BOOK OF ABSTRACTS
PROGRAMMES

6TH PAN AFRICAN ENVIRONMENTAL MUTAGEN SOCIETY CONFERENCE (PAEMS 2008)

Environmental Mutagens and Carcinogens:

Assessing, Managing and Reducing Risk

Cape Town International Convention Centre (CTICC)

Cape Town, South Africa

2 - 5 November 2008

FROM THE CHAIRPERSON

On behalf of the Organising Committee it gives me great pleasure to welcome you to the Sixth Conference of the Pan African Environmental Mutagen Society (PAEMS 2008) taking place at the Cape Town Convention Centre, Cape Town, South Africa, 2-5 November 2008.

The sixth Conference follows on the very successful scientific meetings which were held in different African countries since 1992. Meetings took place every 3-4 years in Egypt (two meetings), South Africa, Zimbabwe and Morocco. Currently the Officers of the PAEMS are Prof Wagida Anwar (Past President, Egypt), Prof Fatima-Zahra Squali (Former President, Morocco), Dr Hester Vismer (President, South Africa), Dr Alaoui Abdelilah (First Vice-President, Morocco), Dr Roland Ndip (Second Vice-President, South Africa), Prof Wentzel Gelderblom (Secretary General, South Africa), Dr Gordon Shephard (Treasurer, South Africa).

The PAEMS 2008 conference will provide scientists from Africa and the rest of the world with a unique opportunity to present their latest research findings, to foster collaboration and to establish long-term relations in science. A PAEMS General Meeting will be held to elect new officers and to discuss, amongst other aspects, the revised constitution of the society.

Participants from all over the world and especially the African continent, will present on topics concerning the conference, i.e. Air-, Water-, Food-borne (including mycotoxins and food safety issues) and Occupational Mutagens and Carcinogens, Antimutagenesis, Chemoprevention, Cancer, DNA Repair, Genomics, Genotoxic Risk Factors, Micro-organisms as Mutagens and Carcinogens, Molecular Mechanisms of Mutagenesis and Carcinogenesis, Radiation as a Mutagen and Carcinogen, Risk Assessment and Intervention Strategies at the meeting. Poster presentations will also form an important part of the programme.

Companies supporting our scientific endeavours, to further establish a wide range of beneficial industrial contacts, will exhibit during the conference.

Participants can also take part in two satellite courses, one on Scientific Writing before the conference and the other on Current Trends in Genetic Toxicity Assessment following the conference.

We are looking forward to a very full programme, which will bring together scientists from many disciplines, studying health and other aspects of environmental mutagens and carcinogens from many countries.

In addition to the stimulating scientific programme planned for PAEMS 2008, Cape Town is one of the most beautiful cities in the world and offers a spectacular range of scenic, artistic, historical, cultural and culinary attractions. We are looking forward to seeing you at PAEMS 2008 in Cape Town and to welcome you with the traditional hospitality of the rainbow nation of South Africa.

Dr Hester Vismer
Chairperson: PAEMS 2008

CONTENTS

ORGANISING COMMITTEE *

Dr Hester Vismer	*PAEMS 2008 Chairperson*
	PAEMS President-Elect
Prof Wentzel Gelderblom	*PAEMS Secretary General*
Dr Gordon Shephard	*PAEMS Treasurer*
	PAEMS 2008 Treasurer
Ms Xoliswa Kupiso	*Conference Secretary*
Ms Hester-Marie Burger	*Poster Sessions /*
	Pre- and Post Conference Tour Information
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Dr David Katerere	*Host to Guests*
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Dr Stefan Abel	*Audiovisual*
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Mrs Lorna Thomson	*Host to Guests*
	Pre- and Post Conference Tour Information

Support staff and Transport
Mr Theodore Leukes
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SCIENTIFIC COMMITTEE *

Dr Hester Vismer
Prof Wentzel Gelderblom
Dr Gordon Shephard
From the Medical Research Council, PROMEC Unit, Tygerberg, South Africa

SATELLITE COURSE 1 (SC1)

Scientific Writing

***Instructor*: Prof John Leslie**
Kansas State University, Manhattan, Kansas, USA

SATELLITE COURSE 2 (SC2)

Current Trends in Genetic Toxicity Assessment

***Co-ordinator:* Dr Jeanine Marnewick**
Cape Peninsula University of Technology, Cape Town, South Africa

PAEMS 2008 ADVISORY COMMITTEE

Dr Carl Albrecht
Cancer Association of South Africa, Cape Town, South Africa

Prof Wagida Anwar
Ain Shams Centre for Genetic Engineering and Biotechnology, Ain Shams University, Cairo, Egypt

Prof Zeno Apostolides
Department of Biochemistry, University of Pretoria, Pretoria, South Africa

Prof William Au
The University of Texas Medical Branch, Galveston, USA

Prof Lothar Bohm
Cape Town, South Africa

Dr David DeMarini
Environmental Carcinogenesis Division, US EPA, North Carolina, USA

Dr Azeddine Elhajouji
Novartis Pharma AG, Genetic Toxicology and Safety Pharmacology, Basel, Switzerland

Prof Mary Gulumian
Toxicology and Biochemistry Section, NIOH, Johannesburg, South Africa

Dr Julia Hasler
United Nations Educational, Scientific and Cultural Organization (UNESCO), Paris, France

Dr Kafui Kpodo
Food Research Institute, Accra, Ghana

Prof Michael Kew
Department of Medicine, University of Cape Town, Observatory, Cape Town, South Africa

Dr Rivka Kfir
Water Research Commission, Gezina, Pretoria, South Africa

Prof John Leslie
Department of Plant Pathology, Kansas State University, Manhattan, Kansas, USA

Prof Walter Marasas
Formerly from the Medical Research Council, PROMEC Unit, Tygerberg, South Africa

Prof David Miller
Department of Chemistry, Carleton University, Ottawa, Ontario, Canada

Prof Piet Steyn
Department of Chemistry, University of Stellenbosch, Matieland, South Africa

Prof Petro Terblanche
Technology and Innovation Directorate, Medical Research Council, Tygerberg, South Africa

Prof Chris Wild
Molecular Epidemiology Unit, Faculty of Medicine and Health, University of Leeds, United Kingdom

IMPORTANT CONTACTS AND ADDRESSES

Information/Conference Website

All information regarding the PAEMS 2008 Conference is also available at the following website: http://www.mrc.ac.za/promec/paems/ The abstracts and PAEMS Newsletter, covering the events, and selected photographs of the conference will also appear on this website in due course.

General Enquiries

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Payments

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Mutagen Societies

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CANSA

Cancer Association of South Africa

WRC

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PAEMS 2008 CONFERENCE PROGRAMME

Sunday, 2 November 2008

08:00 - 09:00 Registration Satellite Course 1 (SC1): Scientific Writing
Muffins and Coffee: CTICC, Roof Terrace

09:00 - 17:00 Satellite Course 1 (SC1): Scientific Writing **(full programme on page 23)**
Venue: CTICC Roof Terrace
Tea/Coffee Breaks and Lunch: CTICC Roof Terrace

15:30 - 18:00 Conference Registration (CTICC, Jasminum Conservatorium)
Loading Presentations (CTICC, Auditorium 2)
Put Posters up (Strelitzia Conservatorium)

18:00 - 20:00 Welcome Reception (Venue: CTICC, Jasminum Conservatorium)

Monday, 3 November 2008

07:30 - 08:00 Conference Registration (Muffins and Coffee), Loading Presentations, Put Posters up (CTICC, Strelitzia Restaurant Area, Auditorium 2 and Jasminum Conservatorium)

SESSION 1 ***Chairpersons: Dr Hester Vismer and Prof Chris Wild***

08:00 - 08:30 **Dr Hester Vismer**
Chairperson PAEMS 2008
Opening and Welcome

08:30 - 09:00 **O1 - Prof Chris Wild** (Plenary Address)
Molecular Epidemiology Unit, Faculty of Medicine and Health, University of Leeds, Leeds, United Kingdom
Mycotoxins and disease: the importance to health in Africa.

09:00 - 09:30 **O2 - Dr Carl Albrecht** (Invited Lecture)
Cancer Association of South Africa, Cape Town, South Africa
How important are man-made molecules as a cause of cancer?

09:30 - 09:50 **O3 - Dr Wolfgang Muster, A Brigo**
F. Hoffmann-La Roche Ltd., Non-Clinical Drug Safety, Basel, Switzerland
Computational toxicology in drug development and early hazard identification.

09:50 - 10:20 **O4** - **Prof Iqbal Parker, D-P Li** (Plenary Address)
International Centre for Genetic Engineering and Biotechnology, ICGEB (Cape Town), University of Cape Town, Observatory, Cape Town, South Africa
Gene-Environment Interactions in Oesophageal Cancer in South Africa.

10:20 - 11:00 Break, Exhibitor and Poster Attended Session 1 (P1 - P7)

SESSION 2 ***Chairpersons:*** ***Dr Jeanine Marnewick and Prof Volker Mersch-Sundermann***

11:00 - 11:30 **O5** - **Prof Theeshan Bahorun** (Plenary Address)
Department of Biosciences, Faculty of Science, University of Mauritius, Réduit, Republic of Mauritius
Cancer chemoprevention: alternative strategies.

11:30 - 12:00 **O6** - **Prof Volker Mersch-Sundermann** (Invited Lecture)
University Medical Center Freiburg, Freiburg, Germany
Modulation of cell cycle regulation and apoptosis caused by sulfur containing food ingredients: molecular mechanisms of chemoprevention caused by isothiocyanates and allyl sulfides.

12:00 - 12:20 **O7** - **Dr Lyndy McGaw, EE Elgorashi, VP Bagla, TA Mokoka, JN Eloff**
Phytomedicine Programme, Department of Paraclinical Sciences, Faculty of Veterinary Science, University of Pretoria, Onderstepoort, South Africa
Genotoxicity, cytotoxicity and biological activity investigation of South African plants used in ethnoveterinary medicine.

12:20 - 12:40 **O8** - **Dr Jeanine Marnewick**[1], **WCA Gelderblom**[2]
[1]*Oxidative Stress Research Unit, Faculty of Health and Wellness Sciences, Cape Peninsula University of Technology, Cape Town, South Africa.* [2]*PROMEC Unit, Medical Research Council, Tygerberg, South Africa*
Rooibos and honeybush – unique South African herbal beverages with chemopreventive activities.

12:40 - 13:30 Lunch, Exhibitor and Poster Attended Session 2 (P8 - P14)

13:30 - 14:00 PAEMS 2008 Group Photograph (Strelitzia Restaurant)

SESSION 3 ***Chairperson: Dr David DeMarini***

14:00 - 14:30 **O9 - Dr David DeMarini** (Plenary Address)
Environmental Carcinogenesis Division, US EPA, North Carolina, USA
Mutagenicity and mutation spectra of disinfection by-products of drinking water.

14:30 - 14:50 **O10 - Dr Virginie Faucet-Marquis[1], L Delgado[1], M DeMeo[2], A Dauta[3], C Albasi[1], A Pfohl-Leszkowicz[1]**
[1]Laboratoire de Genie Chimique, Department of BioSyM, Toulouse, France. [2]Faculté de Pharmacie, Marseille, France. [3]Universié Paul Sabatier, Toulouse, France
Validation of ecotoxicity tests to evaluate the genotoxicity of hospital water waste.

14:50 - 15:10 **O11 - Dr Benedicta Oben[1], PM Oben[1], J-F Akoachere[2], CM Anu[3], P Tebid[4], E Tabi[1]**
[1]Fisheries and Hydrobiology Unit, Department Plant and Animal Sciences, University of Buea, Cameroon. [2]Department Biochemistry and Microbiology, University of Buea, Cameroon. [3]Chair of Freshwater Conservation, Brandenberg Technical University, Cottbus, Germany. [4]Department Medical Microbiology, Faculty of Health Sciences, University of Buea, Cameroon
Tumour–promoting hepatotoxins in the African aquatic environment.

15:10 - 15:40 **O12 - Annatjie Moolman** (Plenary Address)
Water Research Commission, Gezina, Pretoria, South Africa
Water and health-related research.

15:40 - 16:10 Break, Exhibitor and Poster Attended Session 3 (P15 - P20)P

SESSION 4 ***Chairperson: Prof Wentzel Gelderblom***

16:10 - 16:40 **O13 - Prof Roland Ndip** (Invited Lecture)
Department of Biochemistry and Microbiology, University of Fort Hare, Alice, South Africa
Potent *in vitro* antimicrobial activity of two Cameroonian medicinal plants on clinical isolates of *Helicobacter pylori*.

16:40 - 17:00 **O14 - Dr Natalia Vorobyeva[1], AN Osipov[1], EYu Lizunova[1], OV Boeva[1], VK Bozhenko[2]**
[1]NN Semenov Institute of Chemical Physics, Russian Academy of Sciences, Moscow, Russia. [2]Russian Research Center for Roentgenoradiology, Moscow, Russia
DNA double-strand breaks and their repair in blood lymphocytes of prostate cancer patients.

Free Evening

Tuesday, 4 November 2008

08:00 - 08:30 Conference Registration (Muffins and Coffee), Loading Presentations

SESSION 5 ***Chairpersons:*** ***Prof Michael Kew***
Prof Annie Pfohl-Leszkowicz

08:30 - 09:00 **O15 -** **Prof Michael Kew** (Plenary Address)
Department of Medicine, University of Cape Town, Observatory, Cape Town, South Africa
Interaction between aflatoxin B_1 and other risk factors in hepatocarcinogenesis.

09:00 - 09:20 **O16 -** **Dr Gordon Shephard**
PROMEC Unit, Medical Research Council, Cape Town, South Africa
Mycotoxin problems in the food chain: a comparison of developing and developed worlds.

09:20 - 09:40 **O17 -** **Prof Annie Pfohl-Leszkowicz**[1], **M Tozlovanu**[1], **M Baker**[2], **V Faucet-Marquis**[1], **W Gabryelski**[2], **P Mantle**[3], **RA Manderville**[2]
[1]Laboratoire de Génie Chimique, Department BioSyM, Auzeville-Tolosane, France. [2]Department of Chemistry, University of Guelph, Guelph, Ontario, Canada. [3]Imperial College, London, United Kingdom
Overview on molecular mechanism involved in ochratoxin A nephrotoxicity and carcinogenicity.

09:40 - 10:00 **O18 -** **Dr Samir Abbès**[1], **J Ben Salah-Abbès**[1], **Z Ouanes**[2], **MA Abdel-Wahhab**[3], **H Bacha**[2], **R Oueslati**[1]
[1]Laboratoy of Environmental Immunology, Microbiology and Cancerology, Faculty of Sciences Bizerte, Tunisia. [2]Laboratory of Research on Biologically Compatible Compounds, Faculty of Dentistry, Monastir, Tunisia. [3]Food Toxicology and Contaminants Department, National Research Centre, Dokki, Cairo, Egypt
Genotoxicity and clastogenicity of zearalenone mycotoxin: preventive role of aluminosilicate clay.

10:00 - 10:30 Break, Exhibitor and Poster Attended Session 4 (P21 - 26)

SESSION 6 ***Chairperson: Prof Lothar Bohm and Prof Yogi Naik***

10:30 - 11:00 **O19 -** **Prof Yogi Naik** (Invited lecture)
Department of Environmental Science and Health, National University of Science and Technology, Bulawayo, Zimbabwe
The impact of genotoxic pesticides on the environment.

11:00 - 11:30 **O20 -** **Prof Lothar Bohm** (Invited Lecture)
Faculty of Health Sciences, University of Stellenbosch, Tygerberg, South Africa
Neem toxins in agriculture and medicine.

11:30 - 11:50 **O21 -** **Dr Asita Asita, R Makhalemele**
Department of Biology, National University of Lesotho, Maseru, Lesotho
Assessment of pesticides for cytotoxic and genotoxic effects in the onion root tip assay.

11:50 - 12:30 **Presentation by Applied Biosystems, South Africa**
Low level quantification, identification, and characterization of carcinogenic substances in daily food and environmental samples using LC/MS/MS with library searching capabilities.

12:30 - 13:30 **Lunch, Exhibitors and Poster Attended Session 5 (P27 - P32)**

13:30 - 15:30 **PAEMS General Meeting (Auditorium 2)**

15:30 - 16:00 **Break, Exhibitor and Poster Attended Session 6 (P33 - P38)**

18:00 for 18:30 - 22:30 **Conference Dinner and Show (Dress: Smart casual)**

Venue: BMW Pavilion, V&A Waterfront, Cape Town

Buses will leave from the CTICC at 17:30

Wednesday, 5 November 2008

08:00 - 08:30 Muffins and Coffee, Loading Presentations

SESSION 7 ***Chairpersons:*** ***Prof Mary Gulumian and Prof Andreyan Osipov***

08:30 - 09:00 **O22 -** **Prof Mary Gulumian** (Plenary Address)
Toxicology and Biochemistry Section, NIOH, Johannesburg, South Africa
Toxicity and genotoxicity of particles in the environment and in occupational settings.

09:00 - 09:20 **O23 -** **Dr Sohier Korraa**[1], **S Abdel Meguid**[2], **R Khalil**[3], **A Hussein**[4], **N Abdel Khalek**[4]

[1]Department Health Radiation Research, National Center for Radiation Research and Technology. [2]Department Zoology, Girl's College for Arts and Education, Ain Shams University. [3]Department Microbiology, Faculty of Medicine, Ain Shams University. [4]Department Radiological Safety, National Center for Nuclear Safety and Radiation Protection, Atomic Energy Authority, Cairo, Egypt

Apoptosis and mononuclear cell surface markers expression among persons occupationally exposed to X-Rays in Cardiac Catheterization Units.

09:20 - 09:40 **O24 -** **Prof Andreyan Osipov**

NN Semenov Institute of Chemical Physics, Russian Academy of Sciences, Moscow, Russia

Molecular and cellular effects in mice chronically exposed to low dose-rate gamma-radiation.

09:40 - 10:00 **O25 -** **Dr Badal Bhattacharya**[1], **N Biswas**[1], **S Pal**[2], **R Nandi**[2]

[1]Department of Chemistry, Vinayaka Missions University, Tamilnadu, India. [2]Institute of Ecotoxicology and Environmental Sciences, Kolkata, India

Risk assessment from heavy metals accumulation in blood on human populations in urban industrial environment.

10:00 - 10:20 **O26 -** **Sean Doel**

WSP Environment and Energy (Pty) Ltd, Cape Town, South Africa

Formaldehyde Toxicology – Occupational versus Environmental HAP?

10:20 - 11:00 Break, Exhibitor and Poster Attended Session 7 (P39 - P44)

SESSION 8 ***Chairpersons:*** ***Dr Gordon Shephard and Prof John Leslie***

11:00 - 11:30 **O27 -** **Prof Wentzel Gelderblom** (Plenary Address)

PROMEC Unit, Medical Research Council, Cape Town, South Africa

Perspectives on risk assessment paradigms of genotoxic and non-genotoxic carcinogenic mycotoxins.

11:30 - 11:50 **O28 -** **Dr Hussaini A Makun**[1], **TA Gbodi**[1], **HO Akanya**[1], **EA Salako**[2], **GH Ogbadu**[3]

[1]Department of Biochemistry, Federal University of Technology, Minna, Nigeria. [2]Department of Crop Production, Federal University of Technology, Minna, Nigeria. [3]Sheda Science and Technology Complex, Federal Ministry of Science and Technology, Abuja, Nigeria

Studies of mycoflora and mycotoxins contaminating guinea corn and rice in Niger State, Nigeria.

11:50 - 12:00 **O29 -** **Dr Hester Vismer, WFO Marasas**
PROMEC Unit, Medical Research Council, Cape Town, South Africa
Mycotoxins: aspects concerning commercial, organic and genetically modified foods.

12:00 - 12:30 **O30 -** **Prof John Leslie** (Invited Lecture)
Department of Plant Pathology, Kansas State University, Manhattan, Kansas, USA
Genetic variation in mycotoxin-producing species of *Fusarium*.

12:30 - 13:30 Lunch, Exhibitors and Poster Attended Session 8 (P44 - P50)

SESSION 9 ***Chairpersons:*** ***Prof Walter Marasas and Prof Wagida Anwar***

13:30 - 13:50 PAEMS Honorary Membership Award Ceremony

13:50 - 14:20 **O31 -** **Prof Wagida Anwar** (Plenary Address)
Department of Community, Environmental and Occupational Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt
Environmental mutagens and possibilities for prevention.

14:20 - 14:40 **O32 -** **Prof Wojciech Piekoszewski[1], E Florek[2], GH Bręborowicz[3], W Lechowicz[4], MK Kornacka[5], M Kulza[2]**
[1]Department of Analytical Chemistry, Jagiellonian University Krakow, Poland. [2]Laboratory of Environmental Research, Department of Toxicology University of Medical Sciences, Poznan, Poland. [3]Perinatology and Gynaecology Clinic, University of Medical Sciences, Poznan, Poland. [4]Institute of Forensic Research, Krakow, Poland. [4]Neonatology Clinic, University of Medical Sciences, Warsaw, Poland
Exposure of pregnant women on tobacco specific carcinogens.

14:40 - 15:00 **O33 -** **Prof Janusz Blasiak[1], T Poplawski[1], K Wozniak[1], E Pawlowska[2], J Szczepanska[2]**
[1]Department of Molecular Genetics, University of Lodz, Lodz, Poland. [2]Department of Developmental Dentistry, Medical University of Lodz, Lodz, Poland
Genotoxicity of dental materials.

15:00 - 15:20 **O34 -** **Dr Kareemah Gamieldien[1], JD Van der Merwe[2], E Joubert[3], WCA Gelderblom[1]**
[1]PROMEC Unit, Medical Research Council, Tygerberg, South Africa. [2]Department of Food Science, University of Stellenbosch, Stellenbosch, South Africa. [3]ARC-Infruitec-Nietvoorbij, Stellenbosch, South Africa
Possible mechanisms involved in the anti-cancer properties of unfermented rooibos (*Aspalathus linearis*) and honeybush (*Cyclopia* spp) herbal teas.

15:20 - 15:40 **O35 -** **Prof Okezie Aruomo**
Department of Pharmaceutical and Biomedical Sciences, Touro College of Pharmacy, New York, USA
Pharmacoeconomics of cancer treatment and development of adjunct therapy.

15:40 - 16:00 Closing and Tea / Coffee

Thursday, 6 November 2008

08:30 - 09:00 Registration Satellite Course 2 (SC2): Current Trends in Genetic Toxicity Assessment
Muffins and Coffee: Strelitzia Conservatorium

09:00 - 17:00 Satellite Course 2 (SC2) - Current Trends in Genetic Toxicity Assessment
(See full programme on page 24)
Venue: CTICC, Auditorium 2
Tea/Coffee Breaks and Lunch: Strelitzia Conservatorium

PROGRAMME - SATELLITE COURSE 1 (SC1)

Scientific Writing

Instructor: Prof John Leslie
Kansas State University, Kansas, USA
Venue: CTICC, Roof Terrace

08:30	-	09:00	**Registration CTICC Roof Terrace** **Muffins and Coffee**
09:00	-	09:15	**Prof Walter Marasas** Welcome and Opening
09:15	-	10:30	**Prof John Leslie** Organization, Planning and Presentations
10:30	**-**	**11:00**	**Coffee / Tea Break**
11:00	-	13:00	Content and Preparation of a Scientific Paper
13:00	**-**	**14:00**	**Lunch**
14:00	-	15:30	Editors, Reviewers and Manuscript submission
15:30	**-**	**16:00**	**Coffee / Tea Break**
16:00	-	16:45	Practising the Preaching - Revise an Abstract
16:45	-	17:00	Summary, Evaluation and Closing Remarks

PROGRAMME - SATELLITE COURSE 2 (SC2)
Current Trends in Genetic Toxicity Assessment

Coordinator: Dr Jeanine Marnewick
Oxidative Stress Research Centre, Cape Peninsula University of Technology, Cape Town, South Africa
Venue: Auditorium 2, CTICC

08:00 - 08:45 **Registration CTICC, Strelitzia Restaurant Area**
Muffins and Coffee

08:45 - 09:00 **Dr Jeanine Marnewick**
Oxidative Stress Research Centre, Cape Peninsula University of Technology, Cape Town, South Africa
Opening

09:00 - 10:00 **Dr David DeMarini**
US Environmental Protection Agency, North Carolina, USA
Mutagenesis (AMES, COMET, chromosome aberrations, micronuclei).

10:00 - 10:30 Coffee / Tea break

10:30 - 11:30 **Dr David DeMarini**
US Environmental Protection Agency, North Carolina, USA
Genetic biomarkers and molecular epidemiology.

11:30 - 12:30 **Prof Wagida Anwar**
Professor of Community, Environmental and Occupational Medicine, Faculty of Medicine, Ain Shams University, Ain Shams University, Cairo, Egypt
Classical and molecular cytogenetics of human chromosomes.

12:30 - 13:30 Lunch

13:30 - 14:30 **Prof Volker Mersch-Sundermann**
University Medical Center, University of Freiburg, Freiburg, Germany
Fine and ultrafine particles outdoors and indoors: knowledge and hypothesis of their contribution to mutagenicity and carcinogenicity.

14:30 - 15:30 **Dr David DeMarini**
US Environmental Protection Agency, North Carolina, USA
Chemical Carcinogenesis.

15:30 - 16:00 Additional questions

16:00 Closing and Coffee / Tea

HEALTHY LIFESTYLE CHOICES WILL KEEP YOU FIT FOR LIFE

Cancer is the major cause of death worldwide and affects all genders, ages and race groups. In South Africa 1 in 4 people will be affected by cancer at some stage in their lifetime. The good news is that there is a lot you can do to minimise your chances of getting cancer. Eating a healthy diet, exercising regularly, not smoking, being SunSmart, regular self-examination and testing by health professionals can significantly reduce your chances of becoming a cancer statistic.

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Cancer is potentially the most preventable and most curable of the major life-threatening diseases, if detected and treated early on. Monthly self-examination and regular medical check-ups by health professionals are essential for both men and women. Know your body. If you detect any abnormality, see your doctor without delay. Early detection is the key to effective treatment and survival.

Make small lifestyle changes now that can significantly increase your chances of living a long, healthy life. It's the smart thing to do.

For more advice on how you can become Cancer Smart, call CANSA toll-free on 0800 22 66 22 or visit www.cansa.org.za

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ORAL PRESENTATIONS

O1 (Plenary Address)
MYCOTOXINS AND DISEASE: THE IMPORTANCE TO HUMAN HEALTH IN AFRICA

CP Wild

Molecular Epidemiology Unit, Leeds Institute of Genetics, Health and Therapeutics, University of Leeds, Leeds, UK
Email: c.p.wild@leeds.ac.uk

The majority of the world population is exposed to mycotoxins through consumption of contaminated food. Mycotoxins of major concern to human health include aflatoxins, fumonisins, tricothecenes (deoxynivalenol), ochratoxin A and zearalenone. In the economically wealthier parts of the world exposure is controlled or minimised by regulation and surveillance. However, in many geographic regions, including Africa, such protection is lacking. Furthermore a balance often has to be found between food security and food sufficiency. Accurate assessment of human exposure to mycotoxins is a key to assessing the associated human health consequences. Biomarkers of human exposure to aflatoxins, fumonisins and deoxynivalenol have been developed and are in various stages of validation and application to population studies. In West Africa there is a high prevalence and level of dietary exposure to aflatoxins beginning early in life and exposure has been associated with increased liver cancer risk in interaction with chronic hepatitis B virus (HBV) infection. In addition, aflatoxins cause growth faltering and immune suppression in animals and associations between exposure, impaired growth and immunity were observed in young children (Gong et al., Env. Health Per. 112:1334-1338, 2004; Turner et al. Env. Health Per. 111:217-220, 2003). Growth and immune impairment could be critical in pre-disposing children to the infections, including HBV, that result in the high morbidity and mortality in these populations. Intervention strategies to reduce exposure have been explored. In a simple post-harvest intervention in Guinea, aflatoxin contamination of the groundnut crop was reduced, resulting in a >50% reduction in exposure (Turner et al., Lancet 365: 1950-1956, 2005). Current research involves application of urinary biomarkers to study exposure and intervention strategies against fumonisin (Gong et al., Cancer Epi. Bio. Prev. 17: 688-694, 2008) and deoxynivalenol (Turner et al., Env. Health Per. 116: 21-25, 2008) in different populations.

O2 (Invited Lecture)
HOW IMPORTANT ARE MAN-MADE MOLECULES AS A CAUSE OF CANCER?

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Today there is worldwide consensus that cancer is a disease that is mainly caused by environmental factors. This is one of the most hopeful messages from cancer research because it means that very few cancers (less than 10%) are predestined to occur by virtue of inherited genetic malfunction. Rather, in about 90% of cases, cancers are triggered due to one or more environmental factors causing critical damage to the genetic material. While much has been done to prevent cancer by counteracting smoking and vaccinating against oncogenic viruses, very little has been done to decrease the carcinogenic risk of certain man-made chemicals, many of which are in the environment in close and constant proximity to people living mainly in industrialised cities. Furthermore the total cancer risk involving smoking, infections, diet contamination, obesity and UV light is estimated by CANSA to be in the order of 60-70%. If this is so it means that 30-40% of the cancer risk remains unaccounted for. It is quite possible that some of the 100 000 man-made chemicals in the environment could largely fill this gap. This could have an important bearing on the fact that the carcinogens causing breast and prostate cancers, which amount to 25% of all cancer diagnoses in the U.S. and are now reaching epidemic proportions and yet remain unknown at present. In other words, this argument raises the ominous possibility that certain man-made chemicals in our immediate environment could be causing breast and prostate cancers or at least making a major contribution to the carcinogenic processes involved. Recently Rudel et al. of the Silent Spring Institute listed 216 man-made chemicals that have been associated with increases in mammary tumours in test animals (*Cancer* 2007; 109, 2635). In contrast, Michels et al. could not find a strong diet – breast cancer link except for obesity and alcohol intake (*Cancer* 2007; 109, 2712). This scenario is explored in the light of the current international controversy concerning the possible role of bisphenol A which is released from polycarbonate baby bottles possibly causing epigenetic effects in breast and prostate tissue of infants.

O3

COMPUTATIONAL TOXICOLOGY IN DRUG DEVELOPMENT AND EARLY HAZARD IDENTIFICATION

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Computational toxicology (*in silico* toxicity prediction) is widely used in the pharmaceutical industry with the aim of optimizing the efficacy and, at the same time, the pharmacokinetics and toxicological properties of molecules in early drug development. Furthermore, these systems are gaining more and more importance with regards to early hazard identification for a variety of chemicals such as impurities in drug products or pollutants, for which only limited or no toxicological information is available. It has been shown that commercial as well as proprietary systems can be successfully applied in the pharmaceutical industry. *In silico* toxicity prediction methods can be roughly classified into so-called xpert systems and ata driven systems. Expert systems try to formalize the knowledge of human experts who assessed the toxicity of compounds, whereas data driven systems require significant amounts of experimental data to derive predictive models. Expert systems are intuitively more appealing because they promise an easy access to toxicological knowledge. Although some of these programs provide a specificity greater than 80%, all of them suffer from a moderate sensitivity, which is usually in the range of 50%. It is therefore mandatory to customize and continuously update the systems with in-house knowledge in order to maximize the prediction performance. Over the past years, data driven structure-activity relationships have earned special prominence in the effort of creating prediction models for mutagenic properties and chemical carcinogenicity. Beside correct predictions, an important task for data driven systems is the identification of chemical features that are relevant for the observed toxicological effect. This presentation will outline general considerations on commercial systems and proprietary (quantitative) structure-activity relationships ((Q)SAR) models applied to toxicology and, in addition, describe some examples illustrating how computational tools can be advantageously deployed in the early drug development process and hazard identification.

O4 (Plenary Address)
GENE-ENVIRONMENT INTERACTIONS IN OESOPHAGEAL CANCER IN SOUTH AFRICA

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The tremendous variation in the observed susceptibility to complex diseases such as cancer may result as a consequence of an imbalance in the activities of the enzymes involved in the metabolism, conjugation and transport of environmental mutagens and carcinogens. In this study we have investigated the functional polymorphisms in some of the phase I enzymes (CYP3A5, CYP2E1, Alcohol Dehydrogenase 2 and Aldehyde Dehydrogenase.) and phase II enzymes (GSTM1, GSTT1, GST P1 and SULT1A1) in oesophageal cancer patients and controls. A variety of environmental and behavioural factors were identified that were significantly associated with increased risk of developing oesophageal cancer. These factors included the exposure to smoke during the burning of wood or charcoal for cooking and heating purposes (AOR 15.2; $p<0.001$), the consumption of home brewed beer (AOR 6.97; $p< 0.0001$), a combination of tobacco smoking and alcohol consumption (AOR 5.18; $p<0.0005$) and an early age of starting smoking and alcohol consumption (AOR 12.0; $p<0.001$). The homozygous mutant genotypes in the SULT1A1, GSTT1 and GSTP1 genes were associated with increased risk for oesophageal cancer while the homozygous mutant genotype of CYP3A5 was associated with reduced risk. There is a clear association between the different alleles of the various biotransformation enzyme genes and environmental factors investigated in this study. We have also traced the various genetic polymorphisms in various African populations and show a clear segregation of the various genotypes.

O5 (Plenary Address)
CANCER CHEMOPREVENTION: ALTERNATIVE STRATEGIES

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The rising incidence of health related problems in both developing and developed countries has prompted research into the development of potent chemopreventive drugs as an alternative approach to manage disease progression. Many efforts are being invested towards dietary and medicinal plant extracts as prophylactics. The World Health Organisation has initiated global efforts on traditional medicine to increase research on the untapped plant resources that would hopefully identify putative bioactive compounds/extracts with therapeutic relevance. Medicinal plants are an important element of indigenous medical systems of Mauritius with at least 460 known medicinal plants. Several endemic plant species have also been described in the traditional pharmacopoeia and many of their uses are deeply anchored in the Mauritian culture. Literature data strongly suggest that the therapeutic potential of medicinal plant lies in the presence of secondary metabolites including alkaloids, terpenoids and polyphenols. Plant polyphenols, in particular have been greatly recognized for their biological and therapeutic activities including antimicrobial, anti-inflammatory, vasodilatory, expectorant, anti-mutagenic and more partivularly antioxidant properties. The regulatory activity of phenolic antioxidants on cell signal transduction pathways mainly the MAPK, JNK kinases, transcription factors mainly NF-κB, c-Jun, c-myc, c-fos have been highly emphasized as a strategy for reducing the incidence of diseases induced by reactive oxygen and nitrogen species. Bearing this in mind, our group have been working on the screening and analyses of Mauritian endemics/medicinal plants with particular emphasis on the phytophenolic and antioxidant profiles that would provide a molecular basis for their applications. The complex phytophenolic profiles and antioxidant propensities (multi-method analysis systems) of plants from the Rubiaceae, Myrtaceae, Ebanaceae, Celastraceae, Erythroxylaceae and Sterculaceae family were assayed. Their genotoxic and antigenotoxic effects were evaluated. Mauritian endemic plant extracts from the Myrtaceae and Rubiaceae family significantly inhibited cell proliferation of MDAMB 231 and MCF-7 human breast cancer cell lines. In addition plant extracts from the Celastraceae and Myrtaceae family restored gap junction intercellular communication (GJIC), an interesting target of chemoprevention. The rising incidence of cancer worldwide suggests an imperative need to develop alternative approach to manage the disease progression and delineating the mechanism underlying the anti-proliferative effect of the Mauritian endemic plant extracts will provide further details on their chemopreventive nature.

O6 (Invited Lecture)

MODULATION OF CELL CYCLE REGULATION AND APOPTOSIS CAUSED BY SULPHUR CONTAINING FOOD INGREDIENTS: MOLECULAR MECHANISMS OF CHEMOPREVENTION CAUSED BY ISOTHIOCYANATES AND ALLYL SULFIDES

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As shown by *in vivo* and *in vitro* studies, numerous sulphur containing food ingredients are chemopreventive compounds that possess both potent protective and therapeutic properties against carcinogenesis in animals and human cells. Various molecular mechanisms are discussed as being responsible for these chemopreventive actions, e.g. induction or inhibition of xenobiotics metabolizing phase I/II enzymes and phase III transporters, enhancement of DNA repair, anti-inflammatory effects and influences on cell cycle regulation and/or apoptosis induction. For instance, as shown for diallyl disulfide (DADS) isolated from garlic, caspase-mediated proapoptic mechanisms induced by reactive oxygen species (ROS) play an important role via regulation of bcl-2 family proteins and changes in the mitochondrial membrane potential in human lung cell carcinoma cells. Similar ROS-mediated effects on apoptosis were found in primary ovarian carcinoma cells after exposure to isothiocyanates (ITCs). In both cases, cell death induction could be blocked by antioxidants like N-acetyl-cysteine. In contrast, the production of ROS does not seem to play an important role in 4-methylthiobutyl Isothiocyanate (MTBITC)-mediated proliferation inhibition, leading to G2/M arrest and apoptosis induction in human hepatoma cells. In these cells, a strong induction of p53 family members, followed by hTERT suppression and reduction in telomerase enzyme activity was observed. These examples roughly display the dependency of the executed chemopreventive effect on the investigated cell type, experimental design, and, more importantly, on the tested sulphuric compound. On the basis of present knowledge, various or partly contradictory hypotheses can be generated about the underlying mechanisms of chemoprevention mediated by sulphur containing food ingredients. Even though knowledge has grown extensively during the last decade, we are a long way from understanding the meaningfulness of the cellular processes in the context of mutagenesis and carcinogenesis.

O7

GENOTOXICITY, CYTOTOXICITY AND BIOLOGICAL ACTIVITY INVESTIGATION OF SOUTH AFRICAN PLANTS USED IN ETHNOVETERINARY MEDICINE

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Ethnoveterinary medicine (EVM) is an integral aspect of livestock health care in rural parts of South Africa. Extracts of sixteen plants popularly used to treat a wide variety of ailments in domestic animals, from stomach diseases to wounds and infections, were screened for genotoxicity in the Ames test and cytotoxicity against several cell lines. Antibacterial, antifungal and antiviral activity against a panel of microorganisms implicated in causing animal diseases was evaluated. None of the extracts showed mutagenic effects against *Salmonella typhimurium* strains TA98 and TA100 without metabolic activation. Most of the extracts (70%) were not cytotoxic above a concentration of 0.1 mg/ml. However, *Pittosporum viridiflorum* showed strong cytotoxicity comparable to the reference compound, berberine, and *Ricinus communis* and *Combretum caffrum* were moderately cytotoxic in a modified tetrazolium bromide (MTT) assay. These results correlated well with other methods of cytotoxicity determination, including visual observations of the cell monolayers after incubation with plant extracts. Antibacterial minimum inhibitory concentrations (MIC) reached as low as 0.04 mg/ml, and 62.5% of extracts inhibited the Gram-positive bacteria. Average antifungal MICs were 0.56 and 0.59 mg/ml against *Cryptococcus neoformans* and *Candida albicans* respectively. Some extracts showed simultaneous antimicrobial activity and cytotoxicity while others had higher selective activity. Extracts of a quarter of the species, *Combretum caffrum, Ricinus communis*, *Schotia brachypetala* and *Sclerocarya birrea*, showed promising virucidal activity against the sensitive feline herpesvirus type 1 (3 log reduction in viral cytopathic effect at non-cytotoxic concentrations). Further work is focusing on isolating and characterizing active constituents from promising plant species. *Acknowledgements: National Research Foundation for funding, Prof WCA Gelderblom and colleagues of the MRC, PROMEC Unit, for their help with the Ames test.*

O8

ROOIBOS AND HONEYBUSH – UNIQUE SOUTH AFRICAN HERBAL BEVERAGES WITH CHEMOPREVENTIVE ACTIVITIES

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Theoretically cancer is a preventable disease, but in practice, prevention by avoiding exposure can not be achieved and additional approaches are needed. One such approach is an increased intake of chemopreventive compounds that is expected to interfere with the initiation, promotion or progression of carcinogenesis. The past ten years yielded important information from across the world concerning the positive impact of non-nutritive components of plant origin, like teas, on human health. The two most common South African plants used for the preparation of traditional health beverages are rooibos (*Aspalathus linearis*) and honeybush (*Cyclopia* species). The beneficial health effects of rooibos and honeybush are well known, but are mostly of an anecdotal nature. As the popularity of these indigenous herbal teas has increased dramatically, internationally and nationally over the past few years, it has become essential to substantiate some of the beneficial health effects. As oxidants play an important role in the induction of several chronic diseases, such as cancer the antioxidant and antimutagenic properties of rooibos and honeybush extracts could be utilized as chemopreventive agents. Studies were designed to determine the cancer modulating efficacies of various extracts of these indigenous plants that form part of the Western and Southern Cape fynbos flora. A rat liver and mouse skin carcinogenesis models were utilized to determine the possible chemoprotective effects of rooibos and honeybush against cancer promotion. In rat liver diethylnitrosamine and fumonisin B_1, while in mouse skin 7,12-dimethylbenz[a]anthracene and 12-O-tetra-decanoylphorbol-13-acetate were utilised as cancer initiators and promoters, respectively. When dosed orally, both "green" rooibos as well as "green" honeybush effectively reduced the total number of preneoplastic lesions in the liver. In mice skin, topical application of extracts of both "green" and processed rooibos and honeybush significantly ($P<0.05$) reduced the formation of skin tumours. As multiple pathways are involved in skin and liver cancer development, different mechanisms, including the anti-proliferative, anti-inflammatory and antioxidant activity exhibited by the herbal teas may be involved in the protective effects. Results from these studies strongly suggest that the consumption and/or topical application of the two indigenous herbal teas may play an important role in the modulation of cancer promotion that could alleviate the burden of cancer in humans.

O9 (Plenary Address)
MUTAGENICITY AND MUTATION SPECTRA OF DISINFECTION BY-PRODUCTS OF DRINKING WATER

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Recent molecular epidemiology research confirms that an increased risk for bladder cancer is associated with dermal/inhalation exposure to chlorinated water (from bathing/showering and/or swimming), rather than to drinking the water, and that risk is enhanced in people carrying the *GSTT1*-1 gene (i.e., glutathione-S-transferase isoform T1-1). Dermal adsorption permits disinfection by-products to enter directly into the blood stream, bypass the liver, and be transported without significant metabolism to the colon and bladder. The relative proportion of GSTT1-1 activity, which activates brominated trihalomethanes, to the activities of P450 isozymes, is greater in the colon than in other potential target tissues such as the liver. Thus, the disinfection by-products obtained through dermal exposure may be more likely to be activated to mutagens by GSTT1-1 in the colon and bladder, rather than inactivated by P450 isozymes in the liver, explaining the increased cancer risk in these organs. Further studies need to be conducted in both rodents and humans to clarify whether dermal and inhalation exposure to disinfection by-products can increase the risk for colorectal and bladder cancer. Although the mutation spectra of a wide variety of disinfection by-products have been determined in *Salmonella*, no molecular epidemiology studies have been performed to determine if mutation patterns in human tumors associated with chlorinated water exposure contain the spectra of mutations produced by these compounds. Approximately 30% of the municipal water supplies in the U.S. have changed from chlorination to chloramination, which has resulted in the formation of newly identified disinfection by-products, such as the halonitromethanes and brominated forms of disinfection by-products. Studies of these compounds for mutagenicity in *Salmonella* and for DNA damage (comet assay) in CHO cells have shown that the brominated forms are generally more toxic and genotoxic than the chlorinated forms, iodinated forms at the most toxic, and halonitromethanes are generally more genotoxic than the halomethanes. Although more toxic than the regulated disinfection by-products, the newly identified compounds are generally present at much lower concentrations than those that are regulated. [Abstract does not necessarily reflect the policy of the US EPA.]

O10

VALIDATION OF ECOTOXICITY TESTS TO EVALUATE THE GENOTOXICITY OF HOSPITAL WATER WASTE

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The growing use of antineoplastic drugs in cancer therapy is an emerging issue in environmental research. Cytostatics belong to the CMR (carcinogenic, mutagenic and reprotoxic) drugs. They usually enter the hospital effluents partially transformed or even unchanged via urine and faeces of patients under medical treatment. As hospital effluents reach the municipal sewer network generally without any preliminary treatment, they can reach drinking water. Their presence in the environment could affect animal and human health, but also the plants. The aim of this research was to validate biomarkers relevant to follow cyclophosphamide (CPA) and its metabolites in the sewer system of the hospital in-patient treatment and to provide a better understanding of their fate in wastewater and their elimination by activated sludge. The alkylating antineoplastic drug Cyclophosphamide (CPA) which is one of the oldest known cytostatics and is one of the most frequently used agents in cancer chemotherapy has been chosen. Several bioassays have been optimised for this purpose: (i) growth inhibition of the aquatic plant *Lemna minor* (ii) growth inhibition of the algae *Chlorella vulgaris* (iii) cellular viability of human liver cell and renal cell (iv) genotoxicity evaluation by determination of DNA adduct (by postlabelling and HPLC) in cell culture and in vivo (*brachydanio rerio*). At low doses the main cytotoxic metabolites (acrolein, nor-nitrogen mustard and phosphoramid mustard) of CPA induce proliferation of human cells. All these metabolites and CPA induce comet. Phosphoramide mustard damages DNA more than the other compounds. Acrolein formed deoxyguanine adduct detectable by postlabelling and by HPLC. CPA and their metabolites were continuously added to sludge of the bioreactor equipped with a ceramic tubular Membralox®. Preliminary results indicate that water collected after passing through the membrane of the bioreactor is highly genotoxic (increase of cell proliferation, formation of DNA adduct, positive Comet Assay). The metabolites found in water have been analysed by GC/ms. Elimination of the toxic compounds is not enough, and/or some new compounds have been generated into the bioreactor.

O11
TUMOUR –PROMOTING HEPATOXINS IN THE AFRICAN AQUATIC ENVIRONMENT

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Cyanobacteria are true bacteria but are also called blue-green algae because they resemble them in morphology, habitat and photosynthetic ability. They inhabit all natural waters but become a problem when present in excessive number (blooms). In such cases, they are grouped among Harmful Algal Blooms (HABs). Over the last few decades, there has been a dramatic increase in the impacts of HABs globally. Several genera of Cyanobacteria produce algal blooms that can be extremely toxic and they have been linked to the mass death of fish, aquatic mammals, birds and other animals. Human fatalities have occurred from exposure to these toxins from contaminated water supplies. Cyanotoxins are among the most potent tumour-promoting compounds known and are of particular concern in drinking water. Major cyanotoxins include: hepatoxins, which damage liver cells; neurotoxins which damage nerve cells and cylindrospermopsins of which there is a growing apprehension over its possible role in liver cancer. The present study conducted in Cameroon coastal waters indicate that aquatic resources in Cameroon are threatened by these noxious blooms. There are also documented reports of the presence of cyanotoxins in aquatic environments of Nigeria, Ghana, South Africa and other African countries. Knowledge of harmful algal blooms, their toxins and effects on public health is still rudimentary or lacking in most parts of Africa. There is need for concerted multidisciplinary research efforts, exchanged expertise and collaboration between research institutions in Africa and elsewhere so that the extent of the impact of these toxins on public health is assessed and mitigation/management and preventive measures are taken.

O12 (Plenary Address)
WATER AND HEALTH-RELATED RESEARCH

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The quality of our water resources has deteriorated in recent years due to various reasons such as increasing industrial activities, the need for higher food production with the increased demand and use of fertilizers and pesticides , as well as the growing informal settlements around or nearby cities that do not have the capacity to handle the increasing demand for water and sanitation services. Water quality is measured by the amount of microbiological and chemical constituents in the water that could be safe or unsafe for human, animal or environmental health. Water -related health forms thus a crucial and integral component of our daily quality of life. Health related water research is undertaken with the aim of improving water quality and hygiene practices in order to improve quality of life, save lives and reduce the cost and effort in treating diseases and their symptoms. The Water Research Commission(WRC) has established a Water and Health Domain impact area to play and essential role in providing an integrating framework for all the health- related research and development initiatives, identifying gaps and negotiating the initiation of gap-filling research in crucial areas. In fulfilling this role, the impact area assumes the responsibility for the structuring of a needs-driven, dynamic health-related water research portfolio on behalf of the WRC, with contributing projects being funded and managed in the appropriate Key Strategic Areas of water research. A holistic, multidisciplinary approach is followed in order to develop a comprehensive understanding of the origin/sources and special extent of pollution; water quality usage patterns; the effects of degraded water quality on human, animal and environmental health and the need for, and efficiency of various water treatment options. The domain also follows the global trends in handling emerging pollutants and diseases associated with water quality. The emphasis is on a pro-active approach to identify and address causes rather than on a passive response to addressing symptoms. This approach should ensure research products that are relevant, user-friendly, practical and scientifically valid.

O13 (Invited Lecture)

POTENT IN VITRO ANTIMICROBIAL ACTIVITY OF TWO CAMEROONIAN MEDICINAL PLANTS ON CLINICAL ISOLATES OF *HELICOBACTER PYLORI*

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Helicobacter pylori, a gram negative microaerophilic bacterium is a major etiological agent in duodenal, peptic and gastric ulcers. In this study, gastric biopsy samples were obtained from patients presenting with gastroduodenal complications. *H. pylori* was isolated from the specimens following standard microbiology procedures, and isolates subjected to test fractions of plant extracts for antimicrobial assays. Crude methanolic extracts of *Ageratum conyzoides* and *Lycopodium cernua* were fractionated by different methods to obtain pure fractions. *A. conyzoides* was fractionated by silica gel and thin layer chromatography and 16 fractions were obtained and to avoid smearing of the active ingredients through the column *L. cernua* was fractionated by solvent partitioning with solvents of increasing polarity obtaining 5 fractions. Fractions 23-30 and 31-36 of *A. conyzoides* had crystals and showed similarity in their TLC profiles; it was assumed that they had the same active components, so they were combined and considered as Fractions 23-36. The disk diffusion method was used to determine the susceptibility of 15 strains of *H. pylori* to the test fractions. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) for the most active fractions were also determined by the tube dilution method. Results were analyzed by the Student T- test and the Fisher's Exact Test. All the fractions tested demonstrated antimicrobial activity with zone diameters of inhibition between 0-30mm. However, two of the 16 fractions of *A. conyzoides*, 23-36(between elution with 100%Hex-Hex/EA20%) and 69-83(eluted with Hex/EA80%) demonstrated potent activities while the Hex fraction of *L. cernua* was the most active of the 5 fractions. The lowest MIC and MBC recorded were 0.002mg/mL and 0.016mg/mL respectively. However the MIC of the fractions ranged from 0.016-0.500mg/mL for fractions 23-36; 0.002-0.500mg/mL for fractions 69-83 and 0.016-1.000mg/mL for the Hex fraction of *L. cernua*. The MBC of the fractions ranged from 0.063-0.500mg/mL for fractions 23-36; 0.016-1.000mg/mL for fractions 69-83 and 0.125-1.000mg/mL for the Hex fraction of *L. cernua*. There was a statistical significant difference ($P<0.05$) in the potency of the fractions of *A. conyzoides* and *L. cernua* on the different bacterial strains tested, both for the MIC and MBC. It is concluded that these plants may contain compounds with therapeutic activity, which may be found in fractions 23-36 and 69-83 for *A. conyzoides* and the Hex fraction of *L. cernua.*

O14

DNA DOUBLE-STRAND BREAKS AND THEIR REPAIR IN BLOOD LYMPHOCYTES OF PROSTATE CANCER PATIENTS

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Prostate cancer is the most common cancer in men and the second leading cause of cancer mortality. More than 70% of prostate cancer cases are diagnosed in men over age 65. It is supposed that an accumulation of DNA damage and a decline in DNA repair during aging may lead to prostate cancer development. Ionizing radiation is frequently used for therapy of cancer prostate. It well known that late effects of cancer prostate radiation therapy is very differs among humans locally irradiated at similar dose. In the present work, DNA double-strand breaks and their repair, percent of apoptotic cells and chromosome aberrations frequency was studied in blood lymphocytes of healthy donors and prostate cancer patients using comet assay (neutral pH), flow cytometry (antibodies to γ-H2AX, Annexin V) and cytogenetic techniques. 38 men with prostate cancer diagnosis before radiation therapy, 26 patients 2-5 months after radiation therapy starting (local dose on prostate was at range of 41-123 Gy) and 35 healthy men were examined. Our results showed that: 1. DNA double-strand breaks level in blood lymphocytes of prostate cancer patients is significantly higher than in healthy donors; 2. Capacity of DNA double-strand breaks non-homologous end joining repair system in blood lymphocytes prostate cancer patients more variable in comparison vs healthy donors; 3. Blood lymphocytes of prostate cancer patients more sensitivity to ionizing radiation exposure than the cells of healthy donors; 4. Radiation therapy of prostate cancer leads to increase in the DNA double-breaks levels, cytogenetic distributions frequencies and cell death in blood lymphocytes of the patients. In whole, the results suggest that estimation of blood lymphocytes sensitivity of cancer patients to radiation exposure is useful for individualization of cancer therapy strategy.

O15 (Plenary Address)

INTERACTION BETWEEN AFLATOXIN B_1 AND OTHER RISK FACTORS IN HEPATOCARCINOGENESIS

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Chronic hepatitis B virus (HBV) infection and dietary exposure to aflatoxin B_1 (AFB_1) are major risk factors for hepatocellular carcinoma (HCC) in sub-Saharan Africa and the Asian Pacific region. African dietary iron overload is another important risk factor for the tumour in sub-Saharan Africa. HCC not only occurs commonly in the two regions, but the patients are frequently younger than those in other parts of the world, suggesting a possible synergism between these risk factors. Synergistic interaction between HBV and AFB has been well documented in African and Chinese patients with HCC, with relative risks as high as 70 being recorded. Taiwanese HCC patients exposed to both risk factors have an average age 10 years younger than those exposed to HBV alone. Possible mechanisms for the synergism are that the cytochrome P450s that convert harmless AFB to highly reactive AFB-8,9-epoxide may be induced by HBV, and that HBV, specifically its X protein, increases the likelihood of the generation of AFB_1-induced p53 mutation and impairs its removal by nucleotide excision repair. An interaction between the two carcinogens has also been shown in transgenic mice and in woodchucks infected with woodchuck hepatitis virus. There is no convincing evidence of synergism between AFB_1 and chronic hepatitis C virus infection in the genesis of HCC. Although there is as yet no epidemiological evidence of synergism between AFB and dietary iron overload, there is experimental evidence. In Wistar albino rats fed iron alone, AFB_1 alone, or the two together, the Ames Mutagenicity Test was multiplicatively increased in the iron/AFB rats compared with the others, as were levels of lipid peroxidation and 8-hydroxy-2-doexyguanosine, indicators of oxidative stress. Increased levels of polycyclic aromatic hydrocarbons (PAH)-DNA adducts have been demonstrated in liver tissue adjacent to HCC. In a single study a possible synergistic interaction between PAH-albumin adducts and AFB exposure in the genesis of HCC was shown, with a definite interaction between the two in the presence of HBV. The generation of oxidative stress is a possible explanation.

O16

MYCOTOXIN PROBLEMS IN THE FOOD CHAIN: A COMPARISON OF DEVELOPING AND DEVELOPED WORLDS

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Concerns over food-borne mycotoxins are widely acknowledged by food safety authorities around the world. Science-based risk assessments, with components of hazard identification, hazard characterization, exposure assessment and risk characterization, are increasingly being used as a guide to possible health risks. In such risk assessments, both the hazard characterization and the exposure assessment, and consequently the resulting risk characterization, are influenced both by health status and by food quality and consumption differences between the developed and developing worlds. In particular, the risk characterization of aflatoxin B_1 depends on the hepatitis B prevalence of the population and the extent to which foods susceptible to aflatoxin B_1 contamination form part of the staple diet. The health risks posed to populations in the developed world are generally orders of magnitude lower than those posed by contaminated diets in the developing world. Given the dietary variety available and consumed, the market competition for quality food, the presence and ability to enforce legislative regulations and the possibilities for management posed by food processing industries, the populations of the developed world are mostly well protected. Recently published surveys based on food baskets in northern Europe have confirmed this low exposure in the general population. Much the opposite is true in the developing world, where a lack of dietary variation, poor socio-economic conditions and the absence or unenforceable nature of regulations imply great risks from food contamination. This situation is exacerbated in subsistence farming communities with limited choices and resources, as evidenced by recent fatal outbreaks of human aflatoxicosis in rural Kenya. These tragic occurrences have served to highlight that although the chronic effects of mycotoxins have been the most widely considered, instances of acute toxicity are still present in the developing world.

O17

OVERVIEW ON MOLECULAR MECHANISM INVOLVED IN OCHRATOXIN A NEPHROTOXICITY AND CARCINOGENICITY

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Ochratoxin A (OTA) is a nephrotoxic and carcinogenic mycotoxin, suspected of being the etiological agent of Balkan endemic nephropathy (BEN) and associated urinary tract cancers. Conflicting results have been obtained regarding the genotoxicity of OTA and its ability to react directly with DNA upon oxidative bioactivation to yield covalent DNA adducts.This presentation gives an overview on metabolic pathways involved in OTA genotoxicity and the nature of DNA adduction. One hypothesis for ochratoxin A (OTA)-induced tumor formation is based on its genotoxic properties that are promoted by oxidative metabolism. Like other chlorinated phenols, OTA undergoes an oxidative dechlorination process to generate a quinone (OTQ)/hydroquinone (OTHQ) redox couple that may play a role in OTA-mediated genotoxicity. To determine whether the OTQ/OTHQ redox couple of OTA contributes to genotoxicity, the DNA adduction properties, as evidenced by the ^{32}P-postlabeling technique, of the hydroquinone analog (OTHQ) have been compared to OTA in the absence and presence of metabolic activation (pig kidney microsomes) and within human kidney cells. OTHQ generates DNA adduct in the absence of metabolic activation. While OTA does not interact with DNA in the absence of metabolism but the OTQ-mediated DNA adduct noted with OTHQ are also observed with OTA following activation with pig kidney microsomes. Comparison of DNA adduction by OTHQ and OTA in human cell lines shows that OTQ-mediated adduct form in a dose- and time-dependent manner. The adduct form at a faster rate with OTHQ, which is consistent with more facile generation of OTQ from its hydroquinone precursor. These DNA adducts are found in tumoral kidney from human suffering Balkan endemic nephropathy and urinary tract tumors. Several OTA derivatives are found in blood and urine of human contaminated by OTA. One DNA-adduct has been identified as C-C8 dG OTA by LC/MS/MS analysis. On the other hand OTA modulate archidonic acid cascade, known to play an important role in regulation of renal functions and carcinogenic process. It induces c jun expression. Altogether these data indicate that OTA is a complete carcinogen.

O18

GENOTOXICITY AND CLASTOGENICITY OF ZEARALENONE MYCOTOXIN: PREVENTIVE ROLE OF ALUMINOSILICATE CLAY

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Zearalenone (ZEN) is a potent estrogenic metabolite produced by some *Fusarium* species. No treatment has been successfully employed to get rid of the ZEN contained in foods. This study was conducted to evaluate the ability of hydrated sodium calcium aluminsilicate (HSCAS) to protect Balb/c mice against cytotoxicity and genotoxicity induced by ZEN. HSCAS was added alone or simultaneously with a toxic intragastric ZEN dose by orally route. The experimental approach consisted of 7 mice treatments. The first three groups received 400, 600, 800 mg/kg bw of HSCAS. Two experimental groups received respectively ZEN alone (40 mg/kg representing 8% of LD_{50}) and ZEN with the higher dose of HSCAS (400 mg/kg bw). The two control groups received respectively distilled water and olive oil. The positive control groups received Colchicin (4 mg/kg bw) for the micronucleus assay and mitomycin C (1 mg/kg bw) for the chromosome aberrations assay. 48 h after treatment, the femur and tibia are dissected out. The results show that ZEN was cytotoxic and genotoxic to Balb/c mice as indicated by the increase in frequencies of polychromatic erythrocytes micronucleated (PCEMN) and chromosomal aberrations in bone marrow cells. The simultaneous intragastric administration of HSCAS with ZEN resulted in a decrease of PCEMN number and chromosomal aberrations frequency and in an increase of polychromatic erythrocytes (PCE) in bone marrow cells compared with the group treated with ZEN alone. It could be concluded that HSCAS itself was safe and efficient in the prevention of ZEN toxic effects in gastro-intestinal tract.

O19
THE IMPACT OF GENOTOXIC PESTICIDES ON THE ENVIRONMENT

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Pesticides are used widely in Africa to help increase agricultural production and food output. Insecticides fall into several major chemical classes ranging from organochlorines (OCs), pyrethroids (PTs), organophosphates (OPs), carbamates (CMs) and neonecotinoids (NTs). Other pesticides include fungicides and herbicides and include chemicals from a number of different chemical classes. Almost all are targeted at inhibition of nerve function in the target organisms. The bulk of the pesticides applied normally find their way into the environment and adversely affect non target species in the aquatic and terrestrial environment. In the aquatic environment they usually affect species such as fish and mollusks and other invertebrates. Several pesticides have been tested and found to have a number of effects that exclude effects such as inhibition of nerve function and photosynthesis. These effects include alteration of xenobiotic metabolizing enzyme (XME) activity, endocrine disruption and genotoxicity. A survey of the literature indicates that pesticides belonging to almost all classes of compounds induce XME activity, cause endocrine disruption and can be genotoxic and in a variety of different aquatic species ranging from fish to macro and micro invertebrates. Genotoxicity has been confirmed by use of assay such as the micronucleus test and COMET Assay. The data also suggests that where pesticides themselves are not genotoxic they could affect the metabolism of genotoxins through modulation of XME activity. A survey of the literature will be provided and some of the data generated locally will be discussed.

O20 (Invited Lecture)
NEEM TOXINS IN AGRICULTURE AND MEDICINE

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Neem (*Azadirachta indica*, Meliaceae) is a close relative of Mahagoni and the Syringa family. It is native to India and large parts of Southeast Asia including Burma and the Phillipines. Neem has been successfully introduced to tropical regions of Westafrica, parts of Saudi Arabia and South America. Neem products (leaves, juice, bark and seed oil) have found widespread application in subsistence farming for insect control. A wide range of fungicidal, antiviral and bacteriostatic properties have also been reported. The toxic properties have been attributed to a group of terpenoids of which Azadirachtin has been structurally characterized as an acetylated polyhydroxy biphenyl. Plant derived polyphenols are beginning to attract keen medical and nutritional interest in view of their role as antioxidants and free radical quenchers. The Neem group of terpinoids (limonoids) has been widely studied, but for reasons of expense, application in pest control mainly rests on leaves and bark rather than a pure product. The major attraction of Neem toxins is their insect specificity and effect on growth, fecundity, feeding and larval development. Our own studies at Tygerberg have shown that a 1000 to 2000 fold higher concentration of Azadirachtin is required to invoke the same level of cell inactivation (LD 50) in human Hela cells and human A 549 lung fibroblasts than in the insect cell lines Trichoplusia and Heliotis zea. The low toxicity of Neem products to higher animals including humans is generally acknowledged but no satisfying mechanistic explanation has yet been advanced. For insect control Neem toxins clearly pose a low biohazard and have other advantages over conventional acetylcholinesterase inhibitors. It is interesting to note that the Indian tradition of using unrefined Neem products in subsistence farming has not found wide scale application in Africa, nor has the development of Neem plantations in Australia (with spin offs for medicine, cosmetics, nutrition and the timber industry) been repeated. This is the more remarkable as conventional insecticides are expensive and herbivoric and hematophagous insects inflict increasing rather than decreasing costs in Africa. The high level of technical and scientific expertise in South Africa would make it seem attractive to explore the potential of Neem and the related Syringa family for its use in agriculture and medicine as it could safeguard human nutrition at modest cost and ensure a measurable degree of employment and social progress

O21

ASSESSMENT OF PESTICIDES FOR CYTOTOXIC AND GENOTOXIC EFFECTS IN THE ONION ROOT TIP ASSAY

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Pesticide exposure is ubiquitous. Many affect non-target organisms and have been classified as probable mutagens and/or carcinogens. Issues of animal use and care in toxicology research and testing have become of concern for science and ethics so that emphasis has been given to the use of alternatives. We tested three doses (% solution), representing ¼LC50, ½LC50 and LC50 of chlorpyrifos (0.017, 0.034, 0.068), Alpha-thrin (0.183, 0.365, 0.730), Efekto virikop (1.250, 2.500, 5.000), springbok (0.036, 0.073, 0.146), dithane (0.196, 0.391, 0.782), malathion (0.034, 0.069, 0.137) and garden ripcord (1.015, 2.030, 4.060), for cytotoxicity and genotoxicity to onion root tip cells. Onion seeds were germinated on moistened filter paper in petri dish until radicles appeared. Germinated seeds were exposed to the pesticides for 20 hours. About 1-2mm length of root tip was cut, fixed in acetic alcohol, washed in ice-cold water, hydrolyzed in warm 1N hydrochloric acid, stained with aceto-carmine and squashed on glass slide. For each treatment, about 3000 cells were scored and classified as interphase, normal or aberrant division stage. Cytotoxicity was determined by comparing the mitotic index (MI) of treated cells with that of the negative control. The MI of cells treated with chlorpyrifos, Alpha-thrin, springbok, dithane, malathion or garden ripcord was reduced to half or less, that of the control at one or more doses and adjudged cytotoxic. Efekto virikop was not cytotoxic. Genotoxicity was measured by comparing the number of cells/1000 in aberrant division stages at each dose with those of the negative control using the Mann-Whitney statistical test. Chlorpyrifos was genotoxic ($P < 0.05$), inducing chromosome lagging and bridges, pulverized and stick chromosomes, multipolar anaphase and telophase. Dithane induced lagging chromosomes and multipolar anaphases and telophases. Efekto virikop, springbok and Malathion induced lagging chromosomes. Alpha-thrin and Garden ripcord were not genotoxic.

O22 (Plenary Address)
TOXICITY AND GENOTOXICITY OF PARTICLES IN THE ENVIRONMENT AND IN OCCUPATIONAL SETTINGS

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Toxic and genotoxic effects of mineral fibres (asbestos) and particles in micro (crystalline silica) and nano size region (fullerenes, nanopowders, nanotubes, nanowires, nanorods, nanofibers and quantum dots) in the environment and in different occupational settings are determined by a series of specific features and properties that are clearly discernible from non-particulate chemicals. Dissimilar to a soluble/non-particulate genotoxic molecule, a single particle typically contains a multiplicity of intrinsic physicochemical properties that can act simultaneously or consecutively on DNA. In addition, many particles present themselves as having an insoluble or poorly soluble core onto which various adsorbed mutagens or carcinogens can be carried from the environment into and throughout the human body. Chemical composition and surface reactivity of mineral fibres and particles may determine their ability to intrinsically generate oxidants due to surface-associated reactive groups (e.g., $SiO^{\cdot}$ and $SiO_2^{\cdot}$ on quartz), or transition metals such as iron, or due to the ability of particles to generate oxidants in aqueous suspension. Another route for the generation of oxidants by mineral fibres and dusts is via their ability to activate cells for enhancement of intracellular reactive oxygen species (ROS) generation or through particle-elicited inflammation. Of major importance of ROS for genotoxicity is hydroxyl radicals ($^{\cdot}OH$) and superoxide ($O2^{\cdot-}$) as well as reactive nitrogen species (RNS) including nitric oxide ($NO^{\cdot}$), and peroxynitrite ($ONOO^{-}$). Primary genotoxicity of mineral particles is therefore defined as genetic damage elicited by particles, direct or indirect, in the absence of inflammation. Secondary genotoxicity is defined as genetic damage resulting from ROS/RNS and possibly from other mediators that are generated during particle-elicited inflammation. Using these proposed mechanisms, attempts are made to predict the genotoxicity of newly man made mineral fibres or nano-sized particles by using different genotoxicity tests.

O23

DETERMINATION OF OXIDATIVE STRESS AND NITROSATIVE STRESS AND THEIR GENOTOXICITY INDUCED BY NANOPARTICLES AND GAMMA-RADIATION

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An increasing number of applications are being developed for the use of nanoparticles in various fields. Nanotechnology is now at the leading edge of rapid development with many potential human health benefits. Since the release of nanoparticles in an enclosed environment is of great concern, a study of possible genotoxic effects is important. *In vito* effects induced by TiO, mica and clay nanoparticles were evaluated in the presence and absence of γ-radiation at a dose of 2 G so as to assess the dual effects of nano-particles with ionizing radiations on human leucocytes. Nitric oxide and reactive oxygen species induced nanparticles generation was measured in polymorph neutrophils and genotoxicity induced by nanoparticles was evaluated with respect to human lymphocytes using three different test systems: the micronucleus (MN), gene p53 mRNA expression and the hypoxia inducible factors. All investigated agents induced the generation of NO and ROS upon exposure to different nanoparticles, however TiO induced the highest level followed by clay then mica, which exhibited the least levels. Cytotoxicity tests showed loss of viability in a concentration- and time-dependent manner after exposure of cells to different nanoparticles. However mica nanoparticles exhibited some but not significant micronucleus induction, but clay and TiO exhibited significantly higher frequency of micronuclei compared to mica and to controls. All agents induced an increase in gene p53 mRNA expression and the hypoxia inducible factors, which was synergized with dual exposure to ionizing radiation. It is concluded that nanoparticles induce DNA damage, activates gene p53 expression and proteins related to DNA repair, mimicking irradiation-related carcinogenesis pathways.

O24

MOLECULAR AND CELLULAR EFFECTS IN MICE CHRONICALLY EXPOSED TO LOW DOSE-RATE GAMMA-RADIATION

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The results of the 3 independent experiments on study of molecular and cellular effects in CBA/lac male mice chronically (up to 1 year) exposed to gamma-radiation at a dose-rate of 61 cGy/year were summarized and discussed in this report. It was showed using comet assay that low dose-rate irradiation resulted in statistically significant increase in DNA single-strand breaks level in spleen cells, starting from a dose of ~ 20 cGy (120 days). Further prolongation of exposure time and, hence, increase of a total dose did not, however, lead to further increase in the extent of DNA breaks level. A dose-response curve for DNA single-strand breaks is good fitted by a polynomial regression y=0.6209+0.0313*x-0.0004*x2, where y is the average comet index, x is a dose in cGy. At the days 120, 270, and 365 of the chronic irradiation (20, 45, and 61 cGy, respectively), approximately two-fold increase over a control level in the apoptotic cell fraction was observed. It was also found that chronic action of low dose-rate γ-radiation led to a change in the sensitivity of spleen cells to H_2O_2 exposure. A weakening of cellular antioxidant potential and/or repair capacity has been observed at early terms of irradiation (up to 80-120 days). In contrast, prolongation of irradiation resulted in activation of defense system in spleen cells. This effect could be attributed to the development of adaptation processes triggered upon accumulation of a certain dose. The bone marrow micronucleus test revealed that increase in polychromatic erythrocytes with micronuclei over a background level was induced by low-level irradiation with a dose of 61 cGy only, with the extent of the cytogenetic effect being similar to that of 5-10 cGy high dose-rate exposure. Thus, presented results support the hypothesis of non-linear threshold nature of genotoxic action of chronic low dose-rate irradiation.

O25

RISK ASSESSMENT FROM HEAVY METALS ACCUMULATION IN BLOOD ON HUMAN POPULATIONS IN URBAN INDUSTRIAL ENVIRONMENT

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In this research project investigations were carried out in blood samples on human population exposed to risk through exposure of airborne particulate matter and disposal of waste from industries. The industries identified are steel plants, power plants, smelters, mining and battery plants. Investigations were carried out on toxic metals in blood and urine to find out the risk assessment on human population. Statistical correlation was carried out with other pathological parameters. Measurements were carried out for toxic metals like arsenic, mercury by Cold Vapour Atomic Absorption Spectroscopy and Hydride Generation Atomic Absorption Spectroscopy. Lead, Cadmium and Chromium by using Graphite Furnace Atomic Absorption Spectroscopic technique and Inductively Coupled plasma Atomic Emission Mass Spectrometry. Pathological parameters were carried out with analysers as per international protocol. Proficiency testing was carried out with standard reference material. Risk assessment was carried out from interpretation of data and sources identified. The results obtained for the metals in blood samples, As-0.5-4.0 µg/dl. Hg-0.02-1.0µg/dl, Pd-10-80 µg/dl, Cd-0.02-0.30 µg/dl and Cr-0.20-0.50 µg/dl respectively. Of the heavy metals, Arsenic (As), Lead (Pb), Mercury (Hg), Cadmium (Cd) and Chromium (Cr) are included in the list of top 20 hazardous chemicals by the Agency for Toxic Substances and Disease Registry (ATSDR).

O26
FORMALDEHYDE TOXICOLOGY – OCCUPATIONAL VERSUS ENVIRONMENTAL HAP?

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Formaldehyde is the most common naturally occurring aldehyde in the environment. It is, however, also generated by a range of anthropogenic sources including automotive exhaust, cigarette smoke and various products containing formaldehyde-based resins and glues such as particle board and plywood. As a ubiquitous air pollutant in both work and office indoor air the potential adverse health effects from formaldehyde exposure have been subject to numerous critical public health reviews by regulatory agencies over the last ten years. In 2004 the IARC reclassified formaldehyde as Class 1 'carcinogenic to humans'. Public health reviews have, however, been based primarily on the extrapolation of dose-response data from occupational studies where repeated elevated levels of exposure have led to both respiratory irritation and sensitisation as well as proven increased incidences of nasal and oesophageal cancers. In this paper the perils and pitfalls in the interpretation of occupationally derived toxicological information to derive safe levels for public exposure to a key HAP are explored using data from a local case study. The technical background as to why public cancer incidence rates from formaldehyde exposure have been overestimated by a number of international regulatory agencies are demonstrated based on latest knowledge of formaldehyde toxicology and carcinogenesis. Problems in the simple modification of occupational air quality guidelines to derive annual exposure limits for assessment of ambient air quality monitoring data and public health risk assessment are highlighted with reference to case study data. Proposed occupational and ambient limits for formaldehyde in South Africa are tabled for review and debate.

O27 (Plenary Address)
PERSPECTIVES ON RISK ASSESSMENT PARADIGMS OF GENOTOXIC AND NON-GENOTOXIC CARCINOGENIC MYCOTOXINS

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Classification of carcinogens as genotoxic and non-genotoxic forms the basis of setting risk assessment parameters in order to establish permissible exposure levels where no risks are anticipated to humans. For genotoxins, DNA mutations resulting in a strong DNA damage response at the gene expression level include p53 and DNA repair genes which are generally related to cancer initiation. Mutations could lead to oncogene activation or tumor suppression gene inactivation, resulting in increased proliferation and/or decreased apoptosis in the initiated cell. For non-genotoxins the process of cancer initiation is less clear while promotion is likely to be mediated by a strong mitosis induction either directly or via regenerative hyperplasia, which may lead to the fixation of endogenous occurring DNA mutations contributing to or at least enhance both the initiating and promoting phases. Similar mechanisms could also play a role for genotoxins where additional compound specific effects such as oxidative stress or regenerative responses could be key parameters determining cancer induction. This is evident in the liver where both genotoxic and non-genotoxic mechanisms effect the induction of similar endpoints reflecting cancer initiation and promotion. The main difference, however, appear to be the kinetics of events related to initiation, which could either result from tissue specific responses and/or compound specific effects. Despite the similarities with respect to cancer induction, differences exist when determining risk assessment parameters to humans. The major discriminator regarding genotoxic and non-genotoxic carcinogens are centered on threshold and non-threshold responses. As carcinogenesis is readily accept to be a multistage process more support for a threshold effect for genotoxins exists especially at low doses where binding to DNA could be prevented by several means and certain events may not be biologically relevant. Aspects regarding the risk assessment of genotoxic and non-genotoxic carcinogenic mycotoxins will be debated against this background.

O28

STUDIES OF MYCOFLORA AND MYCOTOXINS CONTAMINATING GUINEA CORN AND RICE IN NIGER STATE, NIGERIA

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In a survey for toxigenic fungi, aflatoxin B_1 (AFB_1), zearalenone (ZEN) and ochratoxin A (OTA) contaminating mouldy field, marketed and stored *Sorghum* and *Oryza sativa* samples during the three seasons in Niger State, Nigeria, 884 fungi were isolated from 168 guinea corn samples collected. The commonest fungi found contaminating guinea corn in the state were *Aspergillus niger, Rhizopus oryzae, A. flavus, Mucor spp, Penicillium spp, Rhizopus spp,* and *Trichoderma spp.* The most prevalent fungal species of the 1062 isolates detected in the 196 rice samples were *Penicillium spp, A. flavus, A. parasiticus, A. niger, Mucor spp, Rhizopus spp* and *Alternaria* spp. AFB_1, ZEN and OTA in order of decreasing incidence were found contaminating the two studied grains. Of the 148 (67 and 81 from Sorghum and rice) fungi screened for toxicity, 64.2% were found to be toxigenic and were species of *Aspergillus*, *Fusarium*, *Penicillium*, *Trichoderma*, *Syncephalastrum*, *Alternaria, Phoma, Curvularia, Colletritrochum, Geotrichum, Helminthosporium, Cladosporium, Cryptococcus* and *Mucor.* Preliminary acute toxicity screening test of the very toxic fungi isolated revealed *Fusarium verticillioides* (Sacc.) Nirenberg as the most toxic metabolite producing fungi. The Petroleum Ether Extract (PER) of *F. verticillioides* was acutely toxic to mice and chicks and the organs affected were liver, kidney and gastrointestinal tract. Enlarged spleen, and feathery degeneration and necrosis of hepatocytes were observed in rats chronically fed *F. verticillioides* cultured maize. The total fumonisin content of the fungal extract was 8.233ppm. Acute toxicity studies, and mass and UV spectrophotometric data of the extract of *F. verticillioides* are indicative that the extract contains more than a component (FB_1 inclusive). So there is need for further work to establish the number and structures of toxins produced by the fungus.

O29 (Invited Lecture)
GENETIC VARIATION IN *FUSARIUM* SPECIES PRODUCING MYCOTOXINS

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Fusarium species produce a broad range of mycotoxins including trichothecenes, fumonisins, zearalenone and non-ribosomal peptides. The most genetic information is available on *Fusarium graminearum* (*Gibberella zeae*) and *Fusarium verticillioides* (*Gibberella moniliformis*), which are know primarily for producing deoxynivalenol/nivalenol and zearalenone, and fumonisins, respectively. The genetic regions encoding the mycotoxin biosynthetic pathways are clustered by metabolite and have been sequenced and analyzed in detail. Naturally occurring and laboratory-induced mutations in these genes have been used to confirm the qualitative role of these genes in mycotoxin biosynthesis. Although mechanisms to turn on/off toxin production are known, genes that quantitatively regulate levels from little to much have not been identified. Natural populations of *F. verticillioides* vary greatly with respect to genetic markers such as AFLPs, VCGs and DNA sequences. This variation effectively prevents the identification of genetic markers that are correlated with fumonisin production but are not involved in the biosynthetic pathway. Natural populations of *F. graminearum* also vary greatly with respect to AFLPs, VCGs and DNA sequences, even though the fungus reproduces homothallically and need not have a sexual partner to complete the sexual recombination process. The organization of some of the genetic variation in *F. graminearum* has led to the suggestion that this species be split into 11+ species. Sexual cross-fertility and morphology suggest, however, that *F. graminearum* is a single broad species. In both *F. graminearum* and *F. verticillioides*, the available genome sequences will be invaluable for identifying additional genes involved in the regulation of toxin production and for determining how the various naturally occurring alleles at these loci affect toxin production and the distribution of various toxin phenotypes in agriculturally important populations.

O30
MYCOTOXINS: ASPECTS CONCERNING COMMERCIAL, ORGANIC AND GENETICALLY MODIFIED FOODS

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Food safety, a complex and many-faceted issue, is becoming increasingly important in national and international debates about Agriculture, Nutrition and Health, particularly with regard to mycotoxins, organically grown and genetically modified foods. There is an increasing demand for organic foods in developed countries, while some may argue that people in developing countries have always been eating organically grown foods. Organic foods that are grown without the use of insecticides and fungicides may be expected to be infested by insects and infected by fungi to a larger extent than conventionally grown foods and concomitantly contaminated with higher levels of mycotoxins. An example of this is patulin produced by the post-harvest fungus, *Penicillium expansum*, in apples. In conventionally grown apples, patulin levels in apple juice of up to 4 000 µg/l have been reported compared to 45 000 µg/l in organically produced apple juice. Several other examples of the occurrence of mycotoxins in organically grown crops exist, including fumonisins in maize produced by *Fusarium verticillioides* and *F. proliferatum*. In contrast, significant reductions in fumonisins in some *Bt*-maize hybrids compared to their iso-lines have been achieved. Toxin-producing fungi and their mycotoxins also occur in health foods that further pose a threat to human health. Serious health risks, such as liver cancer, may arise where mycotoxins are not controlled in food commodities, eg. aflatoxin in peanut butter. Peanut butter used in the Primary Schools Nutrition Programme in South Africa was reported to contain high levels of aflatoxin. The liver cancer risk increases significantly if a child with hepatitis B virus infection consumes aflatoxin-contaminated foodstuffs. These and other issues such as the use of fungi and yeasts as biocontrol agents are also of concern, due to the emergence of medically important fungi not previously considered important in human disease, particularly in immune-compromised subjects with, for example, HIV/AIDS and cancer.

O31 (Plenary Address)
ENVIRONMENTAL MUTAGENS AND POSSIBILITIES FOR PREVENTION

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Humans are exposed to many physical or chemical genotoxic agents that can increase the probability to mutation. On the other hand, there are possible ways to prevent this effect. One of them is to prevent cellular injury by augmenting endogenous oxidative defences through the dietary intake of antioxidants such as vitamin C or vitamin E. Also Olive oil proved to have potent antioxidant properties. Several studies were conducted during the last ten years to demonstrate the genotoxic effect of these environmental pollutants and also to investigate the possible protective effect. Examples of these studies will be presented. In one of the studies, we investigated the mutagenic effects of two commonly used pyrethroid pesticides cypermethrin and fenvalerateon on bone marrow cells of adult male rats and the possible protective role played by olive oil and vitamin C. Results revealed that cypermethrin and fenvalerate induced significant increase in the total number of chromosomal aberrations more observed with fenvalerate. Olive oil and vitamin C induced significant improvement of total aberrant cells at high doses (1/10 LD50). Aflatoxins contaminate many food products and are consequently of worldwide heath concern. Prevention of exposure to aflatoxins can be achieved either at community (via good agriculture practices) or individual levels (treatment or dietary interventions). Several trials were carried out to evaluate the effect of processing steps of corn products on destruction of aflatoxins in popcorn and porridge was studied. The results of the trial indicated that the process of popcorn and porridge preparation had a significant effect on Aflatoxins destruction. The temperature of preparing and treatment with 5% salt (Sodium Chloride) yielded the highest destruction rate. Several probiotic bacteria are able to bind aflatoxin B_1 *in vitro*, including *Lactobacillus rhamnosus* LC-705 and *Propionibacterium freudenreichii* subsp. *shermanii* JS. A mixture of these two probiotics is used by the food and feed industry as biopreservative (Bioprofit), making it a promising candidate for future applications. Recent study was carried out to determine whether administration of probiotic bacteria could block the intestinal absorption of aflatoxin B_1. Probiotic administration led to a statistically significant decrease in the urinary excretion of AFB-N7-guanine. Probiotic supplement reduces the biologically effective dose of aflatoxin exposure, and may thereby offer an effective dietary approach to prevent the development of liver cancer. Human intervention study is ongoing now in Egypt in a group of human subjects proven to be exposed to aflatoxins at baseline. Other examples of these studies are the antimutagenic effect of dimethyl sulfoxide on metabolism and genotoxicity of benzene *in vivo* and the radioprotective role of vitamin C and E against gamma radiation-induced depletion in the relative testicular weight and sperm shape abnormalities.

O32
EXPOSURE OF PREGNANT WOMEN ON TOBACCO SPECIFIC CARCINOGENS

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The most important carcinogens of tobacco smoke belong to two chemical groups; polycyclic aromatic hydrocarbons and N-nitrosamines. The aim of the study was to apply the biomarkers 1-hydroxypyrene (1-HP), and 4-(methylnirosoamino)-4-(3-pirydyl)-1-butanol (NNAL) for monitoring the exposure of pregnant women to PAH and tobacco specific nitrosamines. One hundred twenty pregnant women took part in the study, i.e. 31 women who did not smoke, 35 non-smokers exposed to environmental tobacco smoke (ETS) and 54 smokers admitted for the delivery at the Gynaecological-Obstetric Clinical Hospital of the University of Medical Sciences in Poznan and Warsaw. A urine sample was taken from each woman to determine cotinine and 1-hydroksypyrene by means of HPLC and NNAL by LC/MS/MS. In the urine of non smoking women, the level of cotinine tobacco smoke biomarker was below the limit of detection, in women exposed to ETS and smokers were 49,6 and 345,8 ng/mg of creatinine respectively The concentration of 1-HP for smoking women amounted to 0.53 ng/mg of creatinine and was statistically higher than in the case of exposed to ETS and non-smokers (0.23 and 0.19 ng/mg of creatinine respectively). The concentration of NNAL in the urine of smokers amounted to 77.6 pg/mg of creatinine. In the urine of women exposed to ETS concentration of NNAL was 28,8 pg/mg of creatinine and in the urine of non-smokers. In all studied groups no correlations between the concentration of cotinine and NNAL or between NNAL and 1-HP were demonstrated. The results of the study indicate that tobacco smoking is real source of carcinogenic compounds which can cross the placenta and reach the foetus body.

O33
GENOTOXICITY OF DENTAL MATERIALS

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The development of resin-based dental materials bonded to tooth structures stimulated new restorative techniques. Some of these materials may induce harmful biological effects. The co-monomers and monomers of triethylene glycol dimethacrylate (TEGDMA) and 2-hydroxylethyl methacrylate (HEMA) are reported to induce gene mutations *in vitro*. The bioaviability of these materials, leaching from the dentin adhesives into the pulp may be in the milimolar range. Chitosan and its derivatives, due to their adhesive and antioxidative properties, may be considered as protective compounds against detrimental action of dental materials. We investigated the action of chitosan against DNA damage induced by HEMA and TEGDMA in human lymphocytes with the using of alkaline comet assay. Both compounds decreased the viability of the cell in a dose-dependent manner. They also evoked dose-dependent DNA damage. Pretreatment of the lymphocytes with the nitrone spin trap, *N-tert*-butyl- -phenylnitrone or ebselen, which mimics glutathione peroxidase, reduced the extent of DNA damage evoked by HEMA and TEGDMA. The cells exposed to the compounds and treated with endonuclease III and 3-methyladenine-DNA glycosylase II, the enzymes recognizing oxidized and alkylated bases, respectively, displayed greater extent of DNA damage than those not treated with these enzymes. The results obtained suggest that free radicals may be involved in the formation of DNA lesions induced by HEMA and TEGDMA. These compounds can also methylate DNA bases. Moreover, HEMA and TEGDMA increased the activity of caspase-3, which may indicate their potential to induce apoptosis. Preincubation of the cells with chitosan increased their viability and decreases the extent of DNA damage induced by HEMA and TEGDMA. Therefore, chitosan can be considered as a support or additive to restorative dental materials.

O34

POSSIBLE MECHANISMS INVOLVED IN THE ANTI-CANCER PROPERTIES OF UNFERMENTED ROOIBOS (*ASPALATHUS LINEARIS*) AND HONEYBUSH (*CYCLOPIA* SPP) HERBAL TEAS

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Polyphenolic components of two herbal tea plants are being investigated to elucidate their potential anticancer properties. Investigations include studies on (i) anti-mutagenic properties of selected phenolic compounds in rooibos (*Aspalathus linearis*) and honeybush (*Cyclopia spp*), (ii) the effect of aqueous extracts of rooibos and honeybush, as well as their major phenolic compounds on the stability of cytochrome P450 (CYP450) (iii) effect on carcinogen/CYP450 binding and (iv) effect of flavonoids-enriched extracts of rooibos and honeybush *spp.* on the gene expression of selected xenobiotic metabolising enzymes using super array technology. Flavonoid/mutagen interactions manifested in four ways exhibiting antimutagen, comutagen, promutagen and mutagenic properties. Two different parameters (i) CYP450 stabilisation and (ii) interference of the mutagen/CYP interaction appear to determine the antimutagenic potency of the herbal teas and their flavonoid constituents. Unfermented rooibos tea demonstrated the highest CYP450 stabilizing effect which was related to the inhibition of lipid peroxidation. Unfermented *Cyclopia spp.* and rooibos resulted in reduction of type II substrate binding to CYP450. Luteolin, hesperetin, chrysoeriol and eriodictyol exhibiting a high antimutagenic response was more effective in interfering with mutagen/CYP interactions than the weak antimutagens, aspalathin, mangiferin and hesperidin. The antioxidant properties of the herbal tea flavonoids depend on hydrophobic/hydrophilic membrane interactions and variations in structure related activity such as number and position of hydroxyl and sugar groups. The *in vivo* study showed that rooibos and honeybush extracts selective altered the expression of drug metabolizing enzymes in the liver which is likely to play a key role in carcinogen metabolism and certain drug/herb interactions.

O35

PHARMACOECONOMICS OF CANCER TREATMENT AND DEVELOPMENT OF ADJUNCT THERAPY

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Chemotherapy to patients with cancer remains an effective mode of treatment of the disease, but it is associated with many side effects including mild or dose-limiting toxicities such as alopecia (hair loss), myelosuppression, gastrointestinal dysfunctions, neurologic toxicities, and immune suppression which results in infections and cancer cell proliferation. Although economic analysis of treatment in health care systems may be applied to the full range of interventions that make up a cancer service (including cancer screening programmes and early treatments, diagnostic test and referral processes, surgical procedures, radiotherapy, chemotherapy, and palliative care), the economic impact of cancer in health care systems remains one that much attention, in the context of complementary medicine, needs to be directed. Cytosine arabinoside (cytarabine, Ara-C, a cell cycle-specific cytotoxic drug that selectively kills cells in the S phase) has been used in the treatment of human acute myeloblastic and lymphoblastic leukemia, some head and neck cancers, and non-Hodgikin's lymphoma, and its effectiveness has been associated with cytotoxic effects on blast progenitors in self-renewal. Cisplatin (cis-diaminedichloroplatinum (II) or CDDP a platinum-containing anticancer drug, is one of the most commonly used cytotoxic agents in the treatment of a variety of solid malignant tumors, for example in the head and neck, lungs, ovaries, bladder and testicles. Although treatment with CDDP is often effective, serious side effects such as nausea, nephrotoxicity, neurotoxicity, ototoxicity, poor Karnofsky performance status and co-morbidities occur often. Focal encephalopathy and neurological deficits of higher function (including cortical blindness and aphasia with or without seizure and confusion) are also widely documented side effects of CDDP therapy. These side effects interfere with the treatment and often force a reduction of the dosage, frequency and duration of the cisplatin therapy necessitating the search for alternative therapy with less toxicity. In chemotherapy, toxic drug responses are unavoidable and there is a need to minimize these. Thus, the frequency and severity of chemotherapy-induced side effects and their management are primary treatment concerns. It will be important to determine whether in a clinical trial the merit of diet-based adjunct therapy can enable cancer patients to tolerate therapeutic/high doses of cytotoxic drugs and whether this can parallel an improved quality of life following chemotherapy. It is envisaged that supplementation strategies involving diet-based adjuncts could significantly benefit the cost-effectiveness of health care interventions in cancer treatment.

POSTER PRESENTATIONS

P1

THE EFFECT OF SPECIFIC N-6/N-3 POLYUNSATURATED FATTY ACID DIETARY RATIOS ON CELLULAR OXIDATIVE STATUS IN THE PREVENTION OF HEPATOCARCINOGENESIS

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Alteration in fatty acid (FA) metabolism, especially regarding n-6 and n-3 polyunsaturated FA (PUFA), is linked to the modulation of cell membrane structure and oxidative status affecting membrane function, enzyme activity and signalling pathways. A growing body of research supports the use of n-3 PUFA in the prevention of certain cancers. The proposed chemopreventive mechanisms of n-3 PUFA are many and include suppression of arachidonic acid-derived eicosanoid synthesis, inhibition of cell proliferation, enhanced apoptosis and alteration in cellular oxidative status. In rat liver, a characteristic lipid profile is associated with the growth and development of preneoplastic nodules. This profile entails decreases in the PC/PE phospholipid ratio, arachidonic acid PC/PE ratio, n-3 PUFA content and oxidative status as indicated by low TBARS but high GSH levels. Subsequent modulation of the nodule lipid profile by diets containing varying low n-6/n-3 FA ratios (SFO/EPA, 12:1 ratio; SFO/EPA/GLA, 12:1 ratio; SOY, 5:1 ratio) was investigated and compared to a high n-6/n-3 PUFA ratio diet (SFO, 250:1 ratio). The three low n-6/n-3 ratio diets effected alteration in PUFA content and oxidative status indicated by increases in n-3 PUFA and TBARS levels, respectively. However, the SFO/EPA and SFO/EPA/GLA diets decreased the GSH level more effectively than the SOY diet, while only the SFO/EPA/GLA diet modulated the growth of the nodules. Lipid analyses of liver biopsies from human patients with hepatocellular carcinoma indicated a similar altered lipid pattern observed in the rat preneoplastic nodules, i.e. a reduced level of n-6 PUFA in PC, decreased n-3 PUFA in PC and PE phospholipids with a resultant decrease in oxidative status. It is suggested that modulation of tumour oxidative status by diets with a specific n-6/n-3 FA ratio and the subsequent alteration in cell growth are important events in the chemoprevention of hepatocarcinogenesis.

P2

DIETARY MODULATION OF COLON PUFA CONTENT ALTERS MEMBRANE SUSCEPTIBILITY TO LIPID PEROXIDATION

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Fatty acids play an important role in cellular homeostasis with respect to maintaining cell structure and function. Fatty acids, particularly the n-6 and n-3 polyunsaturated fatty acids (PUFA) which are susceptible to lipid peroxidation, affect cell structure and influence cellular processes such as proliferation, apoptosis and differentiation. Studies indicated that neoplastic cells have a decreased PUFA content that contributes to their resistance to lipid peroxidation and therefore cell survival. This study firstly investigates the lipid profile of azoxymethane (AOM) induced colon polyps in rats fed a diet high in n-6 PUFA, and secondly to evaluate the effect of varying dietary n-6/n-3 FA ratios on FA composition and the susceptibility to lipid peroxidation in normal rat colon mucosa and red blood cell (RBC) ghost membranes. Analyses indicated that colon polyp lipid content differs significantly from the surrounding mucosa, characterized by increased phospholipid phosphatidylcholine (PC) and phosphatidylethanolamine (PE) content, a decreased PC/PE ratio and increased arachidonic acid (C20:4n6) level and n6/n3 ratio. These lipid characteristics have also been associated with the growth of tumour tissue in an animal liver cancer model. Investigating the modulation of rat colon mucosa and RBC ghost membrane lipid profile by varying dietary n-6/n-3 FA ratios showed a reduction in the membrane n-6/n-3 ratio due to increased n-3 long chain (LC) PUFA content, particularly by fish oil containing diets. The increased n-3 LCPUFA incorporation in the mucosa and ghost membranes was associated with an elevation in Fe^{2+}-induced lipid peroxidation. Changes in the PUFA content could adversely affect neoplastic lesion development by selectively sensitizing their survival through the induction of oxidative stress resulting in apoptosis. This study suggests that a low n-6/n-3 PUFA ratio diets could potentially be used as a cancer therapeutic tool due to its ability to enhance cell susceptibility to lipid peroxidation.

P3

THE EFFECT OF ROOIBOS AND HONEYBUSH HERBAL TEAS ON THE EXPRESSION OF PHASE I AND II ENZYMES OF CARCINOGEN METABOLISM

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Herbal infusions may interfere with the gene expression, activity and/or translation of drug metabolising enzymes. Inhibition and/or induction of these enzymes, and specifically the cytochrome P450 (CYP) enzymes, could result in an increased toxicity or decreased efficacy of drugs, respectively. Many carcinogens are metabolised by CYPs, which may enhance the formation of DNA-reactive metabolites, leading to an increased risk of tumor formation. The induction of certain phase II enzymes, however, can protect against the adverse effects by enhancing the deactivation and excretion of these DNA-reactive metabolites. South African herbal teas, rooibos (*Aspalathus linearis*) and honeybush (*Cyclopia spp)*, display potent *in vitro* and *in vivo* anti-mutagenic and anti-tumor properties. It is not known at present whether these herbal teas may alter the expression of the phase I and II enzymes. The present study investigated the effect of unfermented rooibos and honeybush *spp.* (*C. genistoides* and *C. subternata*) aqueous extracts on the gene expression of selected xenobiotic metabolising enzymes. Forty male Fisher rats were exposed for 30 days to, either *A. linearis*, *C. genistoides*, or *C. subternata* dried extract mixed in their feed. The control group received only the normal feed. The livers were harvested and RNA was extracted using Trizol®. Following conversion of intact RNA to cDNA, 84 genes of drug metabolising enzymes were screened using Super Array technology and expressed against selected house-keeping genes. Super Array results displaying inhibited or induced genes were selected and quantified using RT-PCR. Findings of the present study will provide additional information regarding the potential health effects of the herbal teas in humans.

P4
BIOLOGICAL DEGRADATION OF AFLATOXIN B_1

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Aflatoxin B_1 (AFB_1), a Group I human carcinogen, is highly mutagenic, toxic, carcinogenic and teratogenic to humans and animals and in particular correlates with the incidence of hepatocellular carcinoma in parts of Africa, China and South East Asia. The biological degradation of AFB_1 by bacteria and fungi was investigated. Degradation of AFB_1 by intracellular extracts of *Mycobacterium fluoranthenivorans* sp. nov. DSM 44556^T, *Nocardia corynebacterioides* DSM 20151 and *N. corynebacterioides* DSM 12676 was demonstrated. Furthermore, AFB_1 was effectively degraded by liquid cultures as well as intra- and extracellular extracts of *Rhodococcus erythropolis* DSM 14303. Significant ($P<0.001$) reduction in AFB_1 was observed following treatment with *R. erythropolis* extracellular extracts with only 33.20% residual AFB_1 after 72 h. The degradation of AFB_1 when treated with *R. erythropolis* DSM 14303 extracellular extract coincided with a total loss of mutagenicity. In addition, treatment of AFB_1 with culture fractions containing recombinant 2,3-dihydroxybiphenyl dioxygenase, which was produced through extracellular expression of the *bph*C1 gene of *R. erythropolis* DSM 14303 in *Escherichia coli* BL21DE3, resulted in significant ($P<0.0001$) degradation (49.32%) and reduced mutagenic potency (42.47%) of the molecule. Significant ($P<0.0001$-0.05) degradation of AFB_1 was obtained following treatment with culture extracts containing laccase enzyme produced by white rot fungi (17.10-76.00%), purified fungal laccase from *Trametes versicolor* (1 U/ml, 87.34%) as well as with recombinant laccase produced by *Aspergillus niger* (0.12 U/ml, 55.00%). Furthermore, treatment of AFB_1 with purified fungal laccase enzyme (1 U/ml) resulted in loss of the mutagenic potency of the molecule. The decrease in the fluorescence and mutagenic properties of AFB_1 following treatment with the microbial preparations imply changes to the furofuran- and/or lactone rings of the molecule.

P5

MODULATION OF LIVER FIBROSIS DEVELOPMENT FOLLOWING SUPPLEMENTATION OF ALOE ARBORESCENS*: IN VIVO* STUDY

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Aloe arborescens Mill var. *natalensis* Berger (designated as 'ALOE'), a member of the family Liliaceae, and is valued as a family medicine for gastrointestinal complaints, skin injuries and burns. Various pharmacological and therapeutic activities of ALOE have been studied, and there have been many reports of anti-inflammatory effects, antidiabetic influence, and antitumorigenic effects of extracts. ALOE contains aloin and aloenin as anthranoid. In human cases, anthranoid-containing laxatives use including ALOE has been suggested a risk factor of colorectal tumors. However, in F344 rats, antitumorigenic effects of ALOE have been reported in colorectal tumorgenesis and liver preneoplastic lesions. Therefore, the associations of cancer risk and anthranoid-containing laxatives including ALOE are controversial. The anti-fibrogenic potential of ALOE was evaluated in relation to hepatic stellate cells (HSCs) activation and apoptosis in dimethylnitrosamine (DMN)–induced fibrotic liver in rats. In brief, hepatic fibrosis was induced by DMN for 4 weeks. At the beginning of the third week, part of DMN-treated rats received ALOE (0.418g/100g/day) for preventing therapy for 2 weeks. Untreated-DMN rats were served as control. Liver histopathology and hydroxyproline content were investigated. Smooth muscle actin alpha (α-SMA) was used as a biomarker for HSCs activation using immunohistochemistry, western blotting and real-time polymerase chain reaction (RT-PCR) analysis. HSCs apoptosis was investigated using laser confocal microscopy. Extracellular matrix (ECM) synthesis interrelated factors such as transformation growth factor (TGF-β1) and tissue inhibitor matrix proteinases were studied by westernblotting or real-time PCR. Matrix metal proteinase 2 and 9 (MMP-2/9) were measured by zymography. Hepatic hydroxyproline content was decreased with improved histopathology in ALOE-treated rats. In comparison to the DMN treated group, α-SMA expression in DMN-AA group was reduced signifcantly, however, α-SMA-positive HSCs apoptosis was not observed by confocal microscopy. Fibrogenic proteins (TIMP-1/2, MMP2/14) and cytokines (TNF-α and TGF-β_1) were decreased; MMP-9 was significantly up-regulated. ALOE preparation attenuates the development of liver fibrosis at least in part by suppression activation of Kupffer and inhibition HSCs activation directly rather than promotion cell apoptosis of activated HSCs.

P6

IN VITRO MUTAGENIC ACTIVITY OF 2,2'-(DI-4-METHOXYPHENYL)-1H,1H'-[5,5']-BIS-BENZIMIDAZOLE AND 2,2'-BIS-(3- METHYLPHENYL)-1H,1H'-[5,5']BISBENZIMIDAZOLE

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In this study 2,2'-(Di-4-methoxyphenyl)-1H,1H'-[5,5']-bis-benzimidazole and 2,2'-Bis-(3-methylphenyl)-1H,1H'-[5,5'] bisbenzimidazole derivatives were tested for the ability to cause *Salmonella typhimurium* strains TA 98 and TA100 to revert to histidine independence (Without metabolic activation). Agents were assayed in five different concentrationsThe results indicate that 2,2'-(Di-4-methoxyphenyl)-1H,1H'-[5,5']-bis-benzimidazole is more mutagenic than 2,2'-Bis-(3-methylphenyl)-1H,1H'-[5,5']bisbenzimidazole. In this test methoxyphenyl ligand in the bisbenzimidazole complex has a slight effect on mutagenic capacity of these complexes.

P7

ABSENCE OF ANTIMUTAGENIC EFFECT OF ASPARAGUS, TOMATO, AND GRAPE JUICE ON CYCLOPHOSPHAMIDE-INDUCED GENOTOXICITY IN MICE

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Studies on agents that modulate carcinogen-induced genotoxic effects in experimental animals provide end points that can be used for assessing the antimutagenic or anticarcinogenic properties of putative chemopreventive compounds and for predicting their protective efficacy in humans. We investigated the potency of Asparagus-, tomato- and red grape-juice to modify the proportion of polychromatic erythrocyte (PCE) and frequency of micronucleated polychromatic erythrocytes (MNPCE) induced by cyclophosphamide (CP) in male NIH mice. Three groups of five mice were given the fruit juices (100%, 50% and 25%, diluted with water) *ad libitum*, for 44 days then intraperitoneally (*ip*) injected with 40 mg/kg CP and killed 24 hours later for cytological preparations and analysis. The control group animals were injected with CP (positive) or purified water (negative). Each group mean of the proportion of PCE and frequency of MNPCE was compared with the group mean for the negative and positive control using the Mann-Whitney U test. No statistically significant difference was found between the proportion of PCE in any of the experimental groups compared with the negative control ($P<0.05$), suggesting that CP treatment alone or after pre-treatment with the plant juices did not induce erythropoietic cell toxicity. Pretreatment of the mice with the plant juices did not modify the frequency of CP-induced MNPCE. Tomato-, asparagus- and grape-juices have been shown to inhibit the mutagenic effects of cyclophosphamide and /or other mutagens in different strains of mice and rats, *in vitro* and/or *in vivo* using different route of administration of juice and mutagen (oral by gavage, or *ip* injection) and treatment regime (short pre-treatment, post or simultaneous treatment with mutagen).

P8

MAURITIAN BLACK TEA: ANTIOXIDANT PROPENSITY AND PROPHYLACTIC APPLICATION AGAINST CARDIOVASCULAR DISEASES

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There is convincing data indicating that excessive free radical production and lipid peroxidation are involved in cardiovascular diseases. In this respect plant phenolics are increasingly being studied for their antioxidant properties. Tea has received considerable attention as a protective agent against cardiovascular disease and cancer, two important targets of preventive medicine. Tea is considered to be an important source of phenolics with more than 35 % of their dry weight. HPLC data of the individual phenolics in Mauritian tea infusate revealed high levels of (+)-catechin, (-)-epicatechin, (-)-epicatechin 3-gallate, (-)-epigallocatechin, (-)-epigallocatechin 3-gallate and gallic acid. Antioxidant data generated using FRAP, TEAC, hydroxyl scavenging, hypochlorous scavenging, and microsome lipid peroxidation assays were strongly correlated to the phenolic contents. The *in vivo* investigation of black tea consumption in a randomised clinical trial revealed that daily consumption of a Mauritian black tea infusate (9 g daily) had a reducing effect on high fasting serum levels of glucose (> 140 mg/dl: 20%), cholesterol (> 220 mg/dl: 16 %), triglycerides (> 200 mg/dl: 56%), LDL/HDL ratio (> 3: 37%), uric acid (> 7 mg/dl: 8.5 %), creatine kinase MB (> 200 U/L: 33%), C-reactive protein (> 4 µg/L: 77%) and GOT/GPT ratio (> 2: 35%) while blood plasma showed an increase in antioxidant status as evaluated by the FRAP assay (0.2-0.8 mmol/L: 175%) and TEAC assays (1-2 mmol/L: 32%). This study was funded by the Mauritius Research Council.

P9

IN VITRO MUTAGENIC ACTIVITIES OF (2,2'-BIS-(4-NITROPHENYL)-1H,1H'-[5,5']BISBENZIMIDAZOLE, 2,2'-BIS-(3-NITROPHENYL)-1H,1H'-[5,5']BISBENZIMIDAZOLE AND 2,2'-BIS-(4- METHYLPHENYL)-1H,1H'-[5,5']BISBENZIMIDAZOLE DERIVATIVES

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The Salmonella Ames test system is a short-term bacterial reverse mutation assay widely used to detect the mutagenicity of various chemicals. Bisbenzimidazole derivatives (2,2'-Bis-(4-Nitrophenyl)-1H,1H'-[5,5']bisbenzimidazol, 2,2'-Bis-(3-Nitro-phenyl)-1H,1H'-[5,5']bisbenzimidazole and 2,2'-Bis-(4-methylphenyl)-1H,1H'-[5,5']bisbenzimidazole) were evaluated for their potential mutagenic effects in *Salmonella typhimurium* TA 98 and TA 100 strains by performing Ames Salmonella test (plate incorporation assay) without metabolic activation. The mutagenic response in *Salmonella*, and the structure of the molecule, reveal that nitrophenyl ligand in the bisbenzimidazole derivatives showed greater inducing ablity than did methylphenyl ligand in the bisbenzimidazole derivatives. Results revealed that 2,2'-Bis-(4-Nitrophenyl)-1H,1H'-[5,5']bisbenzimidazole and 2,2'-Bis-(3-Nitrophenyl)-1H, 2,2'-Bis-(3-Nitrophenyl)-1H,1H'-[5,5']bisbenzimidazole have significant effect on mutagenicity.

P10

EVALUATION OF RANDOMLY AMPLIFIED POLYMORPHIC DNA SEQUENCES (RAPDS) AS BIOMARKERS FOR GENOTOXICITY IN EARTHWORMS: EFFECTS OF HEAVY METALS OCCURRING IN MINE TAILINGS AND SOILS

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Earthworms are one of the most important soil animal taxa. As detritivores they fulfill an important role in nutrient transformations and energy flow in terrestrial ecosystems, because they are in direct contact with soils. Earthworms are exposed to heavy metals in the soil, and therefore well suited as indicators for toxin accumulation. It has already been illustrated that heavy metals can cause DNA damage i.e. genotoxic and that RAPDs can be utilized as a tool in such investigations. Heavy metals are present in mining tailings and surrounding soils and the effect on earthworm DNA may be important as an indicator for possible DNA damage. The latter aspect had been demonstrated using comet assay analysis. The aim of the present study was to evaluate RAPD analysis for demonstrating that genetic variation is possibly induced in earthworms exposed to heavy metal polluted mining soils. Several RAPD primers were compared to select optimally suited testing of the genotoxicity. In this preliminary study one of the Operon primers (Cooperation US) OPA 18 had few polymorphic bands when DNA from control earthworms (unexposed) were analysed. DNA from earthworm that were exposed to different tailing and soil types showed differences in RAPD profiles when compared to the profiles of control earthworms. This observation was supported by statistical and clustering analysis. The observed genetic variability could thus have been due to DNA damage when earthworms were exposed to heavy metal containing tailings material and surrounding soils. However, further testing with more primers and more individuals using controlled experiments are needed.

P11

THE IMPORTANCE OF USING VALIDATED DIETARY ASSESSMENT TOOLS IN HUMAN EXPOSURE STUDIES: *A CASE FOR MYCOTOXIN EXPOSURE IN THE FORMER TRANSKEI REGION, SOUTH AFRICA*

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Mycotoxin contamination of food sources is a major problem affecting animal and human health. Environmental monitoring of human exposure to mycotoxins provides many methodological challenges. As diet and nutritional factors are the bases of human exposure and need to be accurately assessed when determining the risk. In the former Transkei region of South Africa fumonisin-contaminated maize is the staple diet of Xhosa-speaking Africans living in this region. A validated and culturally specific dietary assessment method, the ratio and portion size pictures (RAPP) tool was developed to assess dietary exposure. This tool consists of life size photographic pictures of the types of foods mostly consumed and a food frequency questionnaire, focusing on the dietary intake of the past month. A study conducted in the Centane area (n = 319 volunteers, mean age 45 years, mean body weight 69.7 kg) showed a mean maize intake, of 985 g.person^{-1}.day^{-1} which included maize-based dishes. The basic dietary habits indicated that 77% of the participants consume maize as the main dietary cereal and have two meals per day consisting either of bread and a maize-based dish or only maize. Total fumonisin exposure, estimated as the probable daily intake (PDI), was 2.7 (range 0.031 to 11.3) mg kg^{-1}.body weight.day^{-1} and exceeds the provisional maximum tolerable daily intake (PMTDI) of 2 mg kg^{-1}.body weight.day^{-1} as proposed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Accurate dietary intakes and patterns are therefore important for determining exposure and the health risk, a well as to develop intervention strategies.

P12

LOW LEVEL QUANTIFICATION, IDENTIFICATION, AND CHARACTERIZATION OF CARCINOGENIC SUBSTANCES IN DAILY FOOD AND ENVIRONMENTAL SAMPLES USING LC/MS/MS WITH LIBRARY SEARCHING CAPABILITIES

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The method described enables low level quantification of various carcinogenic substances such as mycotoxins, cyanobacterial toxins as well as different classes of environmental pollutants in our daily food stuff or in drinking and surface waters by using liquid chromatography with electro-spray ionization triple quadrupole mass spectrometry (LC-ESI-MS/MS). A limit of quantification for most toxic substances in the lower ppb range can be achieved. QTRAP™ technology allows for simultaneous quantitation, characterization, and identification of these substances. By switching between triple quadrupole and linear ion trap modes of operation during a single liquid chromatograph run, there is a synergy that provides data opportunities not realized by traditional LC-MS/MS approaches. The linear ion trap can collect and store ions, thus greatly improving the sensitivity of the scan over traditional MS/MS scan modes. Another great advantage of enhanced product ion (EPI) spectra is their ability to be compared to an already analyzed set of standards referred to as a library. In this way, the current database for hundreds of carcinogenic substances can be used to verify the identity of a spectrum collected or to elaborate the transformation or metabolization of carcinogens or pathogens. This methodology provides another level of confidence above traditional MRM only quantitation experiments. The methodology described is part of routine food testing for natural or man-made contaminants as well as part of research driven applications such as the investigation for food supplements to modulate cellular parameters of chemoprotection.

P13

ENVIRONMENTAL CONTAMINATION BY RADON: GENOTOXICAL EFFECTS IN CHILDREN FROM WESTERN SIBERIA

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Chromosomal aberrations (CA) in 48-hour cultures of a peripheral blood lymphocytes of 196 children-teenagers in the age of 10 - 19 years (mean 14,2), living in the same ecological conditions - mountain area in Western Siberia (Gornaya Shoria), has been investigated. Mean 180 metaphases from each subject has been scored. Stable increased aberrant cells level (AB.C, %) was discovered in these cohorts during three periods of time: 5,78 ± 0,63 in 1992; 4,74 ± 0,21 in 2005 and 5,42 ± 0,35 in 2007. The background level of this parameter for the given region (the Kemerovo area) for this period of time was 2,62 ± 0,29. Increasing of frequencies for exchanges of chromosomal type was noted too: 0,32 ± 0,14 in 1992; 0,32 ± 0,05 in 2005 and 0,35 ± 0,09 in 2007. In basic control group this parameter was 0,08 ± 0,03. Furthermore at 6 individuals (4,55 %) rogue cells has been found in 2005 and 1 case (2,8%) in 2007. Our repeatedly radon measurements in living quarters and educational rooms air (winter 2007-2008) shown enlarged maintenance of this radioactive gas (mean 298 Bqm3). The reasons of increase in frequency of CA at inhabitants of the given mountain area are discussed. This study was supported by an the program of presidium of the Russian Academy of Science «Adaptation of people and cultures to changes of an environment, social and technogenic transformations»; by the RFBR grant, 07-04-96031-r_ural_a; by the Russian Federal Agency for Science and Innovations (contract 02.512.11.2233).

P14

ASSESSMENT OF DNA SENSITIVITY IN PERIPHERAL BLOOD LYMPHOCYTE SMOKERS AND NON-SMOKERS IN SPONTANEOUS *IN VIVO* AND γ-RADIATION INDUCED *IN VITRO* CONDITIONS

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The induction of micronuclei and bleomicyn-induced chromatid breaks in cultured peripheral blood lymphocytes in spontaneous *in vitro* conditions and γ-radiation induced *in vivo* were investigated. Peripheral blood sample was obtained from a healthy male and female non-smoking and smoking donors (age 20-25 years). A first aliquot of the whole blood sample from each donor was exposed to gamma rays from ^{60}Co source (Alcyon CGR-MeV). Total exposure to radiation lasted 1.24 minutes and the absorbed dose was 2 Gy. Second aliquot of whole blood sample was not irradiated, but it was handled in the same manner. The levels of cytogenetic damage in peripheral blood lymphocytes were evaluated using cytokinesis-block micronucleus assay (CBMN) and chromatid breakage assay (bleomycin-sensitivity assay). The degree of spontaneous of damage of genome in smokers determined by micronucleus assay was higher compared to nonsmokers and the difference reached statistical significance. However, differences in total number of micronuclei of both donors, male and female donors were not found. After *in vitro* exposure of cultured lymphocytes to γ-radiation smokers had high numbers of micronuclei compare with non-smokers. Chromatid breakage assay established that the differences in break per cell (b/c) values between smokers and non-smokers were increased in cultured peripheral blood lymphocytes in spontaneous *in vivo* conditions and γ-radiation induced *in vitro.* The level of chromosome damage generated by bleomicin varies greatly between individuals and this results indicate inter-individual differences in DNA damage between donors, and differences in genome radiosensitivity.

P15

THE EFFECT OF SUBCHRONIC COMBINED EXPOSURE TO AMOSITE, REFRACTORY CERAMIC FIBRES AND CIGARETTE SMOKE ON THE SELECTED BAL PARAMETERS AND LUNG TISSUE

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Refractory ceramic fibers (RCF) are used as one kind of asbestos substitutes. As RCF are relatively durable and some of them are respirable, they might represent a potential inhalatory health hazard. The aim of this study was: 1) to find and compare the effects of subchronic exposure to amosite (AMO), RCF, cigarette smoke (CS) and the combined exposure to AMO + CS and RCF + CS by analyses of inflammatory, cytotoxic and genotoxic parameters of bronchoalveolar lavage (BAL) and by lung histology, 2) to find out if smoking amplifies the possible adverse effect of RCF as it is known after combined exposure to asbestos + CS. After 6-months exposure, the animals were exsanguinated and BAL was perfomed. Following characteristics were examined: BAL cell count; alveolar macrophages (AM) count, differential cell count (% of AM, polymorphonuclears and lymphocytes), % of immature AM, binucleated cells, viability and phagocytic activity of AM, frequency of micronuclei (MN), comet assay and histology of lung tissue. The results of our work suggest: 1) There are no great differences between AMO and RCF exposure and their combined effects with cigarette smoke in the BAL inflammatory and cytotoxic parameters under our experimental conditions. 2) RCF did not treated MN; comet assay results were not significantly influenced after AMO or RCF exposure. 3) According to histological findings, there are differences in the lung tissue injury (fibrosis) between AMO (grade 8) and RCF (grade 5) exposure and there is no fibrosis effect (grade 0) after cigarette smoke exposure only.

P16
VIABILITY OF TOXIGENIC, PLANT PATHOGENIC AND MEDICALLY IMPORTANT FUNGI

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Cultures of toxigenic, plant pathogenic and human pathogenic fungi are important in research and the conservation of biological diversity. Maintaining fungal cultures under optimal conditions, ensuring long term viability, is essential at the PROMEC Unit of the MRC. All strains (9000) were originally lyophilized from a conidial suspension in lactose phosphate buffer, obtained from a single-conidial culture, and stored at 4ºC. Lyophilized cultures were revived by resuspending the contents of the vial in 2 ml sterile distilled water and inoculating PDA plates, which were incubated at 25ºC for 7 days and examined. The genus *Fusarium* that forms the largest group (>6000 strains and 100 species) showed an overall survival rate of 71%. *Aspergillus* (>520 strains) and *Penicillium* (>450 strains), represented by more than 20 species each, showed survival rates of 90-100% for all species. Whereas *F. verticillioides* and *F. proliferatum* strains had a survival rate of 95% and more, only 25% of *F. graminearum* strains survived. *Stenocarpella* species had the poorest survival rate of 6%. The overall survival rate of the total of 9000 lyophilized fungal cultures was 74%. Thirty percent of the surviving cultures have been stored for 1-10 years, 32% for 11-20 years and 38% for 21-30 years. Alternative methods of preservation, including storage on PDA at 4ºC or -80ºC and in 15% glycerol at -80ºC, were tested on *F. graminearum* complex, *F. pseudograminearum*, *F. crookwellense*, *S. marcosopora* and *S. maydis*. Of these alternative methods, PDA at 4ºC, showed the best survival rates for the preservation of fungi that do not survive lyophilization well. Some variation in the results were recorded for all the fungi tested, which indicates that more than one vial or PDA McCartney slant should be stored using different preservation methods in order to ensure survival of a species or individual strains within a species.

P17

ASSESSMENT OF MULTIPLEX-PCR AND PCR-BASED DNA PROFILING METHODS FOR THE DETECTION AND IDENTIFICATION OF *FUSARIUM* SPECIES

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The genus *Fusarium* is an important plant pathogen that is responsible for severe crop losses due to lower yield and quality of crops. Apart from causing several plant diseases, this genus also produces mycotoxins. Various methods are available for the detection and identification of *Fusarium*, each with distinctive advantages and disadvantages. The most frequently genes used molecular analysis of *Fusarium* include elongation factor 1-α (EF-1α), internal transcribed spacer (ITS) region, beta-tubulin (β-tubulin) and polyketide synthase (FUM1) sequences. The aim of this study was to develop and evaluate multiplex PCR-denaturing gradient gel electrophoresis (DGGE) and single strand conformational polymorphism (SSCP) as DNA profiling methods for the detection of mycotoxigenic *Fusarium* spp.. In the profiling methods (DGGE and SSCP) the EF-1α gene region was used. Multiplex PCR for various *Fusarium* species and strains was performed using the EF-1α and FUM1 primer sets. EF-1α fragments were excised from agarose gels and re-amplified to produce ~500bp fragments with and without a GC-clamp. Fragments were then subjected to DGGE and SSCP analyses. The DGGE approach used in this study could not distinguish between the various *Fusarium* species and strains. Similar banding patterns were observed for most of the *Fusarium* species and strains analysed. Multiple bands were also observed for a single species and strain. On the other hand, PCR-SSCP analysis permitted some differentiation of species when DNA from single species were used. Different banding patterns between the various *Fusarium* species and strains were evident although large EF-1α fragments (~500bp) were used. Therefore, the PCR-SSCP method developed here may have potential to rapidly assess *Fusarium* community composition from contaminated food and feed samples. However, a draw back was that some additional non-specific bands were present in the PCR-SSCP profiles when EF-1α fragments extracted from multiplex PCR were analysed. This aspect is presently being investigated and addressed.

P18

MOLECULAR PHYLOGENY OF VARIOUS *FUSARIUM* SPECIES AND STRAINS USING EF-1α AND β-TUBULIN GENE FRAGMENTS

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Phylogenetic relationships among various *Fusarium* species and strains were investigated by neighbour-joining analyses of the EF-1α and β-tubulin gene sequences. Divergent topologies were observed between the β-tubulin and EF-1α gene trees. Neighbour-joining analysis indicated two main clusters (Cluster A and B) for the β-tubulin gene fragments. Bootstrap support for cluster A and B oscillated between 59 and 100%. The phenentic dendogram grouped the three reference strains, as well as *F. subglutinans*, *F. oxysporum*, *F. proliferatum*, *F. nygamai* and one *F. verticillioides* strain into Cluster A. Cluster B mainly consisted of seven *F. verticillioides* and three *F. oxysporum* strains. Dendogram for the EF-1α fragments were divided into four main groups: *F. verticillioides*, *F. nygamai*, *F. proliferatum* and *F. oxysporum*. The *Fusarium* species and strains used were grouped within the appropriate cluster with sequence similarities above 88%. Thus, genetic relationships between the various *Fusarium* species and strains were more accurate and consistent with the EF-1α gene than with the β-tubulin gene. The results presented in this study demonstrated the high discriminatory power of the EF-1α gene for phylogenetic analysis of *Fusarium* as well as the potential suitability of using these sequences (EF-1α genes) for DNA profiling such as single strand conformation polymorphism (SSCP).

P19

DETERMINATION OF PATULIN IN APPLE JUICE: COMPARATIVE EVALUATION OF FOUR ANALYTICAL METHODS

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Patulin is a polyketide lactone produced by certain *Penicillium, Aspergillus* and *Byssochlamys* species growing on apples, pears, grapes and other fruit. It is considered immunotoxic, genotoxic, embryotoxic and neurotoxic. The presence of patulin is considered a marker of the quality of apples entering the processing factory and levels in the final product are subject to legislative regulatory control. The performance of four purification methods for the analysis of patulin in apple juice was evaluated by high performance liquid chromatography (HPLC). Samples were spiked with patulin at 10, 20, 50, 100 and 150 ppb (ng/ml) and extracted by one of four methods (three solid phase extraction and one liquid-liquid extraction), and then analysed by HPLC – UV under the same isocratic conditions. The methods were validated for recovery, linearity and precision at high and low concentrations. Recoveries were all higher than 70% for spiking range 10 – 150 ppb. The RSD for repeatability was found to meet EU Directive requirements. In addition all the methods showed baseline separation from hydroxymethylfurfural (HMF).

P20

APOPTOSIS AND MONONUCLEAR CELL SURFACE MARKERS EXPRESSION AMONG PERSONS OCCUPATIONALLY EXPOSED TO X-RAYS IN CARDIAC CATHETERIZATION UNITS

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The aim of the present study was to evaluate the immunological status among medical personals occupationally exposed to ionizing radiation at the cardiac catheterization units of three different University hospitals in Cairo, Egypt. The individual annual collective dose information was estimated with thermoluminescence dosimetry system dose for those workers ranged from 0.02- 0.3 mSv/y 0.42-0.94, mSv/y and 1.16-8.44 mSv/y as measured by thermoluminscent personal dosimeters (TLD). Venous blood samples were obtained from 60 medical personals exposed to x-ray during fluoroscopy procedure. At three different hospitals (Ain Shams, Al Azhar and National Heart Centerat Embaba) vs. 20 persons not exposed to ionizing radiation and not working at hospitals vs. 20 persons not exposed to ionizing radiation and working at hospitals. Blood samples were assayed for total and differential blood count, micronucleus formation and cell phenotype for CD4 for T-helper and CD8 for T-cytotoxic. Results revealed significant increase in the frequency of micronuclei (10.1 ± 3 % vs. 3.6 ± 1.2 %, $p < 0.001$), CD4 (38.4 ± 9.7 vs. 13.1 ± 5.8, $p<0.0001$) and CD8 (25 ± 9.2 vs. 8.1 ± 5.5, $p<0.0001$). It is concluded that Total Differential counts of WBCs could not be accurate determinant for low dose exposure effects on the human body, whereas micronucleus formation and cell phenotype analysis for lymphocyte subpopulations populations including CD4, CD8, CD4/CD8 can offer a more precise indicators for radiation exposure to low dose levels of ionizing radiation.

P21

DNA PROTEIN CROSS LINK AND FREQUENCY OF MICRONUCLEI AMONG NURSES DUALLY EXPOISED TO GLUTARALDEHYDE AND IONIZING RADIATION

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Most mutagens are known to stimulate leucocytes. During such stimulation, activation of transcription factors, which are DNA-binding proteins that regulate gene expression of a variety of genes, including cytokines and growth factors, that functions to enhance the transcription-phase proteins and this can be measured in terms of the assay for DNA-protein cross links. The frequency of micronulei in human lymphocytes proved to be a reliable assay for genotoxicity. Thus, to measure the radio-sensitivity among individuals, we assessed the frequency of micronuclei (FMN), DNA-protein cross links and apoptosis percentage in circulating lymphocytes among 20 nurses exposed solely to glutaraldehyde, and 20 dually exposed to glutaraldehyde and ionizing radiation. Our results showed a significant increase in the levels FMN, apoptosis percentage and DNA-cross links among nurses occupationally exposed solely to glutaraldehyde and dually exposed to glutaraldehyde and ionizing radiatio compared to controls compared to controls. Nurses exposed solely to glutaraldehyde showed significant increased DNA-protein cross-links accompanied by significant increase in FMN and apoptosis percentage in circulating lymphocytes compared to those dually exposed to glutaraldehyde and ionizing radiation. Results indicate the genotoxic effects of glutaraldehyde among exposed persons and call for adequate preventive measures to protect such nurses.

P22

INVESTIGATING THE CHEMOPREVENTIVE ACTIVITY OF SELECTED SOUTH AFRICAN HERBAL TEAS, ROOIBOS (*ASPALUTHUS LINEARIS*) AND HONEYBUSH *SPP.* IN NORMAL AND CANCER HUMAN SKIN CELLS

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The multiple stages of skin carcinogenesis include initiation, promotion and progression. Cancer promotion, characterized by uncontrolled cell proliferation and chronic inflammation in the skin often forms the basis of chemoprevention studies. Unfermented rooibos (*Aspalathus linearis*) and honeybush (*Cyclopia spp*) possess anti-carcinogenic properties in *in vitro* and *in vivo* assays. However, there is a lack of knowledge on the protective mechanisms involving the different honeybush species, rooibos and green tea (*Camelia sinensis*) in skin carcinogenesis. This study was aimed at performing a comparative investigation *in vitro* on the anti-proliferative and anti-inflammatory activity of unfermented green tea, rooibos and four honeybush herbal teas (*C. genistoides, C. subternata, C. intermedia, C. longifolia).* Aqueous and methanol extracts were prepared and analysed for total polyphenols, flavonol/flavone and flavanol/proanthocyinidins flavonoid subgroups. The antiproliferative properties of the aqueous and methanol extracts were assessed and compared in normal (CRL 7761) and cancerous (CRL 7762) fibroblasts by monitoring the effect on cell viability (ATP production) and cell-proliferation (BrdU incorporation). Results indicated differential anti-proliferative effect exhibited by the various tea extracts against the normal and cancer cell lines. The parameters investigated will be used to investigate the chemopreventive properties of selected herbal tea extracts in an *in vivo* two-stage mouse skin cancer model.

P23

INVOLVEMENT OF A NOVEL NEUROPEPTIDE EM66 IN THE NEUROENDOCRINE RESPONSE TO IMMUNE STRESS INDUCED BY THE ENDOTOXIN LIPOPOLYSACCHARIDE

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The hypothalamic paraventricular nucleus (PVN) is involved in the neuroendocrine adaptative response to stress through parvicellular effector neurons synthesizing and releasing into the pituitary portal blood the corticotropin releasing hormone (CRH). The CRH neurons have a high potential for phenotypical plasticity, allowing them to modify their neuroendocrine output depending upon circumstances (nature and intensity of a stimulus). Indeed, in addition to CRH, they elaborate several other neuropeptides, such as vasopressin, cholecystokinin, enkephalin or neurotensin, each probably subserving a complementary function to CRH in the control of the pituitary and each depending on different regulatory mechanisms for its expression. For example, vasopressin (VP) is a powerful pituitary corticotropin (ACTH) releaser and VP mRNA is overexpressed in CRH neurons in response to various stressful stimuli. EM66 is a 66-amino acid peptide derived from secretogranin II, a member of granin acidic secretory protein family, by proteolytic processing. EM66 has been first characterized in the adult and foetal human adrenal gland, as well as in the rat pituitary and specific hypothalamic nuclei suggesting putative endocrine and/or neuroendocrine roles for this peptide. EM66 is strongly expressed within parvicellular NPV neurons and may be involved in the response to stress. The aim of the present study was to explore the possible involvement of EM66 in the response to immune stress induced by the endotoxin lipopolysaccharide (LPS) in rat. Immune system activation by LPS induces the release of interleukin-1 (IL-1) that centrally activates PVN CRH neurons, leading to ACTH discharge in order to trigger glucocorticoid secretion from the adrenal which in turn modulates the immune response. Injection of LPS is known to induce an array of peripheral and central responses associated with increased activity of the hypothalamic–pituitary–adrenal axis by increasing PVN CRH mRNA and circulating corticosterone levels. A single dose of LPS (Xmg/ml) was administered intraperitoneally to adult male rats that were killed 8 h later. The EM66 intraneuronal expression was evaluated by immunocytochemistry using polyclonal antibodies directed against EM66. Compared to control animals, LPS-injected rats showed increased expression of paraventricular EM66 (52% increase of the number of EM66-immunopositive neurons). Taking into account the similarity of the patterns of distribution of EM66 and CRH neurons within NPV, and the positive fluctuation of the two neuropeptides following immune stimulation, our results suggest that EM66 constitutes an additional accessory neuropeptide expressed in CRH paraventricular neurons which may participate to phenotypic plasticity of these neurons in order to regulate the corticotrope axis activity. These data argue for the involvement of the novel neuropeptide EM66 in the neuroendocrine response to immune stress.

P24

ASSESSMENT OF *MICROCYSTIS AERUGINOSA* BLOOM TOXICITY ASSOCIATED WITH WILDLIFE MORTALITY IN THE KRUGER NATIONAL PARK, SOUTH AFRICA

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Cyanobacterial blooms in man-made water impoundments in the Kruger National Park (KNP) were associated with wildlife mortality. Water samples were collected from four dams (Nhlanganzwani, Mpanamana, Makhohlola and Sunset Dams) from the south eastern part of the KNP during episodes of wildlife mortality that occurred during January and July 2007. The toxicity of the algal blooms was investigated using the Enzyme-Linked Immunosorbent Assay (ELISA), Protein Phosphatase Inhibition (PP*i*) assay and Mouse Bioassay. Both the ELISA and PP*i* assays indicated that the water sample collected, during February 2007, from the Nhlanganzwani Dam and samples collected from the Nhlanganzwani and Sunset Dams, during June-July 2007, were toxic. These dams, containing toxic *Microcystis aeruginosa* blooms, were also the dams associated with wildlife mortality. Mice injected intraperitoneally with water samples from Nhlanganzwani Dam (February 2007) induced hapatotoxicity and mortality within an hour. These laboratory results confirm that the wildlife mortality in the KNP was due to toxic *M. aeruginosa* blooms. The eutrophication and blooms appear to have been caused by high Hippopotami (*Hippoppotamus amphibious*) numbers in specific dams.

P25

MEASUREMENT OF BIOMARKERS OF OXIDATIVE DNA DAMAGE IN SYSTEMIC SCLEROSIS

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Background: Reactive oxygen species (ROS) are derived from the metabolism of molecular oxygen. The metabolic reduction of oxygen results into highly reactive species, e.g. superoxide anion radical ($O_2^{-\cdot}$) and hydroxyl radical ($^{\cdot}OH$). The major sources of endogenous ROS are generated as by-products of cellular metabolism, e.g. mitochondrial respiration. ROS can cause tissue damage by reacting with lipids in cellular membranes, e.g. systemic sclerosis (SSc). Moreover, ROS can cause oxidative DNA damage and this has been implicated in human diseases, e.g. cancer. Markers of oxidative DNA damage in human biomonitoring studies include single and double DNA strand breaks (SSB and DSB), and oxidized nucleosides such as 8-hydroxydeoxyguanosine, etc., which can be measured using Comet assay with restriction enzymes and in serum and urine using ELISA methods. Objective: To determine the occurrence of oxidative DNA damage in SSc using various genotoxicity biomarkers. Subjects and Methods: Ten patients fulfilling the American College of Rheumatology (ACR) criteria for SSc and attending the Connective Tissue Diseases Clinic, Chris Hani Baragwanath Hospital, Soweto were studied. Oxidative DNA damage was assessed by the Comet assay as described by Singh et al, with modifications using Formamido pyrimidine (FPG) restriction enzyme and by measurement 8-OHdG adducts in urine and serum using an ELISA assay (Assay Designs). Results and Discussion: Positive results were obtained with all methods tested with certain biomarkers, notably FPG sites by Comet assay and 8-OHdG (ELISA), being significantly higher in the SSc group than in age- and ethnically-matched healthy controls. Positive correlation was observed between Comet % Tail DNA and urinary levels of 8-OHdG in both study groups. Conclusion: These results indicate oxidative DNA damage in SSc in the form of SSB, DSB, and oxidized bases, DNA FPG sites and 8-OhdG.

P26

MEASUREMENT OF OXIDATIVELY MODIFIED DNA LESIONS IN URINE OF SYSTEMIC SCLEROSIS PATIENTS

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Background: Oxidative stress, including oxidative damage to DNA is a result of interaction of DNA with reactive oxygen species (ROS), has been thought to contribute to the general decline in cellular functions that are associated with many human diseases including human cancers. Oxidative stress is implicated in the causation of tissue damage in systemic sclerosis (SSc). Lipid peroxidation, measured by a number of different methods, has been found to be increased in SSc[1]. Several studies have presented evidence to suggest that oxidative DNA damage is increased in certain autoimmune diseases, e.g. systemic lupus erythematosus[2], but there is no published data in SSc. Markers of oxidative DNA damage in human biomonitoring studies include oxidized nucleosides such as 8-hydroxydeoxyguanosine which can be analyzed from isolated DNA and urine. Objective: To investigate the excretion of 8-hydroxydeoxyguanosine (8-OHdG) in urine of SSc patients in comparison with healthy controls. Subjects and Methods: Ten patients fulfilling the American College of Rheumatology (ACR) criteria for SSc and attending the Connective Tissue Diseases Clinic, Chris Hani Baragwanath Hospital, Soweto, and 15 age- and ethnically-matched healthy controls were studied. Oxidative DNA damage was assessed by measuring urinary 8-OHdG adducts using an ELISA assay (Assay Designs). Results and Discussion: Levels of 8-OHdG were significantly higher (p=0.0003) in SSc group (0.85±0.54µg/mg creatinine) than in the control group (0.2±0.136µg/mg creatinine); suggesting increased urinary excretion of this lesion in SSc as further evidence of oxidative stress in general and oxidative DNA damage in particular in SSc. Conclusion: Measurement of urinary 8-OHdG can be a useful biomarker for evaluating in vivo oxidative DNA damage in SSc. References: 1. Tikly *et al.* Clin Rheumatol 2006; 25:320. 2. McConnell *et al.* Clin Exp Rheumatol 2002; 20:653.

P27

THE ANTI-PROLIFERATIVE EFFECTS OF AQUEOUS AND ORGANIC EXTRACTS OF *SUTHERLANDIA FRUTESCENS* IN HUMAN LIVER, COLON AND OESOPHAGEAL CANCER CELL LINES

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Cancer development is a multistep process in which a carcinogen interacts with DNA in the presence of an environment containing promoting agents which stimulate proliferation of cells. Most cancer treatments have numerous drawbacks, most importantly severe effects and resistance. The continued search for new drugs is indispensable. The use of natural products is considered of utmost importance in the control of cancer, hence our exploration of *Sutherlandia frutescens. S. frutescens* also known as cancer bush (English), kankerbos (Afrikaans) and unwele (Zulu), is a multipurpose herb which has displayed anti-cancer properties *in vitro*. This study is aimed at determining the antiproliferative effect of aqueous and organic (DCM:MeOH) extracts of *S. frutescens* in human liver (Hep-G2), colon (HT-29) and oesophageal (WHCO5) cancer cell lines. ATP production was determined using the CellTiter Glo® Luminescent Cell Viability assay and the IC_{50} values calculated. Anti-proliferative effect of the extracts was monitored using a luminescence-based bromodeoxyuridine (BrdU) incorporation assay at concentrations below IC_{50}. Oesophageal cancer cells were more sensitive to the aqueous and organic extracts in disrupting ATP production with the colon cancer cells the most resistant. Overall, the organic extract was more effective than the aqueous extract at inhibiting ATP production in all cancer cell lines. The different extracts showed selective effects on cell viability in the three cancer cell lines with the organic extract exhibiting the highest response. The anti-proliferative properties of the aqueous and organic extracts in the three cancer cell lines are currently in progress.

P28

INDUCTION OF DNA STRAND BREAKS AND MICRONUCLEUS FORMATION CAUSED BY TONER PARTICLES AND TONER PARTICLE EXTRACTS FROM LASER PRINTERS IN HUMAN LUNG CELLS

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Toners for laser printers are generally a particulate mixture of plastic resin and carbon black (CB) or iron oxide, often with numerous other additives. A study carried out recently for the German Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung, BfR) has shown that laser printers and photocopiers emit fine and ultrafine particles into indoor air that may partly consist of toner particles. Additionally, exposure to toner particles is possible via dermal contamination and inhalation while operating and servicing laser printers and photocopiers. Therefore, in the present study we investigated the cytotoxic and DNA-damaging potency of three commercial toners and their dimethyl sulfoxide (DMSO) extracts in human A-548 lung adenocarcinoma cells. In the present study, cytotoxicity was assessed using the lactate dehydrogenase (LDH) assay. Additionally, the mutagenicity and genotoxicity (DNA migration) was evaluated by the micronucleus (MN) assay and the single cell gel electrophoresis assay (Comet assay). Benzo(a)pyrene (Bap) and quartz DQ12 were used as reference controls. All toner particles showed cytotoxicity in A-549 cells when using higher concentrations. Furthermore, all toner particles caused significant and dose-dependent DNA migration and micronucleus induction, albeit to varying extents. With respect to the investigation of DMSO extracts, only the extract of one toner showed cytotoxicity. All toners caused significant DNA damage in the Comet assay, but only two toners induced micronuclei formation. Taken together, our results showed that toner particles based on CB and iron oxide may cause cytotoxicity and DNA damage in human lung carcinoma epithelial cells.

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GENOTOXIC AND ANTIGENOTOXIC PROPERTIES OF THREE STRUCTURE RELATED ISOTHIOCYANATES IN HUMAN HEPG2 HEPATOMA CELLS

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Isothiocyanates (ITCs) belong to a class of chemopreventive compounds derived from cruciferous vegetables of the *Brassicaceae* plant family. In numerous epidemiological and experimental data, ITCs have been shown to possess a potent inhibitory effect on cancer development and are effective protectors against dietary carcinogens such as polycyclic aromatics hydrocarbons (PAHs) or aflatoxins. However, there is evidence that ITCs can also exert genotoxic and co-carcinogenic effects. In the present study, we used the single cell gel electrophoresis (SCGE) assay and the micronucleus (MN) test to investigate the DNA damaging effects, the antigenotoxic potencies and the influence of DNA repair capacities of three structurally related ITCs, which differ only in the length of the alkyl chain, on human HepG2 cells. Cell viability was determined by the tetrazolium dye-forming WST-1, erythrosine B and the nuclei division index. Our results show that all three ITCs possess both genotoxic and antigenotoxic potential, dependent on the applied concentration. Interestingly, the comet assay showed significant DNA damage at much lower concentrations compared to the results derived with the MN test. Experiments on the cellular repair capacities of HepG2 cells revealed that ITC-induced DNA migration could be significantly reduced for a period of 1 h, which could partly explain the differences obtained with the two test systems. The increase in the genotoxicity parameters was accompanied by a decrease in cell viability and proliferation, as assessed by the Erythrosin B method and the WST-1-assy, respectively. These results could help to weigh up the pros and cons of ITC intake.

P30

REAL-TIME PCR ANALYSES OF FUMONISIN BIOSYNTHETIC *FUM* GENES IN *FUSARIUM VERTICILLIOIDES* MRC 826 SUBCULTURES

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Fumonisins were first implicated in various animal diseases such as equine leukoencephalomalacia. These mycotoxins have been established to cause liver cancer in rodents and pulmonary edema syndrome in pigs. They also have epidemiologically been linked to oesophageal cancer in both South Africa and China and more recently it has been proposed that fumonisins be considered a potential risk factor for birth defects, including human neural tube defects (NTD) in populations consuming fumonisin-contaminated maize. *F. verticillioides* strain MRC 826 isolated from maize collected from the Transkei region in 1975, originally produced unsurpassed high levels of fumonisins, particularly FB_1, up to 17900 µg/g of cultured material. Several subcultures of this isolate have been established over the past 25 years and a reduction, as well as fluctuation in the ability of this strain to produce total fumonisins has occurred. In order to elucidate the mechanism by which *Fusarium verticillioides* produces fumonisins, a study into the gene regulation of fumonisin production is being done. The fumonisin biosynthetic gene cluster consists of 15 genes, namely *FUM* genes. A set of *F. verticillioides* MRC 826 subcultures that were previously grown under varying cultural conditions, including diverse media, and were shown to exhibit fluctuating fumonisin levels is being studied. AFLP analysis of 14 MRC 826 subculture strains confirmed the homogeneity of the subcultures. Quantitative Real-time PCR was performed to ascertain whether the *FUM* genes are differentially expressed or absent in the strains with varying fumonisin profiles. Elucidating the roles of the *FUM* genes and investigating what genes are expressed to a different extent in high producing strains, may enable the blocking of the expression of the *FUM* genes, thereby reducing the synthesis of the carcinogenic mycotoxins. Through understanding the regulation of fumonisin biosynthesis, specific measures can be developed to control fumonisin production by identifying possible target areas for reduction of toxin production.

P31

GENOTOXIC PROFILE OF FURAN AND ITS KEY METABOLITE CIS-2-BUTENE-1,4-DIAL IN MAMMALIAN CELLS *IN VIVO* AND *IN VITRO*

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Furan, a possible human carcinogen present in a wide variety of human foods is formed during its processing results in widespread human exposure. It is a potent carcinogen in rats and mice showing a dose-dependent increase in hepatocellular adenomas and carcinomas. In rats, dose-dependent increases in mononuclear leukaemia and a very high incidence of cholangiocarcinomas of the liver are also seen at dose-levels as low as 2 mg/kg b.w., which is very close to the possible human exposure. The mechanism for carcinogenicity of furan is not well understood, though genotoxicity is regarded as a plausible mechanism. Furan is metabolized by cytochrome P450 2E1 to a bifunctional electrophilic metabolite, cis-2-butene-1,4-dial which potentially binds proteins and DNA and could probably be responsible for its carcinogenic properties . However, the available data on the genotoxicity of furan and cis-2-butene-1,4-dial are highly inconsistent and controversial both *in vivo* and *in vitro*. In the present study we discuss positive cytogenetic effects in the absence of rat liver S9 metabolism (CYP 450, 2E1) in human lymphocytes cultured *in vitro* and in two lymphoblastoid cell lines both in the presence and absence of rat liver S9 metabolism (CYP 450, 2E1) from Fanconi's Anemia Patients with different mutations in the gene Fanc A (which are hypersensitive to DNA cross-linking agents). Positive findings obtained with cis-2-butene-1,4-dial *in vitro* are also discussed. In rat *in vivo* we show positive cytogenetic effects in splenocytes at dose-levels of 2mg/kg b.w. but negative results for chromosomal aberrations and micronuclei in bone marrow erythrocytes. Significant increases in DNA breakage (alkaline comet assay pH 13.1) were observed following 4 weeks daily treatment at dose-level of 2 mg/kg b.w. and recovery of two weeks. Generation of relevant mechanistic information on induction of chromosomal damage both in vivo and *in vitro* is an important support for the ongoing risk assessment of human furan exposures with food. Acknowledgements: The work is financially supported by European Commission, call FP6-2005-SSP-5A (Contract no. SSPE-CT-2006-44393, Specific Targeted Research Project) "Role of genetic and non-mechanisms in furan risk.

P32

AFLATOXIN M_1 AND FUMONISIN B_1 CONTAMINATION IN FRESH MILK FROM SELECTED RURAL AREAS OF SOUTH AFRICA: THE CASE OF THE LIMPOPO PROVINCE

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The occurrence of mycotoxins in commercial animal products has been well investigated, particularly the carryover of aflatoxin into milk as aflatoxin M_1 (AFM1). This is hardly surprising considering that AFM_1 is a hydroxylated product of aflatoxin B_1, both metabolites being considered highly carcinogenic and classed as group 1 carcinogens causing liver cancer. Far less attention has been placed on the situation in Africa rural areas with respect to the impact of mycotoxins on rural animals and in turn their impact on the rural people who farm them. Animals and their feed were studied in two rural areas in Limpopo Province for exposure to and carryover of mycotoxins into dairy products, meat, etc. In general the animals, cattle, goats, chicken and sheep were allowed to forage for themselves, whilst pigs were penned and fed whatever was available from the household. For cattle this usually meant browsing in old maize fields and other plots. Altogether 100 samples of animal feed and 50 samples of fresh milk obtained from cattle and goats were analyzed for fungi and mycotoxins contamination. *Aspergillus niger, A. clavatus*, *A. flavus*, *A. fumigatus*, *Fusarium verticillioides*, *F. graminerium* and *F. proliferatum* were the most prevalent fungi in analysed fodder (all samples showed contamination). Aflatoxin M_1 was detected at 25.0 - 108.4 µg/l in 100% of the milk samples on ELIZA (Neogen) analysis with validation by HPLC. Traces of fumonisin B_1 (100-200ppb) were detected in 2 % of milk samples by ELISA and HPLC. Finally a cytotoxicity essays were carried on lymphocytes using fumonisins and aflatoxins standards and extracts with positive dose response toxicity results. There concern for alarm with these results, considering the prevalence of AFM1 found in the milk samples.

P33

IN VITRO STUDIES ON THE TOXICITY OF AFLATOXINS AND ZEARALENONE IN PRIMARY HEPATOCYTES OF THE AFRICAN SHARPTOOTH CATFISH (*CLARIES GARIEPNUS*)

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In vitro assays using isolated fish cells are increasingly used to measure the induction of cytochrome P4501A (CYP1A) and its associated enzyme activity, 7-ethoxyresorufin-*O*-deethylase (EROD). The induction of CYP1A is used as a biological marker in response to xenobiotic exposure. The use of the primary hepatocytes of the African Sharptooth catfish to assess EROD activity, cytotoxicity and ultrastructural alterations when exposed to the xenobiotic models, aflatoxins and zearalenone was investigated. Results obtained showed that aflatoxins and zearalenone are able to induce CYP1A activity in a biphasic manner at concentrations ranging from 10^{-6} M to 10^{-8}M. Cytotoxicity using the methyl thiazol tetrazolium (MTT) assay was not observed at all concentrations used (10^{-5} M to 10^{-10}M). Ultrastructural alterations observed using transmission electron microscopy showed swollen mitochondria, and endoplasmic reticuli (ER), and whorls of ER in mycotoxin exposed hepatocytes. This study shows that the primary hepatocytes of the African Sharptooth catfish may be used to determine the mechanism of toxicity of mycotoxins.

P34

FUNGI AND MYCOTOXINS ASSOCIATED WITH FOOD COMMODITIES IN CAMEROON

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Spoiled maize grains and numerous types of snacks that are consumed in the Western Highlands of Cameroon are infected by several mycotoxin producing fungi. The extent of contamination of these food commodities by secondary metabolites of fungal origin has not been well studied. This study aimed to identify the microorganisms that infect maize grains and snacks sold at road side markets, and to sensitize the population on the health risks that are associated with consumption of contaminated commodities. Maize and snack samples were collected from various locations in Cameroon. Contaminating microorganisms were isolated and identified using conventional techniques. *Staphylococcus* and *Salmonella* species were the most frequently isolated bacteria while *Fusarium* and *Aspergillus* species were isolated in highest frequency ranging from 20 to 100 % presence in the samples analysed. Chemical analyses revealed the presence of fumonosins (50-26000 ng/g), deoxynivalenol (100-1300 ng/g) and zearalenon (50-180 ng/g) in the sampled maize. Contamination of agricultural products by microbial toxins is an important but often underestimated risk to public health and can have long-term health implications. Appropriate sanitary measures need to be taken to ensure that conditions for microbial contamination and toxin production are reduced or eliminated during the handling, transportation, packaging and storage of all agricultural products.

P35
LATE POST-IRRADIATION EFFECTS IN CHO CELLS

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Changes in the genome damage level, radiosensitivity and apoptotic cells number were studied in generations of irradiated Chinese Hamster Ovary cells (CHO K1 cell line). Three independent experiments were conducted. Using the neutral version (neutral pH) of DNA comet assay we registered 1.5-2.0 folds increase in DNA fragmentation (mainly due to double-strand DNA breaks) in cells immediately after gamma-rays irradiation in dose of 1 Gy. The DNA fragmentation level in generations of irradiated cells 2-4 days after exposure was similar to control values. However, the significant increase of DNA fragmentation (*de novo*) was registered 7 days after exposure to gamma-radiation that is probably appearance of the radiation-induced genome instability. The increase of DNA fragmentation remains up to 21st day of experiments with maximum values for 11th and 18th days. Nevertheless, the DNA fragmentation level in generations of irradiated cells for 23-28 days after exposure was reduced to control values. The results on the apoptotic cells level using “DNA-halo” method showed significant increase of the apoptotic cells fraction in generations of irradiated cells for 7-21st days after exposure. Most probably, the increase of DNA fragmentation level described above is conditioned by significant level of apoptotic cells with high-fragmented DNA. The most interesting results were obtained after investigations of the irradiated cells generations radiosensitivity. Thus, the significant increase of cells sensitivity to additional gamma-rays irradiation in dose of 10 Gy was shown for 9, 11, 16 and 18th days after exposure but there was an converse effect (resistant to additional irradiation) since 21st day up to the end of experiments (28th day). In conclusion, the obtained results are recent and demonstrate a selective pressure of the genome instability leading to the radioresistant cell clones forming.

P36

MODULATION OF OXIDATIVE STRESS IN THE SKIN BY EXTRACTS OF HONEYBUSH ON THE ACUTE AND CHRONIC EFFECTS OF UVB

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The acute effects of ultraviolet B (UVB) light on the skin include erythema, oxidative stress, DNA damage and inflammation, while the chronic effects include skin cancer and aging. These acute effects of UVB exposure may contribute to the chronic effects of UVB, therefore reducing the acute effects could help prevent the development of skin cancer. Previously, it was shown that topical application of extracts of honeybush (*Cyclopia intermedia*) prevented DMBA-initiated, TPA-promoted skin cancer in ICR mice and also that oral administration of aqueous extracts of honeybush reduced oxidative stress in the livers of Fisher rats. In this study, ethanolic extracts as well as purified compounds of unfermented and fermented honeybush were prepared and total polyphenols, flavonoids and antioxidant capacity was determined. In a short term (acute) animal study, female SKH-1 mice were irradiated daily with 180mJ/cm^2 UVB for 10 days and treated with the honeybush extracts and purified compounds before irradiation. Both honeybush extracts showed evidence of protection against UVB-induced depletion of antioxidant enzymes, erythema, edema and hyperplasia. In a long term (chronic) animal study, female SKH-1mice skin tumours were initiated once with DMBA and promoted with 180mJ/cm^2 twice a week for 22 weeks. The mice were treated with extracts and purified compounds of fermented and unfermented honeybush before irradiation. Preliminary results show that both unfermented and fermented honeybush extracts reduced the number and volume of tumours per mouse. Unfermented honeybush extract showed a higher protection than fermented honeybush in all these activities, as well as higher antioxidant capacity, polyphenols and flavonoids content.

P37

THE EXPOSURE OF A RURAL VILLAGE POPULATION IN LIMPOPO PROVINCE TO FUNGI AND MYCOTOXINS WITH PARTICULAR REFERENCE TO FUMONISIN B_1

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Today's global concern on food security is quantity but mainly quality to minimize consumer's health risk. Fumonisins mycotoxins and particularly fumonisin B_1 has been associated in the aetiology of oesophageal cancer in South Africa and in the world. The main objectives of this study were to determine fumonisin B_1 and its metabolites in faeces from members of the rural population as a means of estimating their exposure to this toxin via their diet and to assess their health risk potential. Staple food (maize, porridge) and human faecal samples were collected from selected households of rural areas in Limpopo Province. Maize (38) and porridge(30) samples were cultured and sub-cultured on Ohio Agricultural Experimental Station Agar (OAESA) or Potato Dextrose Agar (PDA), Czapek 20 (CY20S), Czapek (CZ) and Malt extract agar (MEA) under aseptic conditions and incubated at 28°C for 4 to 7 days for fungal isolation, microscopically and polymerase chain reaction (PCR) for fungal identification and mycotoxins production. Faecal samples (29) were freeze-dried and fumonisin B_1 and metabolites extracts using C18 cartridges and analysed on Thin Layer Chromatography and High Performance Liquid Chromatography. *Fusarium verticillioides*, *F. graminerium* and *F. proliferatum* as well as *Aspergillus* spp. *and Penicillium* spp. *were isolated* from all food samples. The *fusarium* cultures were confirmed producing fumonisins B_1 on YES media. And fumonisin B_1 or its metabolites were also confirmed present at 22% on TLC plates and 57% of faecal samples analysed at a range of 4.0mg/g to 18mg/g on HPLC. There is a need in regard to the obtained results to improve food crops storage in these rural areas to prevent any contamination and minimize human exposure.

P38
TOXIC EFFECTS OF METABOLITES OF INDOOR MOULDS

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There are many reports of allergies, chronic intoxication or even acute lung hemosiderosis of worker and occupants in buildings contaminated with indoor moulds. Mechanisms of the potential pathological effects of fungal toxic compounds on airways of healthy humans have not been sufficinetly clarified yet. *In vitro* and *in vivo* toxicity of the most frequent indoor micromycetes – under Slovak dwellings´ conditions *(Aspergillus versicolor, A. ustus, Penicillium expansum, P. chrysogenum)* and top risky *Stachybotrys chartarum* – from the public health point of view – with extrolites profile characterized by TLC and LC/MS/MS – was studied by microbiological methods (employing *Bacillus subtilis*), by a bioassay on chick tracheal cultures and by analyses of histological and biochemical alterations of rat organs or cell cultures and cytotoxic, inflammatory and hematological parameters in bronchoalveolar lavage fluid or blood. Pure solvent (2 % dimethylsulphoxide – negative control) and standards of mycotoxins, all carcinogenic, potentially produced by the fungus tested (sterigmatocystin for *A. versicolor* and *A. ustus,* patulin for *P. expansum,* ochratoxin for *P. chrysogenum*, trichothecene diacetoxyscirpenol for *S. chartarum* as there are no commercially available stachybotrytoxins yet) were used – 20 µg/ml (*in vitro* studies) and 4 µg/ml (the *in vivo* ones – intratracheal instillation), exposure for 3 d. All fungal metabolites tested showed certain toxic effects (bacterial growth inhibition, ceasing of tracheal epithelial cells´ beating, statistically significant changes in hematological parameters and lung injury – cytotoxic and inflammatory – detectable by bronchoalveolar lavage) that were concentration and cell origin of the toxicant (exo- or endocellular metabolite) dependent. Generally, exometabolites were able to damage natural cell and organ functions of airways *in vitro/in vivo* much stronger.

P39

DIETARY MODULATION OF LIPID METABOLISM IN FUMONISIN B_1 INDUCED PRE-NEOPLASTIC LESIONS IN RAT LIVER

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Fumonisin B_1 (FB_1) was classified as a group 2B carcinogen based on toxicity and carcinogenicity studies in rats and mice. Altered lipid metabolism involving arachidonic acid and other fatty acid (FA) in membrane phospholipids were suggested as key elements underlying the carcinogenic properties. Numerous studies have focussed on the potential of fish oil derived ω3 FA in the treatment and prevention of diseases such as cancer and their health benefits are now widely acknowledged. This study investigated the influence of dietary ω6/ω3 FA ratios on the prevention of FB_1-induced pre-neoplastic liver lesions in male Fischer 344 rats utilising a cancer initiation/promotion regimen with diethylnitrosamine (DEN-200mg/kg body weight) or FB_1 as initiator and FB_1 (250mg/kg diet) as promoter. The dietary fat consisted of sunflower oil (ω6/ω3 ratio 700:1) or sunflower oil supplemented with eicosapentaenoic acid and γ-linolenic acid (SEG diet-ω6/ω3 ratio 6:1). Liver lipids were subjected to FA, cholesterol and phospholipid analyses while liver sections were stained for placental glutathione-S-transferase positive ($GSTP^+$) foci. The SEG diet resulted in replacement of long-chain ω6 FA with ω3 counterparts. FB_1 decreased ($p<0.05$) long-chain polyunsaturated FA in phosphatidylcholine and increased ($p<0.01$) cholesterol significantly regardless of the diet. The number of $GSTP^+$ single cells decreased in the SEG/FB_1 group compared to SO/FB_1 without DEN initiation. However, with DEN the number of foci sized >50000µm^2 was significantly increased ($p<0.05$) in the SEG/FB_1 group compared to SO/FB_1. The data indicate that the SEG diet reduced initiation in the absence of DEN, while exacerbating promotion in the SEG/DEN/FB_1 group. More research on the dual role of dietary FA and FB_1 interactions is needed for the modulation of FB_1-induced hepatocarcinogenesis.

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BIODEGRADATION OF CHLORPYRIFOS BY SOME BACTERIAL STRAINS ISOLATED FROM EGYPTIAN POLLUTED SOILS

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Five bacterial isolates *Pseudomonas stuzeri*-B-CP5, *Enterobacter aerogenes*-B-CP6, *P. stuzeri*-B-CP7, *P. maltophila*-B-CP8 and *P. vesicularis*-B-CP9) were isolated form indigenous soils in Egypt and were tested for their natural biodegradability to degrade on of the most toxic chlorinated compounds; Chlorpyrifos (CP) (commercial name Dursban). The isolates were completely characterized by the traditional microbiological methods. The production of halo zone around the bacterial colonies and growth in the presence of high concentrations of CP (100-300 mg/l) and the production of phenolic compounds were the most important criteria on which the bacterial isolates identified. The isolate B-CP5 (*P. stuzeri*) was selected as the most potent CP-utilizing bacterial isolate. Molecular genetic characterization (fingerprinting) for the isolates under study was performed using RAPD analysis and 16S ribosomal DNA. The digestion ability of 16S patterns by the restriction endonuclease (RE) have been performed for further analysis of the differences between the tested isolates.

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A COMPARATIVE STUDY ON THE ANTI-PROLIFERATIVE EFFECTS OF ROOIBOS (*ASPALATHUS LINEARIS*), HONEYBUSH (*CYCLOPIA* SPP) AND GREEN (*CAMELLIA SINENSIS*) TEAS IN RAT PRIMARY HEPATOCYTES AND HUMAN LIVER AND COLON CANCER CELLS

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Growing scientific evidence indicates that tea consumption has beneficial health properties. The health promoting potential of the South African herbal teas, rooibos (*Aspalathin linearis*) and honeybush (*Cyclopia* spp) is of interest as they exhibit anti-oxidative, anti-mutagenic, anti-viral and anti inflammatory properties. In the present study the anti-proliferative effects of rooibos and four *Cyclopia* spp were monitored in rat primary hepatocytes and human liver ($HepG_2$) and colon (HT-29) cancer cell lines. Green tea (*Camellia sinensis*) was also included as a benchmark, as it is well known for its anti-proliferative properties. Cell viability was determined based on the assessment of ATP production using the CellTitre Glo® assay. Cell proliferation assay was based on the measurement of chemiluminescence detection of bromodeoxyuridine (BrdU) incorporation. Based on cell viability (IC_{50}), rooibos was more effective than green tea, followed by the honeybush teas in all the different cell types. The IC_{50} values of the different honeybush teas differ between the various cell types with *Cyclopia intermedia* exhibiting the highest adverse effect against HT-29 and primary hepatocytes while *C. subternata* was more effective against $HepG_2$ cells. *C. genistoides* and *C. longifolia* were the least effective in all the cell types. Preliminary studies showed that rooibos tea displayed the highest anti-proliferative effect in the HT-29 cells while green tea, *C. intermedia* and rooibos exhibited similar properties in $HepG_2$ cells. A similar response was observed in primary hepatocytes. The selective responses of the different teas on cell viability and cell proliferation in the different cell types could be important in developing herbal tea extracts as possible tools for cancer prevention.

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THE ANTIOXIDANT POTENTIAL OF OLEIC ACID AND EFFECT ON CELL SURVIVAL IN CARCINOGENESIS

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Cancer cells exhibit low levels of lipid peroxidation due to low levels of PUFA resulting from an impaired delta-6 desaturase enzyme. PUFA are key substrates for lipid peroxidation which plays a role in cellular oxidative status affecting processes such as cell proliferation and apoptosis. Studies demonstrated that changes in the PUFA profile and lipid peroxidation status due to an abnormal FA metabolism, involving a decrease in delta-6 desaturase activity, are associated with potentially neoplastic hepatocyte lesions. Furthermore, cancer cells contain high levels of antioxidants such as vitamin E and oleic acid (OA, C18:1n-9), which has been reported to display antioxidant properties. In the present study the antioxidant properties, of OA was compared to known antioxidants such as vitamin E, quercetin, reduced glutathione (GSH), ECGC and catechin in an *in vitro* microsomal assay. In addition the antioxidant properties of OA were compared to vitamin E in rat primary hepatocyte cultures treated with the mycotoxin fumonisin B_1 (FB_1), known to induce lipid peroxidation *in vitro.* In the microsomes, OA demonstrated a protective effect against lipid peroxidation exhibiting an IC50 of 760µM, half as effective as vitamin E with an IC50 of 320µM, while GSH was approximately 1000x less potent with an IC50 of 10mM.The polyphenols showed strong inhibitory effects at low concentrations (EGCG, IC50 42µM; catechin, IC50 90µM; quercetin, IC50 17µM). In the primary hepatocytes, vitamin E (10µM) tended to counteract the FB_1-induced depletion of PUFA, while both OA (100µM) and vitamin E counteracted the FB_1-induced lipid peroxidation. The present data suggest that OA plays a key role in the control of the oxidative status of a cell and contribute to the survival of a cancer cell.

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COMPARATIVE CYTOTOXIC AND ANTI-PROLIFERATIVE PROPERTIES OF SOUTH AFRICAN HERBAL TEAS IN A HUMAN OESOPHAGEAL CANCER CELL LINE

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The cytotoxicity and anti-proliferative properties of freeze-dried aqueous extracts (FDE) of unfermented and fermented rooibos (*Aspalathus linearis*) and honeybush (*Cyclopia intermedia*) herbal teas, as well as that of green and black (*Camellia sinensis*) teas were investigated in a human oesophageal cancer (WHCO5) cell line. The effect of the various FDE on cytotoxicity and/or cell viability was determined using flow cytometry, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT), lactate dehydrogenase (LDH) release colorimetric assays, and the CellTiter Glo® Luminescent Cell Viability assay, which measures ATP production. The effect of the unfermented FDE on cell proliferation was monitored using a luminescence-based bromodeoxyuridine (BrdU) incorporation assay. Cytotoxicity could not be assessed accurately when using the LDH and MTT assays due to colour interference. Based on IC_{50} values, flow cytometry and the luminescent-based cell viability assay indicated that green and black teas exhibited higher cytotoxic effects than rooibos and honeybush. Unfermented rooibos was the most effective in inhibiting cell proliferation, followed by green tea and unfermented honeybush. Differences in the cytotoxicity (IC_{50} values) could be explained by the total polyphenol (TPP) content, more specifically the flavanol/proanthocyanidin, flavonol/flavone and the xanthone/flavanone subgroups. Variations exist between the type of polyphenol involved in cytotoxicity and inhibition of cell proliferation by the herbal teas. The selective cytotoxic effects and impairment of the proliferative capacity of the cancer cells could be important in developing chemopreventive agents against oesophageal cancer.

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MALNUTRITION AND MICRONUTRIENT DEFICIENCIES

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Epidemiological studies make it possible to clarify the way in which a disease appears and the extent of the problem that it can cause. They make it possible to identify a vulnerable group and facilitate the methodology of assumption of responsibility. Yet over 800 million people around the world are chronically malnourished because of nutrient deficiencies. In Morocco malnutrition is a public health problem since one in every four children between the ages of 6 to 60 months old suffers from protein-calorie malnutrition (PCM). The aim of this study is to define malnutrition from an epidemiological as well as a biological point of view. In order to set up the best nutritional program, forty-four children, aged 6 to 60 months, were divided into three groups and the groups were investigated in parallel. We determined blood antioxidant vitamins, trace elements as well as blood oxidative stress index in children suffering from severe and mild malnutrition, and in healthy control children. Our studies showed that in the malnourished children, selenium, zinc, the retinol, alpha tocopherol and their carotenoids are significantly decreased. Conversely, the TBARS, the ferritin and the prognostic inflammatory and nutritional index (PINI) are significantly increased in the children suffering from malnutrition. Reduction in the antioxidant micro-nutriments and increase in markers of stress confirm an imbalance of pro-oxidants and anti-oxidants in malnourished children in bond with the inflammatory syndrome and stunting (growth delay). Factors affecting the bio-availability of vitamin A deficiencies are varied, but there are three major types of interventions: (i) Dietary modification: the environment meets all the nutritional needs for vitamin A intake. The knowledge of its sources and the organization of the life of family should ensure a normal vitamin A status. (ii) Supplementation: WHO recommends the administration in liquid form or capsule of vitamin A according to several diagrams; and (iii) Fortification: addition of a deficient nutrient such vitamin A to basic food of a given population. Malnutrition also varies according to the area geography. This reveals that interventions must be adapted to the local conditions of each country.

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INVESTIGATION OF GENOTOXIC ACTIVITIES OF 2,2'-(DI-3-HYDROXYPHENYL)-1H,1H'-[5,5']-BIS-BENZIMIDAZOLE, 2,2'-(DI-4-HYDROXYPHENYL)-1H,1H'-[5,5']-BIS-BENZIMIDAZOLE, AND 2,2'-(DI-3-METHOXYPHENYL)-1H,1H'-[5,5']-BIS-BENZIMIDAZOLE IN *SALMONELLA TYPHIMURIUM* TESTER STRAINS

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The aim of this study was to evaluate the mutagenic potential of bisbenzimidazole derivatives. Agents were tested for mutagenicities using Ames/Salmonella tester strains TA 98 and TA 100, without metabolic activation. The mutagenic response in *Salmonella*, and the structure of the molecule, reveal that 2,2'-(Di-3-methoxyphenyl)-1H,1H'-[5,5']-bis-benzimidazole slightly mutagenic. 2,2'-(Di-3-hydroxyphenyl)-1H,1H'-[5,5']-bis-benzimidazole and 2,2'-(Di-4-hydroxyphenyl)-1H,1H'-[5,5']-bis-benzimidazole showed no mutagenicity on tester strains. Methoxyphenyl ligand molecule of TA 100 and TA 98 resulted in slight mutagenicity. The presence of mutagens causing frameshift mutation in TA98 and base-pair substitution mutations in TA100 strains.

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ANTIFUNGAL ACTIVITY OF WEEDY PLANT EXTRACTS

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Food and feed are subject to infection by a variety of microorganisms that can induce spoilage or produce secondary metabolites that are toxic to man and animals. In many cases the natural contaminants are mycotoxigenic fungi most frequently the *Fusarium* and *Aspergillus* species. Fungicidal products currently available on the market are expensive and harmful to the users as well as to the environment. Therefore there is a need to develop safer alternatives for use in resource-poor farmers. This study investigated the antifungal activity of extracts of *Tagetes minuta, Lippia javanica*, *Amaranthus spinosus* and *Vigna anguiculata* against four agricultural fungi, i.e. *Fusarium verticillioides*, *F. proliferatum*, *Aspergillus flavus* and *A. paraciticus* using a microtitre assay. Amphotericin B and Cantus were used as positive controls. All extracts except for the water extracts showed activity on all isolates of the *Fusarium* spp. tested. The most active were the methanol and hexane extracts of V*. anguiculata* (MIC: 0.02 mg/ml – 0.32 mg/ml) and *A. spinosus* (MIC: 0.02 mg/ml – 0.08 mg/ml). No inhibition of fungal growth was observed for isolates of the *Aspergillus* spp. tested, but conidium formation was enhanced on treated plates when compared to the controls. The results obtained indicate that these plants contain chemicals that can be developed as potential antifungal agents, which may reduce the risk of mycotoxins exposure and diseases associated with food contamination in rural areas.

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REDUCING FUMONISIN CONTAMINATION OF MAIZE STAPLE FOODS BY SIMPLE INTERVENTION PROCEDURES IN A RURAL AREA OF SOUTH AFRICA

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Fumonisins are carcinogenic food-borne mycotoxins produced mainly by *Fusarium verticillioides* occurring ubiquitously in maize. Previous studies in Eastern Cape Province have revealed that high levels of fumonisin exposure occur in populations reliant on subsistence maize as a dietary staple. Home-grown maize collected from households in the Centane district, Eastern Cape Province, were analysed for the major naturally occurring fumonisins (FB_1, FB_2 and FB_3) by HPLC. Sorting of maize kernels by removing the visibly infected kernels by hand reduced the total fumonisin from 1.99 mg/kg to a mean of 0.68 ± 0.42 mg/kg (66% reduction). Although the discarded kernels had a mean total fumonisin level of 53.69 ± 15.03 mg/kg, they comprised only 2.5% by weight of the original maize. Following the removal of the infected kernels, the remaining kernels were hand washed with water for between 5 and 60 minutes at 22°C. A mean fumonisin reduction of 25% was achieved and a 40°C water wash did not improve the reduction. Thus, the mean total fumonisin reduction achieved by removing the infected kernels by hand and washing the remaining maize kernels in room temperature water was 74%. Although soaking periods of 15 and 24 hours achieved a mean reduction of 51%, the prolonged soaking period was deemed impractical. Therefore, simple intervention procedures to be recommended would be the removal of the infected kernels by hand followed by a 10-minute hand wash of the sorted maize kernels. *This work was supported by the Sir Halley Stewart Trust.*

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DETERMINATION OF FB_1 EXPOSURE IN A POPULATION AT RISK OF LIVER CANCER

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Fumonisin B_1 (FB_1) is a fungal secondary metabolite produced by *Fusarium verticillioides*, which grows in maize, and might be implicated in the aetiology of oesophageal and liver cancer in humans. FB_1 induces liver tumours in rats and kidney tumours in mice which are sex and strain specific. FB_1 is deposited in hair and nails in a dose-dependant manner and these matrixes can be quantitatively analysed to determine FB_1 exposure. A case-control study was conducted in a population-based cohort from Linxian county, Henan province in central China, to test the association between FB_1 exposure and the incidence of primary liver cancer. Nails from woman (18 cases with 38 controls) and men (54 cases with 109 controls) with primary liver cancer were analysed by LC-ESI-MS/MS. The levels of FB_1 in the nail samples ranged from 12 ng/g to 2267 ng/g. In the women 33% of the cases and 11% of the controls tested positive for FB_1 exposure. In men 22% of the cases and 20% of the controls tested positive for FB_1 exposure. Corrections were made for hepatitis exposure. FB_1 exposure was associated with an increased risk of primary liver cancer in Chinese woman but there was no association in men. Whilst FB_1 exposure levels have been measured, aflatoxin B_1 (AFB_1) co-exposure cannot be ruled out since it's also known to occur in mouldy maize contaminated with the fungus *Aspergillus flavus.* This toxin has been shown to be a promoter of primary liver cancer in Shanghai (China) and therefore further investigations are required to determine the AFB_1 exposure levels in this high risk population.

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FUMONISIN LEVELS IN TRANSGENIC AND CONVENTIONAL MAIZE FROM RURAL AREAS IN KWAZULU-NATAL

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The genetically modified *Bt* maize contains *cry* genes from *Bacillus thuringiensis*, which upon expression produce insecticidal proteins toxic to *Lepidopteran* insects, among others the maize stalk borer, *Busseola fusca*. *B. fusca* causes wounds in maize, which is consequently infected by certain *Fusarium* species, particularly *F. verticillioides* and *F. proliferatum*. The fumonisin mycotoxins produced by these fungi have adverse health effects in humans and animals, thus IARC classified fumonisin B_1 (FB_1), the most abundant fumonisin analogue, as a group 2B carcinogen. Following the 2006/2007 crop season *Bt*, RR (resistant to Roundup herbicide) and conventional maize were collected from subsistence farmers in the rural areas of Simdlangentsha, Hlabisa and Paulpietersburg in the Kwazulu-Natal Province of South Africa. Following extraction with methanol/water, the main naturally occurring fumonisins were analysed utilizing reversed-phase HPLC. The mean total fumonisin (FB_1 + FB_2 + FB_3) level in the *Bt* maize (n = 20) was 0.181 ± 0.420 mg/kg compared to 0.917 ± 2.52 mg/kg in the RR maize (n = 19) and 1.39 ± 2.78 mg/kg in the conventional maize (n = 36). However, the large variations in fumonisin contamination between individual farmers' lots resulted in large standard deviations and consequently the overall differences between maize types were not statistically significant ($p>0.05$). The exception was in Simdlangentsha where the mean total fumonisin levels were significantly lower ($p<0.05$) in *Bt* maize (0.051 ± 0.070 mg/kg) than in the non-*Bt* maize (1.83 ± 3.22 mg/kg). The overall trend observed was the numerically lower levels of fumonisins in the *Bt* maize compared to the conventional maize.

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MATERNAL NICOTINE EXPOSURE AND NEONATAL LUNG DEVELOPMENT: INVESTIGATING THE MODULATING EFFECT OF ROOIBOS (*ASPALATHUS LINEARIS*) ON OXIDATIVE STATUS OF RAT LUNG

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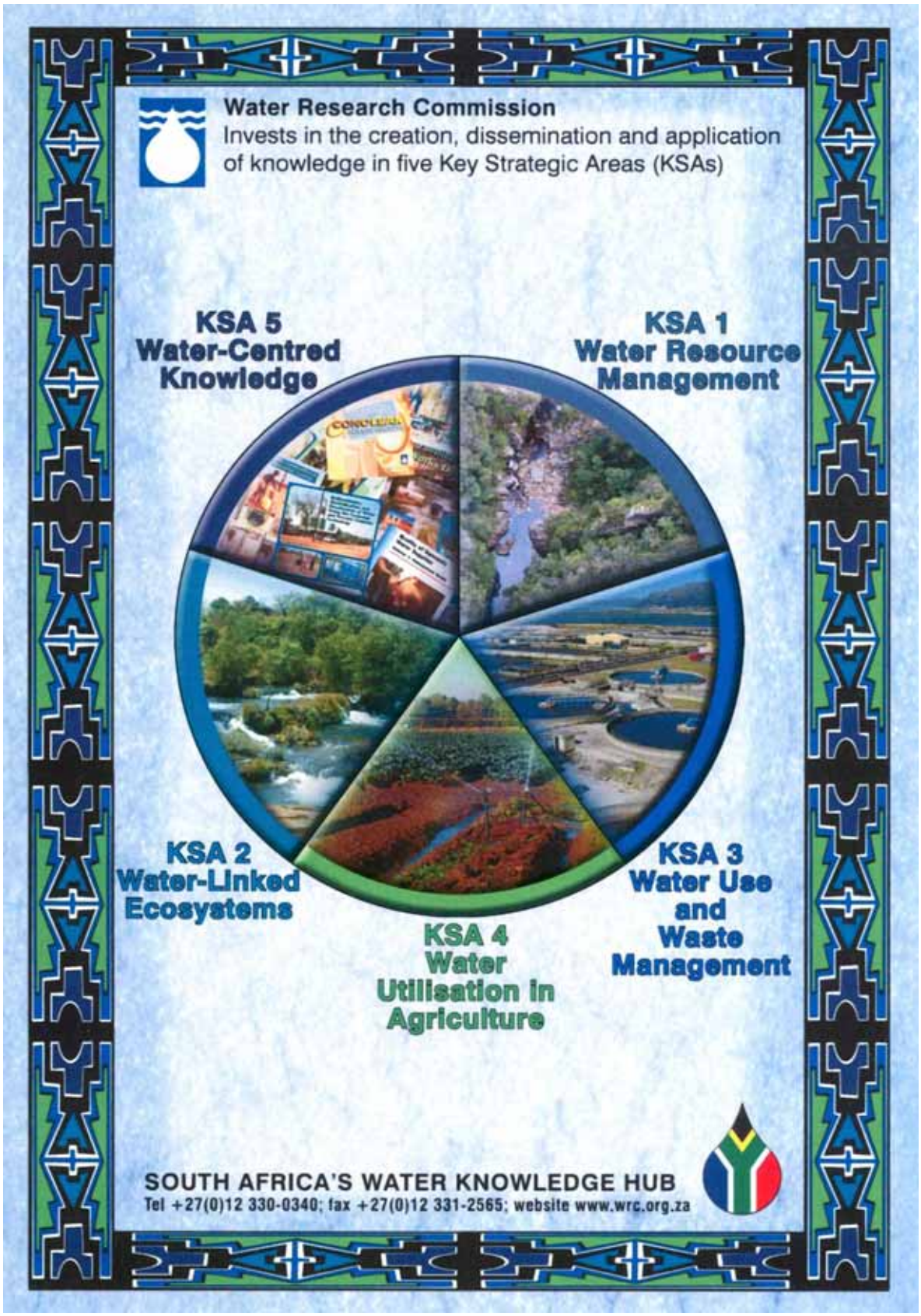
Tobacco smoking is the leading preventable cause of cancer deaths worldwide. Nicotine, the major alkaloid in tobacco smoke, is metabolised to the carcinogen 4- (methylnitrosamino) - 1 - (3-pyridyl) - 1 - butanone (NNK). An increased uptake of NNK in infants is associated with exposure to tobacco smoke, suggesting that environmental tobacco smoke exposure in young children may be related to the development of cancer in later life. Nicotine is associated with increased oxidative stress and also acts as a chemo-attractant for polymorphonuclear leukocytes, leading to oxidative damage by releasing reactive oxygen species. Oxidative stress is characterised by a disturbance in the free radical homeostasis, favouring the formation of pro-oxidants and associated inflammation, tissue damage and tumourigenesis. Effective enzymatic antioxidant defences rely on different antioxidant systems within the cell of which the cytosolic enzymes, superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) are of importance. Stabilisation of the oxidative status within the cell is therefore, likely to reduce the adverse effects of nicotine. Rooibos (A*spalathus linearis*) is known to exhibit antimutagenic, antioxidant, as well as anti-tumour properties. It alters the oxidative status in the liver by stabilising the level of reduced glutathione (GSH). The aim of the present study was to investigate the modulating properties of fermented rooibos on the susceptibility of the neonatal lung to oxidative stress related to the carcinogenic properties nicotine and NNK exposure. Results indicate differences in the modulation of oxidative enzyme activities by fermented rooibos after exposure to nicotine and NNK, reaffirming the sensitive nature of the pro-oxidant/antioxidant balance in the lung.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OTHER CONFERENCE AND GENERAL INFORMATION

Conference Badges
Delegates are kindly requested to wear their badges at all times in order to allow them to participate in conference events.

Airport Tax
Please consult with your own travel agent about airport tax payable when entering or leaving South Africa.

Credit cards
Most shops and hotels will accept major credit cards.

Currency/Banks
The local currency is the South African Rand (Notes: R200, R100, R50, R20, R10; Coins: R5, R2, R1 and 50c, 20c, 10c and 5 cents). Foreign exchange facilities can be found at the airport, Bureaus de Change and the Cape Town Tourism Visitors Information Centres. International bank and credit cards can be used at most Automatic Teller Machines (ATMs). Most banks are open from 09:00 and close at 15:30 on weekdays, and Saturdays from 09:00 to 12:00.

Value added tax (VAT)
South Africa has a VAT system of 14% on purchases and services. Foreign visitors can reclaim VAT on purchases of items more than R250 that are taken out of the country. Forms need to be completed and can be obtained in the International Departure Hall of the Cape Town and Johannesburg International Airports or if your time is limited before departure, at the VAT Refund Office in the Victoria Wharf at the V&A Waterfront, CapeTown - open daily from 08:00 - 20:30, or at Cape Town Tourism City Centre (Mon - Fri: 08:00 - 17:00, Sat: 08:00 - 13:00) - *Telephone:* 021 426 4260.

Tipping
A 10% tip is acceptable in restaurants and for taxis. R2 to R5 per piece of luggage is generally given to porters in hotels and at airports.

Shopping
Most shops are open between 09:00 and 17:00 or in some cases until 21:00 at the large malls, particularly at V&A Waterfront, Canal Walk and Tygervalley (Bellville) throughout the week. Shops open later over weekends, mostly 10:00 and closing times vary from 14:00 to 16:00.

Public Transport
An airport bus service operates between Cape Town International Airport and the City Centre. Tickets can be purchased at the airport.

Bus/Train Services
Bus and train services are limited in and around Cape Town. Contact your travel agent for details regarding luxury bus services for travelling.

Car Hire/Taxis
All major car hire companies operate from the airport and have depots in the city. There are no roving taxis in Cape Town but services are available from hotels, the airport and in the city ***(be sure to ask about fares beforehand and check that the driver is familiar with your area of destination).***

Internet Access/Business Centre

The Mahisha Business Centre is situated on the ground floor of the CTICC and provides internet access, phone, fax, photocopying, printing and other office services.

Electricity

Electricity systems are 200/230 volts, 50hz AC. Plugs have 3 cylindrical pins and it is essential to have an adaptor for foreign appliances.

Safety in Cape Town

Considerable efforts are made to safeguard tourists and residents. Cape Town's Central Business District is monitored by surveillance cameras and security guards monitor major shopping malls and areas. Nonetheless, visitors should take sensible precautions like they would in any other large city in the world to ensure their safety.

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O = Oral presentation; P = Poster presentation

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