification of blood protein biomarkers of arsenic exposure is being employed for developing a database of protein profile in blood samples from toxicant exposed and unexposed population. This would help to delineate the molecular mechanisms of actions of the test pollutants, he added.



40th Foundation Day of ITRC : Dr. Nitya Anand being felicitated by Dr. C.M. Gupta, Director ITRC

While delivering the Foundation Day address, Dr. S.S. Agrawal explained the concept of toxicology in the post-genomic era. He opined that a qualitative shift has emerged in the scope of toxicology. He emphasized that understanding delineation of gene-environment interaction is of great importance to all human diseases.

Dr. Nitya Anand released the report of Assessment Environmental Status of Lucknow city – A Post Monsoon Survey.

National Science Day – 28th February, 2006

The centre observed National Science Day on February 28, 2006 as open day for general public and students.



School children taking keen interest in demonstrations during exhibition on National Science Day, 2006



Seminars (April 2005 to March 2006)

Sl. No.	Name of speaker	Topic
1	A Jamal Khan	Study of functionally important Single Nucleotide Polymorphisms in cytochrome P450 2E1 gene in Indian Population
2	Abhishek Ojha	Detection of GM Food by ELISA
3	Alok Pandey	Micronucleus assay in genetic toxicology
4	Amita Mishra	Allergenic potential of various food crops of India
5	Amresh Mahapatra	Bioinformatics: an overview
6	Anoop Raj Tilak	Genetic polymorphism of microsomal epoxide hydrolase and its association with cancer risk
7	Anwar	Studies on association of functionally important genetic polymorphisms in cytochrome P-450 2E1 gene with alcoholic liver cirrhosis
8	Arvind Pratap Singh	Automated DNA sequencing
9	Ashu Johri	Effect of prenatal exposure to Lindane and post natal expression of hepatic and brain cytochrome P450
10	Ashu Johri	Prenatal exposure to deltamethrin and persistent over expression of cerebral and hepatic cytochrome P450s
11	Beer Bahadur Singh	Comparative chronic toxicity of pyridine, alpha-picoline and beta-picoline to <i>Lemna minor L.</i> and <i>Chlorella vulgaris B.</i>
12	Chaitali Sinha	Developmental neurotoxicity of pyrethroid based mosquito repellent exposure in rat offspring
13	Chandra Kumar Singh	Genetically engineered plants: bane or boon
14	Chandra Shekhar Seth	Accumulation of cadmium and its toxicity to hydroponically grown <i>Brassica campestris</i> plant
15	Chitra Tripathi	The role of Survivin in cancer chemoprevention
16	Chitra Tripathi	Effect of 6-gingerol on testosterone induced alterations of cell growth regulatory genes in mouse prostate
17	Devyani Bhargava	Toxic potential of municipal solid waste leachates using <i>Drosophila</i> as a model
18	Divya Gupta	Identification of plasma proteins associated with lead exposure
19	GC Kisku	Conservation of natural resources for sustainable development
20	Ghanshyam Upadhyaya	An introduction to DNA microarray
21	Hifzur R Siddiqui	Validation of <i>Drosophila melanogaster</i> as <i>in vivo</i> model for genotoxicity assessment using modified alkaline comet assay



22	Jyoti	Trace elements and breast cancer
23	Jyoti	Comparison of some trace elements concentrations in blood, tumor free breast and tumor tissues of women with benign and malignant breast lesions
24	K Babu	Influence of pyridine nucleotides and glutathione redox potential on erythrocyte cellular defense in epidemic dropsy patients
25	Kavita Seth	Possible role of astrocytes in 6-hydroxydopamine induced degeneration of dopaminergic neurons
26	Kiran Verma	Degradation of endosulfan by Rhodococcus species
27	Madhu Lata	Neurobehavioral toxicity of monocrotophos in developing rats
28	Madhu Singh	SNP cytochrome P450 2D6 gene
29	Mahima Vajpayee	Short term test for the evaluation of genotoxicity, mutagenicity and carcinogenicity of environmental chemicals
30	Mahima Vajpayee	Genotoxicity of endosulfan: its isomers and metabolites
31	Maqsood Ahmad Ansari	Environmental exposure to lead and assessment of associated health risks among children
32	Munish Kumar	Genetic polymorphism in CYP1A1, CYP2D6 and GSTs gene and susceptibility to disease following exposure to xenobiotics
33	Naveen K Reddy	Effect of Argemone alkaloid on cytochrome P450 isoform profile in rats treated with P450 inducers
34	Neelima Pathak	Cadmium induced apoptosis in mouse thymocyte cells
35	Neelima Pathak	Cadmium induced apoptosis in murine splenocytes
36	Neetu Kalra	Modulation of ras signaling pathway by diallylsulfide in DMBA induced mouse skin tumors
37	Pankaj Chaudhary	Degradation of beta-hexachlorocyclohexane by haloalkane dehalogenase LinB
38	Parag P Shah	Studies on functionally important polymorphisms in CYP1A1 gene in head and neck cancer
39	Pramod Kumar Mishra	Molecular approaches for early detection of gall bladder cancer
40	Rajneesh K Chaturvedi	Co-transplantation of fetal neural cells with Zuckerkandl's cells: functional restoration in rat model of Parkinson's disease
41	Rajnish Kumar Chaturvedi	Restorative potential of dopaminergic grafts in presence of antioxidants in rat model of Parkinson's disease



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42	Rakhi Agarwal	Validation of cyclic voltammetry for the trace estimation of mercury in various aqueous samples
43	Richard E Goodman, USA	GM allergenicity assessment including the use of animal model: pros and cons
44	Sahdeo Prasad	Evaluation of antioxidant potential of mango pulp extract against testosterone induced oxidative stress in Swiss albino mice
45	Sanjaya Yadav	Expression of cytochrome P-44502E1 (CYP2E1) in rat brain
46	Sanjaya Yadav	Region specific modulation of brain CYPs by Lindane
47	Shikha Tewari	Round up ready: genetically modified soybean
48	Shikha Tewari	Real time PCR based detection of GM Foods
49	Shubha Shukla	Co-transplantation of carotid body with fetal neural cells: functional restoration in rat model of Parkinson's disease
50	Siya Ram	Drug resistance profile of <i>Escherichia coli</i> isolates from river gomati and ganga
51	Smita Nair	Study to evaluate antioxidant capacity in some selective herbs using primary rat hepatocytes
52	Subhash Chandra Gupta	Studies on Hsp70 expression and antioxidant enzymes against dichlorvos toxicity in <i>Drosophila</i>
53	Shubha Shukla	Parkinson's disease
54	Suman Patel	Oxidative stress in Parkinson's disease
55	Sushila Patel	Genotoxic potential of cypermethrin in multiple mouse organs using Comet assay
56	Vipul Kumar Singh	Chemical and biochemical studies of the subjects occupationally exposed to pesticides
57	Vipul Kumar Singh	Comparison of blood polycyclic aromatic hydrocarbon levels in the patients of breast cancer with controls
58	Virendra K Singh	Study of the SNP in tumor suppressor gene (p53) and toxicant responsive gene and their association with the development of breast cancer in Indian women



Honours and Awards

- Dr. Mukul Das** was invited as Chief Guest on the 91st Annual Day Function of State Public Analysis Laboratory, Lucknow on April 27, 2005.
- Dr. Mukul Das** was elected as Executive Committee Member of Environmental Mutagen Society of India for 2005-2007.
- Dr. G.S.D. Gupta** was elected Treasurer of the Academy of Environmental Biology for the period 2006-2007.
- Dr. A.K. Agarwal** has received Jotsana Mai Raghunath Bhattacharya Award for the best paper published in the area of neuroscience at Annual Meeting of Indian Academy of Neurosciences, Bangalore
- Dr. A.P. Sahu** was awarded Gold Medal and Honorary Fellowship (FIAES) of Indian Academy of Environmental Sciences, Hardwar in recognition of the valuable contribution to Environmental Sciences in General and Toxicology in particular, November 28, 2005, Jaipur, India.
- Dr. R.K. Upreti** was awarded the Surjaben Jethalal Thaker Award – 2005 by Academy of Science for Animal Welfare.
- Dr. Krishna Gopal** was awarded the “Scientist of the year 2006” by Bioved Research Society, Allahabad on the occasion of 8th Indian Agricultural Scientists and Farmer’s Congress held on Feb., 21, 2006 at Banaras Hindu University, Varanasi.
- Dr. Poonam Kakkar** has been appointed as member of Joint Implementation Committee by CSIR in August 2005 for monitoring collaborative research on Herbal Drugs between CSIR and CCRUM (Central Council for Research in Ayurveda & Siddha) under an MoU for five years.
- Dr. Poonam Kakkar** was selected by CSIR as one of the 40 technopreneurs to participate in the “Indo-US initiative on technopreneurship in academia” organized by Indo-US Science & Technology Forum, Jan 23-25, 2006.
- Dr. Yogeshwer Shukla** has been elected as member of The National Academy of Sciences, Allahabad, (India)
- Dr. Yogeshwer Shukla** has been elected as member of the National Academy of Medical Sciences, New Delhi
- Dr. Yogeshwer Shukla** has been elected as General Secretary of Environmental Mutagen Society of India
- Dr. V.P. Sharma** has been accredited as QMS Lead Auditor by Management Systems Institute, Noida. This is registered with National Registration Board for Personnel and Training a constituent QCI and member of IPC.
- Dr. Alok Dhawan** was awarded Shakuntala Amir Chand Prize 2002 of ICMR in the field of Biomedical Research during 2005.



Dr. Alok Dhawan has been elected as Vice President of Environmental Mutagen Society of India.

Dr. A.B. Pant has been elected member of National Academy of Sciences and National Academy of Medical Sciences, India

Dr. Adekunle A. Bakare (TWAS Fellow) won the prize for oral presentation at the International symposium on environmental mutagenesis and public health and XXXI Annual Conference of Environmental Mutagen Society of India, Hyderabad, February 23-25, 2006.

Mr. Siya Ram, SRF received best Oral Paper award for the paper entitled 'Probing goes *in Silico*: Detection of diarrheagenic *Escherichia coli* serotypes in water by Taqman probes' in the International Conference on *Toxicology, Environmental and Occupational Health*, 14-17th November, 2005 at ITRC, Lucknow .

Ms. Neetu Kalra, SRF got the best paper award in 31st Annual Conference of Environmental Mutagen Society of India held at National Institute of Nutrition, Hyderabad for her paper entitled 'Mechanism of apoptosis induction by black tea in human prostate cancer cell line LNCaP'.

Miss Pushpa Lata, JRF received best Poster award for her paper entitled 'Probing enterococci in surface waters: plate to PCR' in the International Conference on *Toxicology, Environmental and Occupational Health*, 14-17th November, 2005 at ITRC, Lucknow.

Mr. L.K. Dwivedi received best poster award for his paper entitled Human health risk assessment: in silico approaches at national symposium on Issues and Challenges for Environmental Management, Vision 2025, held at BBAU, Lucknow from February 27-19, 2006.

Intellectual Property

Patent filed for a novel device for quantification of mercury in aqueous/non aqueous and biological samples and a process thereof. Rajiv Prakash, Rakhi Agarwal and Jai Raj Behari (0052/NF2006).

Patent filed for a cost effective chemical process for formaldehyde removal from pyridine containing industrial wastewater for environmental safety. R. Chandra, B.B. Singh, K.P. Singh and Y.K. Gupta (0184/NF 2005)

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For developing a working tool "Biocalculators" for the rapid and precise calculations of biological and statistical endpoints including parameters of oxidative stress, xenobiotic metabolizing P450s, student 't' test, ANOVA, Chi square etc. (No. 013/CR/2006/748854). A.B. Pant, U. Prasad, N. Garg, V.K. Khanna, V.P. Sharma



Ph.D. Awarded

Ph.D. Awarded

Name of student	Supervisor	Title of thesis	University	Year of award
Ms Archana Srivastava	Dr. Ram Chandra	Microbial detoxification of various industrial wastes and their toxicological evaluation for environmental safety	Dr. R.M.L. Avadh University, Faizabad	2005
Mrs. Kshama Pandey	Dr. Krishna Gopal	Studies on water with special reference amphizoic amoebae	Lucknow University, Lucknow	2005
Mr. Saurabh Chandra	Dr. S.K. Gupta	Genotoxicity studies of leachates of industrial solid wastes	Dr. R.M.L. Avadh University, Faizabad	2005
Mr. K.M. Ansari	Dr. Mukul Das	Studies on genotoxic and carcinogenic potential of argemone oil/alkaloid	Lucknow University, Lucknow	2005
Mr. Vinay Kumar Yadav	Dr. Yogeshwer Shukla	Mutagenic and carcinogenic evaluation of respirable air borne pollutants	Lucknow University, Lucknow	2006



Visits Abroad

- Dr. A.P. Sahu, Scientist visited Beijing, China from April 19-22, 2005 to attend 10th International Conference on Occupational Respiratory Disease (10th ICORD)
- Dr. Krishna Gopal, Scientist visited Nancy, France from May 8 -15, 2005 for carrying research work on IFCPAR project No. 2500-WI on use of natural products as drinking water purifiers.
- Dr. Krishna Gopal visited Bangkok, Thailand for attending International training course on Detection of environmental pollutants, testing and screening of toxicity from January 23 to February 10, 2006.
- Dr. Yogeshwar Shukla, scientist visited University of Wisconsin, Madison (USA) as visiting Associate Professor in the Department of Dermatology. Dr. Shukla worked on the role of NF-Kappa B pathways in cancer chemoprevention by nutraceuticals from September to December 2005.
- Dr. Deepak K. Agarwal was invited by World Health Organisation, Geneva to attend Refresher course for GLP Trainer at University of Ghana from August 6-12, 2005.
- Dr. Deepak K. Agarwal, Scientist attended Society of Toxicology meeting held at San Diego, USA from March 5-9, 2006.
- Dr. Alok Dhawan, Scientist was deputed to United Kingdom from August 16-20, 2005 to attend meeting under the India-UK Young Scientists Networking programme of British Council at Lhasa Limited, U.K.
- Dr. P.D. Dwivedi, Scientist visited Montreal, Canada from May 28 to June 3, 2005 to attend second meeting of the Parties (MOP2) to the Cartagena protocol on biosafety preceded by a preparatory meeting and to visit Department of Animal Biology, School of Veterinary Biology, Philadelphia from June 4th to June 10th.
- Dr. P.D. Dwivedi was invited by USDA/ USGC as panelists to attend an International Biotechnology Information Conference from October 10-14, 2005 at Iowa, USA.
- Dr. P.D. Dwivedi, Scientist attended Third meeting of the Parties (MOPs) to the Cartagena Protocol on Biosafety preceded by a preparatory meeting held at Curitiba, Brazil from March 11-17, 2006.
- Dr. Ranjan Kumar, Scientist was deputed to Seoul, South Korea from August 29 to September 2, 2005 to attend annual meeting of TIAFT.
- Mr. Kishore Babu, Sr. Research Fellow, was awarded International Redox Network Fellowship to attend the 3rd meeting of International Redox Network from November 9-11, 2005 at Kyoto, Japan.



Externally Funded Research Projects (2005-2006)

Title	Funding Agencies	Principal Investigator
Neuro-genotoxicity assessment of lead and ethanol : an <i>in vitro</i> study	ICMR, New Delhi	Aditya B. Pant
Neurotransmitter receptor screening of herbal extracts	Ranbaxy Res. Lab., Gurgaon	Ashok K Agarwal
Clinical trials with RISUG regarding genotoxicity and mutagenicity studies with RISUG	Min. of Health & Family Welfare, Govt. of India, New Delhi	Ashok K Agarwal
Biotechnological approaches for the detection and amelioration of pollutants	DBT, New Delhi	Ashwani Kumar
Assessment of oil field soil (with special reference to polyaromatic hydrocarbons) for their eventual remediation and reclamation	DBT, New Delhi	Ashwani Kumar
Genetic and environmental interactions in Parkinson's disease	ICMR, New Delhi	Devendra Parmar
Indo-US project: Fingerprints of blood cytochrome P-450 (CYPS) biomarker of exposure and effect	ICMR, New Delhi	Devendra Parmar
Imprinting of cerebral and hepatic cytochrome P-450s (CYPs) in rat offsprings following prenatal exposure to lindane	ICMR, New Delhi	Devendra Parmar
Third party testing and monitoring of stack emission, ambient air quality monitoring and water effluent testing and annual environmental audit of UPRVUNL, ATPS, Anpara	UPRVUNL, ATPS, Anpara	Ganesh C. Kisku
Monitoring of pollution parameters by outside laboratory	NTPC, RSTPS, Rihandnagar	Ganesh C. Kisku
Environmental monitoring and occupational health status of workers in asbestos-cement based industries : an epidemiological and cytogenetic approach	ICMR, New Delhi	Iqbal Ahmad
Evaluation of arsenic in water samples of hand pumps	UP Jal Nigam, Lucknow	Jai Raj Behari
Analysis of 8 pesticides in 13 water samples	RSAC, UPSLR, Lucknow	Jai Raj Behari



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Identification and quantification of polycyclic aromatic hydrocarbons (PAHs) in soil and Gomti river sediments in Lucknow city	Min of Env. & Forests New Delhi	Jai Raj Behari
Setting up a CDM cell and to develop capacity to support small scale CDM projects in the state	UNDP, New Delhi	Kr. P. Singh
Analysis of ground water to ascertain their potability	U.P. Ground Water Deptt., Lucknow	Kr. P. Singh
Safety evaluation of Decol for the use in sericulture	Silkworm Seed Technology Lab., Bangalore	Krishna Gopal
Molecular mechanism of caffeine and nicotine mediated neuroprotection in MPTP induced Parkinson's disease phenotype in mouse	DBT, New Delhi	Mahendra P Singh
Microarrays and proteomics based approaches to assess the modulation of multiple genes and proteins involved in maneb and paraquat induced Parkinson's disease phenotype in mouse	DBT, New Delhi	Mahendra P Singh
Proteomics based approaches for the development of peripheral protein biomarker(s) and assessment of contribution of selected environmental chemicals in the onset of Parkinson's disease	ICMR, New Delhi	Mahendra P Singh
Statutory medical examination of employees engaged in painting and shot blasting operations in Tata Motors, Lucknow	Tata Motors Ltd., Lucknow	Mohan Das
Genome - wide detection of microbial communities involved in pollutants biodegradation using DNA microarray technology	DBT, New Delhi	N. Manickam
Development and validation of protocols for allergenicity evolution of GM foods.	DBT, New Delhi	Premendra D. Dwivedi
Safety evaluation of selected herbs used in Ayurveda and Siddha medicines	Deptt of Ayush, Min. of Health & Family Welfare, New Delhi	Poonam Kakkar
Heavy metal and persistent pesticide analysis in selected Indian medicinal plants – Phase II	ICMR, New Delhi	Poonam Kakkar
Subchronic toxicity study of Namkeen Herbal tea and medicated soft drink	DARL, DRDO, Pithoragarh	Rajendra B Raizada
Toxicological studies of herbal preparations	Dabur Res. Foundation, Sahibabad, Ghaziabad	Rajendra B Raizada
Toxicological evaluation of Polycleanse	Vikram Sarabhai Space Centre, ISRO,	Rajendra B Raizada

Externally funded projects



Toxicity evaluation of PAC powder (30% as Al ₂ O ₃) and liquid (9.5% Al ₂ O ₃)	Gujarat Alkalies & Chemicals Ltd., Distt. Vadodara	Rajendra B Raizada
Biosafety evaluation of the entomo-pathogenic bacterium	Vivekanand Parvatiya Krishi Anusandhan Sansthan, Almora	Rajendra B Raizada
Rapid EIA of the proposed 10,000 TCD sulfur free sugar plant in village Dhadha Bujung tehsil Hata, Distt-Kushinagar	New India Sugar Mills, Gorakhpur	Rajendra B Raizada
Annual contract for monitoring of air, water, soil, effluent quality and process stack emission	ITI Mankapur, Distt. Gonda	Subash K. Bhargava
Monitoring of environmental parameters of HIL-RPD	Hindalco Industries Ltd., Renuagar, Sonebhadra	Subash K. Bhargava
Assessment of hazardous waste incinerator stack emissions, effluent sludge and soil analysis at Ranbaxy Ltd., Paonta Sahib	State CST, HP, Kasumpti, Shimla	Subash K. Bhargava
Environmental parameters monitoring at GAIL, PATA	GAIL (India) Ltd., PATA Distt. Auraiya	Subash K. Bhargava
Acute-oral toxicity of Cleanfloc-1018	Deioners Speciality Chemicals, Delhi	Vinod P. Sharma
Suitability of GRP pipe for potability of water	Thermoset Poly Products (I) Pvt. Ltd., Navi, Mumbai	Vinod P. Sharma
Long term study on packaging of wheat and rice in PP/HDPE bags	Indian Grain Storage Management & Research Institute, Hapur	Vinod P. Sharma
Antioxidant potential of black tea on prostate cancer	National Tea Research Foundation, Kolkatta	Yogeshwer Shukla
Flowcytometric and cytogenetic analysis of cancer cervix	ICMR, New Delhi	Yogeshwer Shukla
Potential of black tea and its constituents in reversal of multidrug resistance and as bio ehnacer in cancer chemoprevention	DBT, New Delhi	Yogeshwer Shukla
Cancer chemoprevention properties of resveratrol: a mechanistic approach.	ICMR, New Delhi	Yogeshwer Shukla



Research Council (2004-2006)

Prof. M.S. Valiathan
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Madhav Nagar, Manipal-576119

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Dr. Indrani Chandrasekharan Director (E) , Room No. 705, Ministry of Environment & Forests CGO Complex, Paryavaran Bhavan, Lodi Road, New Delhi-110 003	Member (Agency representative)
Dr. C.M. Gupta Director Industrial Toxicology Research Institute Lucknow	Member
Dr. O.P. Agarwal Head, RDPD Council of Scientific and Industrial Research New Delhi	DG's Nominee
Dr. D.K. Saxena Dy Director Industrial Toxicology Research Centre, Lucknow	Secretary



Industrial Toxicology Research Centre

Management Council (1.7.2005 to 30.6.2007)

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Dr. Rakesh Tuli Director NBRI, Lucknow	Member
Mr. B.D. Bhattacharji Sc. E-II & Head, RPBD ITRC, Lucknow	Member
Dr. Ashwani Kumar Scientist 'F' ITRC, Lucknow	Member
Dr. (Mrs) Poonam Kakkar Scientist E-II ITRC, Lucknow	Member
Dr. Rishi Shanker Scientist E-II ITRC, Lucknow	Member
Dr. M.P. Singh Scientist 'C' ITRC, Lucknow	Member
Shri B.K. Mishra F&AO ITRC, Lucknow	Member
Mr. Raj Kumar Upadhyay Assistant Engineer ITRC, Lucknow	Member
Mr. Tariq Qutubuddin COA, ITRC, Lucknow	Member Secretary

Management Council



Publications

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Chapters in Books

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2. D. Mohan and Kunwar P. Singh (2005). Competitive adsorption of several organics and heavy metals on activated carbon in water. In: Water Encyclopedia: Domestic, municipal, and industrial water supply and waste disposal. Eds. J. Lehr. J. Keeley, J. Lehr. T.B. Kingery III Wiley-Interscience
3. Yogeshwar Shukla, S.K. Pal, Annu Arora, Neetu Kalra and Y.K. Gupta. Beneficial health effects of black tea: Increasing evidences. Medicinal properties of Tea. Editors: B. Banerjee & T.C. Chaudhary, Oxford & Eivich Publishing Company Pvt. Ltd. 2005. pg. 49-73.
4. Yogeshwar Shukla, S.R. Shaw and Nihal Ahmed. Resveratrol as a radioprotective agent. Editors. D.B. Aggarwal & Shishir Shishodhia; Taylor & Francis Publications-2005. pg. 431-438.
5. Yogeshwar Shukla and Annu Arora. Antigenotoxic activity of tea. CABI 2006. protective effects of tea on human health (N.K. Jain, M. Siddiqui and Welsbergur), pg. 45-57.
6. Y. K. Gupta, Chitra Tripathi and Yogeshwar Shukla. Antidiabetic effects of tea and its constituents. CABI 2006, Protective effects of tea on human health (N.K. Jain, M. Siddiqui & Welsbergur), pg. 102-108.
7. Yogeshwar Shukla, Neetu Kalra and Y.K. Gupta. Hepatoprotective properties of tea. CABI 2006, protective effects of tea on human health. (N.K. Jain, M. Siddiqui & Welsbergur) pg. 120-130.
8. Ram Chandra and Sonal Chaturvedi (2005) Characterization and identification of numerically abundant bacteria isolated from distillery effluent contaminated site growing *Cyperus papyrus* Rhizosphere. Proceedings of Second International Conference on Plant Environmental Pollution (ICPEP-2) entitled Plant response to environmental stress. pp. 161-172.

Publications	Number
Research Papers	88
Book Chapters	8
Average Impact Factor	1.545



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Mr. Balkishan, Gr. II(3)

Mr. A.K. Pathak, Gr. II(3)

Mr. Parvez Ahmad Khan, Gr. II(2)

Mr. Umesh Chandra Srivastava, Gr. II(1)

Staff



Promotions

Sl. No.	Name	Present Group	Group Grade after Promotion	Due date of Promotion
1.	Dr. A.K. Agrawal	IV(4)	IV(5)	01.04.2003
2.	Dr. Shashi Dogra	IV(4)	IV(5)	01.02.2004
3.	Dr. (Mrs.) F.N. Jaffery	IV(1)	IV(2)	19.05.2003
4.	Dr. Altaf Husain Khan	IV(2)	IV(3)	19.01.2004
5.	Dr. A.K. Khanna	IV(2)	IV(3)	01.02.2004
6.	Dr. P.D. Dwivedi	IV(2)	IV(3)	10.08.2003
7.	Smt. Sushma Sharma	III(6)	III(7)	01.11.2004
8.	Sh. Saaduzzaman	III(6)	III(7)	01.02.2006
9.	Sh. Ashok Kumar	II(2)	II(3)	15.10.1999
10.	Sh. Nand Kishore	II(2)	II(3)	15.10.1999
11.	Sh. Abdul Aziz	II(3)	II(4)	01.01.2004
12.	Sh. A.K. Pathak	II(2)	II(3)	01.01.2004
13.	Smt. Mumtaz Jahan	II(2)	II(3)	01.01.2004
14.	Ms. Mona Hemrajani	II(2)	II(3)	01.01.2004
15.	Sh. Tajuddin Ahmad	II(2)	II(3)	01.06.2003
16.	Sh. Ajay Kumar	II(3)	II(4)	17.11.2004
17.	Sh. Fazlur Rahman	II(3)	II(4)	30.12.2004
18.	Sh. H.N. Roy	II(3)	II(4)	01.01.2005
19.	Sh. M.L. Kanojia	II(3)	II(4)	30.12.2004
20.	Sh. Ram Prasad	II(3)	II(4)	02.06.2004
21.	Sh. S.K. Shukla	II(3)	II(4)	30.12.2004
22.	Sh. Jagdish Prasad	I(3)	I(4)	27.09.2004
23.	Smt. Shanti Devi	I(3)	I(4)	07.11.2004
24.	Sh. R.K. Kanojia	II(3)	III(3)	26.12.2005
25.	Sh. Tariq Qutubuddin	COA	Sr. COA	07.08.2006

Staff



Superannuation

Name of staff	Date of superannuation
Mr. Ram Prasad	30.4.2005
Dr. M.M. Hussain	30.6.2005
Dr. (Mrs.) S. Dogra	30.6.2005
Dr. Mohd Waseem	30.6.2005
Dr. S.K. Hasan	31.7.2005
Dr. (Mrs). P.P. Kaul	31.8.2005
Mr. Zahid Husain	30.9.2005
Mr. Jagdish Ram	30.9.2005
Mr. Pyare Lal	31.10.2005
Mr. Fazlur Rahman	31.12.2005
Mr. S.D. Pandey	31.12.2005
Mr. Rajapati Prasad	31.1.2006
Mr. S.K. Shukla	28.2.2006
Mr. V.B. Singh	28.2.2006

Staff Strength

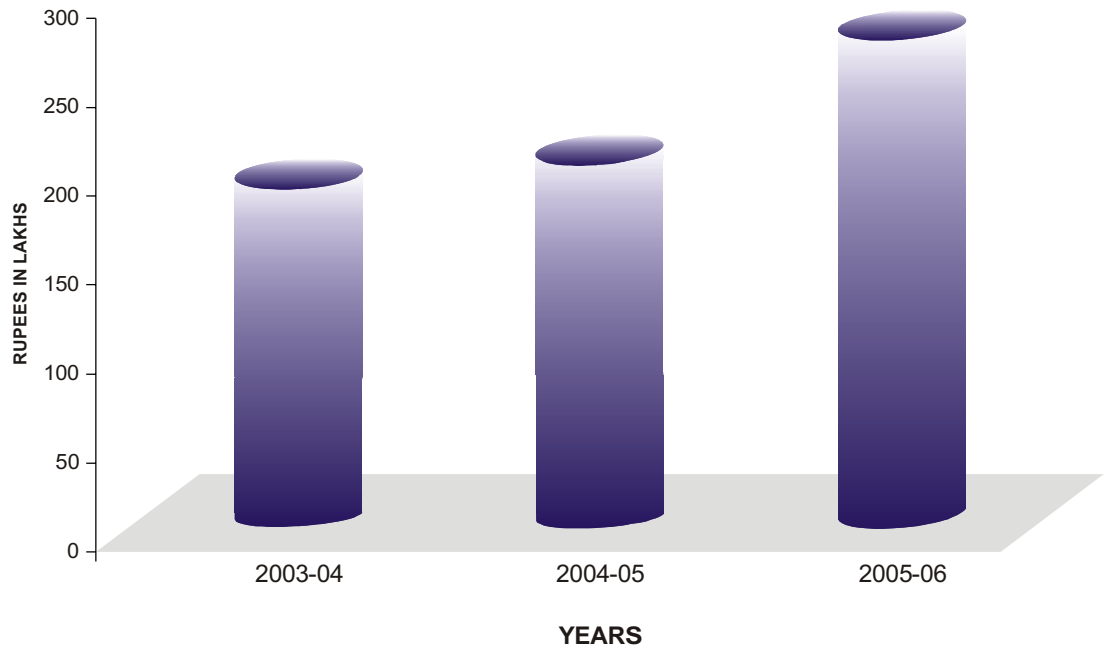
Scientific Group IV	75
Technical Group III	45
Technical Group II	56
Technical Group I	21
Administration A	04
Administration B	32
Administration C	23
Administration D	16

Total	272

Staff

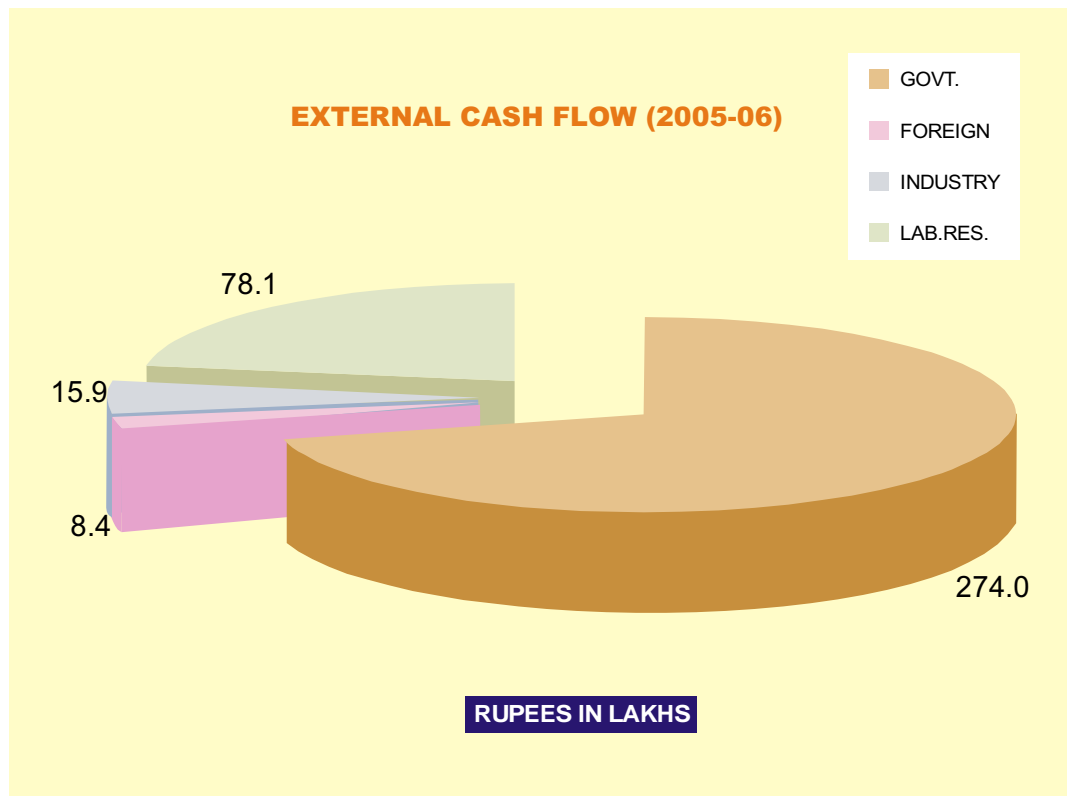


EXTERNAL CASH FLOW (2003-2006)



ECF

EXTERNAL CASH FLOW (2005-06)





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