Guest Editorial Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

An Integrated Approach to Diagnosis and Therapy in Cancer

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Abstract

Cancer is one of the major non-communicable diseases (NCD) worldwide, accounting for 22% deaths in 2012 worldwide. The number of cases is projected to increase to 17 million by 2020. According to ICMR, almost half of the cases will be in Asia with more than 17 lakh cases expected to occur in India by 2020. In such a scenario, early diagnosis and cost-effective treatment will play a major role in effective patient management. Developing the infrastructure required to cater to a vast population requires substantial effort in research and development. The National Symposium on "An Integrated Approach to Diagnosis and Therapy in Cancer" aims to create awareness about cancer etiology and stimulate the interest of students in cancer research. It has become unequivocally evident that tumor development depends on the intricate reciprocal interplay of tumor cells with their local and distant environments. Mutations in genes regulating cell cycle/cell proliferation can also contribute to tumorigenesis and is of great relevance in both diagnosis and disease management. One of the major focus of the symposia is developing diagnostics and therapeutics through translational research. The invited speakers will make presentations on emerging areas in cancer research like nanomedicine, personalized medicine, etc. Reputed clinicians and researchers will provide different perspectives on cancer biology. Thus, this symposium aims at a comprehensive functional understanding on the integrated role of physical and life sciences in diagnostics and therapeutics of cellular and molecular events that are responsible for the plasticity of tumor cells. Moreover, it will bring together experts in cancer and molecular biology who will share their expertise on a new generation of effective diagnostic tools and therapeutic approaches in cancer. One of the objectives of the symposium is to provide students and researchers a platform for exchange of knowledge and innovative ideas towards a comprehensive approach in cancer biology. It provides them with an ample opportunity to present their research work related to the conference theme.

Keywords: Cancer, NGS, MLACW, Integrated approach

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Recent Advances In Cancer Diagnosis

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Abstract
New generation healthcare and the diagnosis of cancer. The role of next generation sequencing (NGS) of genomes in the diagnosis of cancers is now about a decade old. Genomics has represented a paradigm shift in the standards of care of cancer patients and in preventive strategies for high citizens at risk for hereditary forms of cancer. In this talk we will address three topics. (i) Hereditary breast and ovarian cancer in Indian women. (ii) Deep somatic profiling of tumor DNA using NGS. (iii) Emerging technology of liquid biopsies for cancer care.

Keywords: Cancer, NGS

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

How big data is changing biology?

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Abstract
Rapid advancements in technology in the last decade are aiding our understanding of many fundamental biological processes. Introduction of large amount of data, especially those coming out from the second- and third-generation DNA sequencing instruments, is helping us identify key mutations in cancer to unraveling genome and transcriptome sequences in important plant species. The amount of data produced by these high-throughput instruments is massive, often in the range of tens to hundred of terabytes, even from a small single-investigator driven lab in a year. Managing such large amount of data along with its storage, analysis, sharing and interpretation remain the hardest task for any biology-driven lab today. I shall discuss how tackling biology-driven problems have changed in the face of this challenge with a few examples from diseases like cancer and plant biology.

Keywords: Big data, Mutations, Genome

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Cancer: a disease of stem cells?

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Abstract
A fundamental property of cancer cells is uncontrolled growth. Yet, very few cancer cells initiate colony formation in soft-agar assays – an *in vitro* assay for carcinogenicity. Furthermore, injection of less than one million cancer cells fails to initiate tumor formation in nude mice. These observations suggest that not every cell within a cancer possesses unlimited growth potential. Based on this, a '*cancer stem cell*' hypothesis has been put forward which predicts the existence of a small sub-population of cells within a cancer that alone has the potential to initiate new tumors, while the bulk of the cancer cells are non-tumorigenic. Owing to their similarities with normal stem cells, specifically in their ability to self-renew and differentiate to give rise to other cell types, this sub population of cells has been termed as *cancer stem cells (CSCs)*. Recently, such CSCs have been identified in a wide variety of cancers, thereby lending strong support to the '*cancer stem cell*' hypothesis. The identification of *CSCs* has tremendous therapeutic implications. Conventional anti-cancer therapies kill the majority of tumor cells, thereby causing the tumor to shrink; however, tumor relapses within months. It is predicted that current therapies kill the bulk of tumor cells leaving behind the *cancer stem cells,* which then regenerate the tumor. Therefore, to eradicate cancer completely, one must target these *cancer stem cells*. I will discuss possible origins of CSCs and strategies to target them.

Keywords: Cancer stem cells

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Inhibition of DNA Repair as a Strategy to Treat Cancer

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Abstract

Repair of DNA breaks is critical for maintenance of genomic integrity. DNA double-strand breaks (DSBs) are the most deleterious types of DNA damage. Nonhomologous end joining (NHEJ) is the predominant DNA DSB repair pathway in higher eukaryotes. DNA Ligase IV is one of the most critical components of NHEJ, involved in final sealing of DSBs. Inhibition of DSB repair pathway proteins can be used as a strategy to induce apoptosis in cancer cells. Recently we have chemically synthesized and characterized a novel inhibitor of Ligase IV, SCR7. Using radioactively labeled oligomeric substrates mimicking various *in vivo* DSBs, we showed that addition of SCR7 to rat testicular extracts abolished joining by NHEJ. Further, SCR7 interfered with the joining of compatible DSB ends catalysed by purified Ligase IV. Electrophoretic mobility shift and circular dichroism studies suggest that SCR7 binds to Ligase IV and interferes with its interaction to DNA ends. Further using animal models, we find that SCR7 treatment can inhibit progression of breast adenocarcinoma but not haematopoeitic cancers, resulting in a significant increase in life span. Interestingly, SCR7 impedes tumor progression in haematological cancers significantly, when coadministered with existing DSB inducing therapeutic modalities. More importantly, we show that when coadministered, SCR7 could reduce the effective dosage of g-radiation from 2 Gy to 0.5 Gy, in cancers derived from breast cancer, colon cancer and B-ALL. Histopathological and immunofluorescence evaluation of tumor and other tissues suggest that the cytotoxicity induced is mostly restricted to the tumor. We also find that encapsulation of SCR7 in micelles can improve its efficacy by ~4-fold. Thus, by using various biochemical and biophysical approaches, we show that SCR7 is a potent inhibitor of NHEJ, can be used as a chemotherapeutic agent against multiple cancers.

Keywords: Cancer, DNA Ligase

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Genomics and Childhood Cancer- What's new?

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Abstract

Cancer in children is not uncommon. It is estimated that approximately 1 in 10,000 kids suffer from cancer in India. Globally, unfortunately every 4 hours a child dies from cancer. Approximately 70 to 80 % of childhood cancers are curable, if diagnosed and treated correctly. In India, unfortunately the figures are much poorer; this may be due to lack of awareness, affordability and access to health care. Leukemia, Lymphoma and Brain tumors are the commonest cancers in children, followed by kidney tumors, Bone and soft tissue tumors, eye tumors, liver tumors and others. Majority of the childhood cancers do not have a known cause. A few cases may have genetic, environmental or infectious cause (especially viruses).

In recent times, there has been a tremendous turnaround in understanding the biology of cancer. These developments have aided and have been instrumental in changing the outcome of this dreadful disease. We are moving from evidence based medicine to personalized medicine wherein the treatment is tailor made as per the requirement of the person who is having the problem. Every living thing is made of cells. Inside the cells, there is chromosomes which is a thread-like structure of nucleic acids and protein found in the nucleus of most living cells, carrying genetic information in the form of genes. Genes are a portion of a DNA molecule that serves as the basic unit of heredity. Genes control the characteristics that an offspring will have by transmitting information in the sequence of nucleotides on short sections of DNA. In humans, genes vary in size from a few hundred DNA bases to more than 2 million bases.

Genome is an organism's complete set of DNA, including all of its genes. Genomics is the study of the collection of a person's genes and their interactions with each other and the internal and external environment they are exposed to. Cancer Genome is very complex and strikingly heterogeneous at the whole genome level between histologically similar tumors. Genomics is very important to understand the cancer biology and for Individualized/ personalized therapy for a better outcome.

Cancer is not a single disease. It basically represents uncontrolled growth and spread of abnormal cells. There is aberrant expression of genes with a variety of cellular functions and also there is variation in the number of deregulated genes. The genomic instability in cancer may be accumulation of extra copies of DNA or chromosomes,

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chromosomal translocations, inversions, deletions or single-strand breaks in DNA or double-strand breaks in DNA etc.The causes of cancer are mutlifactorial and include an interplay of genetics, environmental factors like radiation/ carcinogens and infections especially viruses.

Cancer is a genetic disease and all cancers involve genetic changes in somatic cells, the germ line, or both. Most gene mutations in cancer occur in somatic cells and are acquired (multifactorial etiology). However, some mutations do occur in the germline and may be inherited and passed on to future generations. The goal is to detect the mutations at the genetic level which are actionable, and use treatment strategies to break that particular pathway in causation of cancer because some standard treatments in some cancers do not get the desired outcome. In other words, common cancers with usual treatment fail, implicating a genetic basis and unless that particular pathway is tackled (if feasible), cancer cannot be conquered. Currently testing is available for both somatic and germline mutations.

The role of genomics in planning treatment in adult cancers is relatively better understood and is being done in specialized centers. Similar approach in childhood cancers is in the developing phase. Some of the childhood cancers with well known genetic basis are Wilm's tumor, Retinoblastoma, Osteosarcoma, Leukemias, and Neuroblastoma etc.

Besides these there are also some inherited/genetic syndromes with stronger predisposition to development of cancers like

- Beckwith-Wiedemann syndrome
- Bloom syndrome
- Diamond-Blackfan
- Down syndrome
- Fanconi anemia
- Neurofibromatosis type I and II
- Gorlin syndrome (basal cell nevus syndrome)
- Rothmund-Thomson syndrome
- Tuberous sclerosis
- Werner syndrome

Then there are some inherited cancer syndromes like

- Hereditary Breast/Ovarian Cancer Syndrome
- Li-Fraumeni Syndrome
- Lynch syndrome
- Familial Adenomatous Polyposis (FAP)
- Diffuse Gastric Cancer Syndrome
- PTEN Hamartoma Tumor Syndrome
- Peutz Jeghers Syndrome
- Cowden Syndrome

Currently most of the childhood cancer treatment protocols take into account the genetic and molecular analysis both for diagnosis as well as planning treatment strategies essentially aimed at improving the outcome. An index case will be presented to highlight the importance of understanding the genomic basis of childhood cancer while managing, otherwise if the child had been managed with usual protocols, the outcome would have been inferior.

To conclude, the future of cancer treatment is looking bright with better understanding of the disease biology, availability of better diagnostic methods with radiology and nuclear medicine attaining the molecular imaging techniques, better pathological tests, and genetic and molecular tests to further not only refine the diagnostic methods but also to plan treatment in a rational and personalized manner.

Keywords: Cancer, Genome

Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Mechanism of DISC Formation-a Prerequisite for Initiation of Extrinsic Cell Death Pathway

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Abstract
Apoptosis or programmed cell death is a key phenomenon in multicellular organisms that are essential for embryonic development, cellular homeostasis, and immune regulation. Imbalance in this tightly controlled process results in severe pathologic conditions, such as cancer, autoimmune diseases, and neurodegenerative disorders. Classical apoptotic cascades follow two distinct pathways: the intrinsic pathway, which originates in the mitochondria, and the extrinsic pathway, which is triggered by ligation of cell-surface death receptors, followed by formation of a multiprotein death-inducing signaling complex (DISC). The caspases, a family of cysteinyl proteases that initiate and execute apoptosis, rely on these events for their activation and subsequent proteolytic functions. In the Fas-receptor-mediated extrinsic cell death pathway, activation of the initiator caspase-8 is achieved through interaction of its pro-form (procaspase-8) with an adapter protein, Fas-associated death domain (FADD). This interaction is mediated via their similar death effector domains (DEDs) leading to a functional DISC formation and subsequent activation. Although much progress has been made in decoding the major players in this pathway, the structural overview of DISC is still elusive, mainly because of its complicated interaction networks and lack of information on DED proteins. Dissecting the precise mode and the binding interface of DED–DED interaction network holds the key to identifying the missing links in deciphering the unknown steps in DISC formation and subsequent cell death. Here, we provide an intriguing insight into the molecular basis of DED chain formation and define the surface for the physical interaction between FADD and procaspase-8 using interdisciplinary tools. Based on the detailed analyses of the interface for DED–DED interactions, together with data on the FADD–procaspase-8 complex, we propose a new model for DISC formation, regulated at the level of DED-containing proteins.

Keywords: Apoptosis, DISC

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Structural Assessment of Cancer-Causing Mutations for Translational Research

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Abstract
The overall aim to study the three dimensional protein structure is to visualize the complexities of disease associated molecule at atomic level. Precisely determined protein structure helps in understanding the function associated to protein. However, it is still a challenge to correlate the structural information for translational research. BRCA1 (Breast Cancer Susceptibility gene 1) is one of the most studied genes for breast and ovarian associated cancers. Familial inheritance of breast and ovarian cancer is also due to mutations in different domains of BRCA1. We have analysed different mutations from Indian families and from Breast Cancer Information Core (BIC). Now, challenges lays on scientists/clinicians for the possibilities to explore the pathogenicity of mutations identified in different genes. Hence, we decided to evaluate pathogenicity of mutations discovered in different domains of BRCA1. BRCA1 comprises different functional domains like N- terminal RING domain, tandem repeats of C-terminal and the central DNA binding domain. N-terminus, RING domain of BRCA1 interacts with BARD1 whereas C-terminal region of BRCA1has been reported for transactivation function through the protein-protein interactions. Different regions of BRCA1 have been evaluated to categorise the pathogenic mutations. The protein-protein interactions (PPIs) with the binding partners of BRCA1 like RAP80, MERIT40, and ABRAXAS have been explored. Furthermore, germ -line mutations screening in BRCA1 has helped in clinical management.

Keywords: BRCA1, Translational research

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Personalized Medicine for Cancer

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Abstract
The overall aim to study the three dimensional protein structure is to visualize the complexities of disease associated molecule at atomic level. Precisely determined protein structure helps in understanding the function associated to protein. However, it is still a challenge to correlate the structural information for translational research. BRCA1 (Breast Cancer Susceptibility gene 1) is one of the most studied genes for breast and ovarian associated cancers. Familial inheritance of breast and ovarian cancer is also due to mutations in different domains of BRCA1. We have analysed different mutations from Indian families and from Breast Cancer Information Core (BIC). Now, challenges lays on scientists/clinicians for the possibilities to explore the pathogenicity of mutations identified in different genes. Hence, we decided to evaluate pathogenicity of mutations discovered in different domains of BRCA1. BRCA1 comprises different functional domains like N- terminal RING domain, tandem repeats of C-terminal and the central DNA binding domain. N-terminus, RING domain of BRCA1 interacts with BARD1 whereas C-terminal region of BRCA1has been reported for transactivation function through the protein-protein interactions. Different regions of BRCA1 have been evaluated to categorise the pathogenic mutations. The protein-protein interactions (PPIs) with the binding partners of BRCA1 like RAP80, MERIT40, and ABRAXAS have been explored. Furthermore, germ -line mutations screening in BRCA1 has helped in clinical management.

Keywords: Protiens, Cancer, Ring domain

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Novel Molecular Targets and New Strategies on The Path from Bench to Bedside

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Abstract
In this talk, I will briefly introduce the concept of drug targets and the many means by which such targets are identified or discovered. Within this definition and scope I will bring to focus how an enzyme involved in seemingly unimportant job of routine protein turnover namely the proteasome, took the centre stage as an important anticancer drug target. We will see some of the retrospective arguments for: why anti proteasome active site inhibitors are effective as anticancer drug targets, why they are tumor specific (if they are) and why they are not universally applicable to all cancer types. Then we will see how such discoveries both by their success and limitations open up other avenues of opportunities for new target discovery. I will illustrate this using an example from our own investigations which branches off from where the proteasome inhibitor was proposed to have had its maximum influence and highlight the challenges and promises on the road ahead.

Keywords: Molecular diagnostics

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

From Bench To Bed Side: Theranostics

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Abstract
Imaging plays a vital role in oncology, because it gives the clinician, objective evidence of the response of the tumor to therapy. Imaging with form only has its limitations, hence fusion imaging with PET (POSITRON EMISSION TOMOGRAPHY) plays a vital role in every step to assess disease status and also therapy planning. Similarly targeted radionuclide therapies is gaining a vital role is oncology. This presentation gives a bird's eye view of the various molecules and their use in clinical practice.

Keywords: Tumor, PET

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Nanoscale Materials for Engineering Improved Cancer Nanomedicine

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Abstract
The development of new materials and technologies has enabled nanotechnology an exciting platform to impact medicine in a paradigm shift manner. Nanoparticles confer promises to improve the efficacy of current cancer therapeutics by providing enhanced drug's half-life and targeting efficacy, sustained release of drugs and reduced drug toxicity. The development of adaptive resistance is the major cause of mortality in cancer. Nanoparticle mediated combination therapy could emerge as powerful strategy for targeting adaptive resistance, resulting in increased antitumor efficacy. In my talk, I will discuss several nanobiotechnology approaches to formulate next-generation therapeutic molecules for translating basic research into clinical applications.

Keywords: Nanotechnology, Cancer

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Effect of Hypoxia and Intermittent Hypoxia on Hif-1α Mediated Neuroblastoma Cell Metastasis

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Abstract

Neuroblastoma is the most common extracranial pediatric solid tumor, containing cells derived from the developing sympathetic nervous system (SNS) and results from improper differentiation of neural crest cells. Hypoxia and Intermittent Hypoxia (IH) can influence the stabilization of HIF-1α and which may further affect the cells to undergo metastasis to specific sites mainly to bone. Hence, understanding the exact biochemical mechanism of metastasis will be a salient objective in finding key drug targets. This study is carried out to understand the effects hypoxia mediated HIF-1α stabilization and its influence on metastasis of SHSY5Y neuroblastoma cells. Neuroblastoma cell lines of SHSY5Y were subjected to 1% hypoxia and normoxia for ten cycles to get IH conditioned SHSY5Y cells. The effect of IH on HIF-1α stabilization was analyzed by real-time RT-PCR, western immunoblotting, and immunofluorescence analyses. Effect of IH on CXCR4 and other osteoclastogenic factors were analyzed by RT-PCR analysis. Stable cell lines of shHIF-1α and HIF-1α overexpressing SHSY5Y cells were studied for altered inductive abilities of RAW 264.7 cell osteoclastogenic tendencies by TRAP assay, CaSR expression status, and effects of MAPK inhibitors. Further, the effects of shHIF-1α and HIF-1α overexpressing SHSY5Y cells on osteoclastogenesis were also observed *in vivo* by injecting the stable cells into the tibia of SCID mice. IH conditioning of SHSY5Y cells, which are parental or untreated, shHIF-1α stable expressing cells, HIF-1 overexpressing stable cells showed influence of HIF-1α on osteoclastogenic factor production and abilities to induce RAW 264.7 cell osteoclastogenesis. Higher tumorigenic and osteoclastogenic effects of IH conditioned SHSY5Y cells over the parental cells were observed in intra-tibial SCID mice. Our results clearly show that Hypoxia and IH conditionings are responsible for enhanced stabilization of HIF-1α, which is an important event associated with CXCR4 up regulation and osteoclastogenic induction in neuroblastoma cells.

Keywords: Neuroblastoma; metastasis; hypoxia; HIF-1α

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Seasonal variation in the production of Psoralen, Bergapten and Xanthotoxin in *Ruta graveolens* L., an anticancerous plant

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Abstract
Furanocoumarins namely psoralen, bergapten and xanthotoxin which are novel potent topoisomerase I inhibitors from *Ruta graveolens,* is of interest as they can be applied as anticancer agents. Hence, Reversed – Phase HPLC analysis was done to analyse the content of psoralen, bergapten and xanthotoxin during different seasons of the year April 2014- January 2015, before and after flowering. The leaves harvested after flowering during the month end of September 2014 contained more of psoralen, bergapten and xanthotoxin. In general the stem and leaf of *Ruta graveolens* contained more of bergapten followed by psoralen whereas the concentration of xanthotoxin was very less.

Keywords: Furanocoumarins; Cancer

Acknowledgement*:* The authors wish to thank funding agency, UGC [(MRP(S)/13-14/KABA023/UGC-SWRO] and management, KLE society for providing facilities.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Causes of Carcinogens from Environmental Pollution

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Abstract
Toxic substances that can lead to cancer are called carcinogens. Inventions, developments and changes in technology and lifestyle of mankind are indirectly affecting the growth and development rate of all living organisms. Recent studies show that the disease burden due to environmental pollution has contributed 3.2 million premature deaths in people worldwide during 2010, largely due to cardiovascular disease and lung cancer. Pollutants are unwanted chemicals or other materials found in the environment, at high concentrations to endanger the environment and mortality rate. A pollutant may cause long or short term damage by changing the growth rate of living organism. Cancer may be defined as a group of disease characterized by an abnormal growth of cells and may occur in any type of cells or tissues of the body. Most cancers start due to gene changes that happen over a person's lifetime and are related to environmental, lifestyle or behavioral exposures. According to World Health Organization, the environment in which many of us live poses serious health risks like cancer. Environmental pollution is the occurrence of harmful substances present in the atmosphere and sources may be man-made, such as smoke from vehicles and burning fuels. Both indoor and outdoor air pollutants have been shown to increase the risk of cancer.

Keywords: Lung cancer; Pollutant; Carcinogens; Environmental pollution.

Acknowledgement*:* The authors wish to thank management, Surana College for providing facilities.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Assessment of Antineoplastic Potential of *Annona muricata* on Human Cancer Cell Lines

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Abstract
The plant *Annona muricata* possesses potent bioactive principles in all its parts. The antitumor effects of the extracts from *Annona muricata* include interfering with microtubule polymerization and depolymerization (G2/M phase), inducing cell apoptosis, altering the cell cycle and interrupting signal transduction. The present study with its methanolic leaf extract was undertaken to establish the anti-neoplastic potential of *Annona muricata* by MTT, Cell cycle (, DNA Tunnel (FITC-dUTP), Apoptosis-Necrosis (AnexxinV-FITC) and Caspase 3 (Caspase-3 FITC) assays. The extracts showed dose dependant growth inhibition of MCF-7(Breast cancer), A549 (Lung Cancer) and HCT116 (Colorectal Cancer) cells. Extract treated HCT116, MCF-7 and A549 cells exhibited significant cytotoxicity with an IC50 value of 292.71, 339.52 and 347.7 µg/ml respectively. In cell cycle analysis, cells were arrested in G0/G1 (MCF -7), but significant cell arrests were absent in A549 and HCT116. 84.79% of HCT116 and 91.97% of A549 cells exhibited DNA damage in DNA tunnel assay. Apoptosis was observed in MCF-7 (6.85%), HCT116 (75.04%) and A549 (40.78%) cells respectively. Significant results were shown in caspase -3 assay on HCT-116 and A-549 cell lines with a mean value fluorescence of 18.91 and 24.26 respectively. The above results derive inference that *A. muricata* is a good lead as an anticancer agent.

Keywords: Cancer; *Annona muricata*; MTT

Acknowledgement*:* The authors wish to thank management, Indian Academy Degree College and CMR Institute of Management Studies for providing facilities.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Bioremediation for the Harmful Effects of Phenolic Pollutants that Cause Lymphoma

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Abstract
Environment pollution results in the uptake and accumulation of toxic chemicals in food chains and drinking water thereby posing a health hazard in present and future generations. Aromatic compounds and their derivatives can exist in the environment at a higher concentration than desired due to anthropogenic activities and can be a source of environment pollution. Lymphoma is a group of cancers that affect the cells that play a role in the immune system. Exposure to toxic chemicals is one of the factor being linked to an increased risk of developing lymphoma. Toxic chemicals include pesticides, herbicides or benzene and/or other solvents. Most of these are phenolic derivatives which cause harmful effects to mankind even in small concentrations. Studies have revealed that they cause skin cancer and lymphatic cancer. Bioremediation is a cost effective technique to remove phenolic pollutants from the environment. In bioremediation microorganisms convert these substrates to cell biomass, carbon dioxide and water which are readily accommodated in the ecosystem. In the present study a microorganism which is promising for bioremediation of phenolic compounds was isolated from contaminated soil and it has shown degradation of high concentrations of phenols. Taxonomic evidences have suggested that the bacterial strain is a novel species within the genus *Arthrobacter*. Results presented here indicate that the microorganism has the ability to degrade various aromatic pollutants that are harmful for the mankind. Thus there is a high potential for its use in the development of microbial technology for bioremediation as well against harmful effects of phenols which cause cancer.

Keywords: Bioremediation; Phenols; *Arthrobacter*; Lymphomas

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Evaluation of Antioxidant Properties of *Cyperus rotundus* Rhizomes

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Abstract

Free radicals or reactive oxygen species (ROS) such as singlet oxygen ,super oxide, peroxyl radicals ,hydroxyl radicals and peroxynitrite can damage the body by cellular or oxidative stress This leads to the development of diseases like diabetes, cirhossis, cardiovascular and cancer. The efficacy of plant extract as an antioxidant is long been well established. Many more plants or plant extracts are under way. Plants contain a rich source of free radical scavenging molecules. *Cyperus rotundus* (Family Cyperaceae) is used both as a functional food and as a drug. The rhizome of *Cyperus rotundus* was selected in this present study to evaluate the antioxidant activity, which is capable of treating various diseases including cancer. The objectives of this studies are findings for phytochemicals which are proven to possess antioxidant properties such as flavonoids, tannins, phlobatannins, alkaloids, total phenols from the qualitative analysis of *Cyperus rotundus.* The antioxidative potential of alcoholic extract of *C. rotundus* (CRE) was also evaluated by various antioxidant assays, 1,1- diphenyl-2-picrylhydrazyl (DPPH), superoxide, hydroxyl radicals, and nitric oxide (NO) scavenging system. The effect of Plant extract on cell cycle as analyzed by flow cytometry showed to possess anti cancerous, antioxidant, and anti-diabetic property. Thus our findings reveal *Cyperus rotundus* exhibit anticancerous, antidiabetic because of the presence of bioactive compounds which exhibit antioxidant property.

Keywords: *Cyperus rotundus;* anti-oxidants; anti-cancerous; anti-diabetic

Acknowledgement: Authors thank Principal, staff and students of RISM for their support.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Immunotherapeutics in Cancer

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Abstract
The human body has the ability to retort back to the presence of any foreign body by the activation of its immune system, which is called as the immune response. The treatment of any disease by inducing, enhancing or suppressing this immune response is known as Immunotherapy. Immunomodulators are the active agents of immunotherapy, which are a diverse array of recombinant, synthetic and natural preparations. The molecular identification of cancer antigens has opened new possibilities for the development of effective immunotherapies to boost the body's natural defences to fight the cancer. The immunotherapy for cancer includes Monoclonal Antibodies, Non-specific Immunotherapies like Interferons and Interleukins, Oncolytic Virus Therapy, T-Cell therapy and Cancer Vaccines including DC vaccine, Tumour vaccine. The scope of Immunotherapy also encompasses research areas such as allergy, autoimmunity diseases, transplantation and other infectious diseases like HIV, hepatitis.

Keywords: Immune response; Immunomodulators; T-Cell Vaccines; Immune Cells; Cancer Vaccines; Tumour vaccines.

Acknowledgement: The authors wish to thank management, ABBS, Bangalore for the providing facilities.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Lifestyle and Cancer

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Abstract

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. It is a degenerative process that develops over a long period of time and goes through many stages which start out with damage to a cell.

Around 134,000 cancers each year are the result of a poor lifestyle, Cancer Research UK has found. In the most wide reaching study yet conducted into the issue, it was found that 14 different lifestyle factors ranging from smoking, to lack of exercise, eating too much salt, not having babies, drinking too much and being overweight contributed to four in every ten cancers diagnosed in the UK.

Smoking is a leading cause of cancer and death from cancer. It causes cancers of the lung, oesophagus, larynx, mouth, throat, kidney, bladder, liver, pancreas, stomach, cervix, colon, and rectum. Alcoholic beverages are classified by the International Agency for Research on Cancer (IARC) as a Group 1 carcinogen (carcinogenic to humans.3.6% of all cancer cases and 3.5% of cancer deaths worldwide are attributable to consumption of alcohol. There is now a clear body of evidence that bowel cancer is more common among those who eat the most red and processed meat.

Psychological stress describes what people feel when they are under mental, physical, or emotional pressure. When it comes to beauty products, the effects of the ingredients they contain can be more than just skin deep. Getting to and staying at a healthy weight is important to reduce the risk of cancer and other chronic diseases, such as heart disease and diabetes. These are few of the factors that can lead to cancer. And thus by making healthy changes to our lifestyle in this fast paced world we can reduce the risks of cancer.

Keywords: Carcinogen; cosmetics; cancer; overweight; smoking.

Acknowledgement: The authors wish to thank management, ABBS, Bangalore for the providing facilities.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Human Umbilical Cord Blood (HUCB) Proteins from Aged Pregnancy as Validated Biomarkers for Cancers

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Abstract
To assess oxidative stress (OS) status in aged pregnancy (HUCB) and non-pregnant normal blood samples (NPNB), isolation and identification of protein biomarkers from HUCB in aged pregnancy. Validation of isolated proteins such as Periostin and Alpha-fetoprotein as validated probable biomarkers. Human umbilical cord blood was obtained from the first pregnancy between the age group of 19-30 were considered (N=4). The subjects were pre-evaluated in terms of gestational complications such as diabetic, hypertension, thyroid etc., and not included in the studies. Biochemical analysis of oxidant biomarkers (Total AOA, GPx activity, GR activity, SOD activity, PXn, AOPP and LPO) was analyzed. The proteins present in the sample were identified by SDS-PAGE. Our results revealed oxidative stress as an associated parameter with aged pregnancy as hypothesized. Protein expression increased with increase in age from which it is evident that these protein biomarkers could be an early diagnostic tool for validating the risk factors. This data has to be further validated and confirmed. The current project has successfully investigated OS status in aged pregnancy. The current study showed that advanced pregnancy exerts a maximal oxidative stress, but is characterized by minimal compensatory upregulation of antioxidant enzymes. The protein biomarkers such as Periostin and alpha-feto protein were over-expressed in HUCB with advancing age. Oxidative stress is associated with pregnancy, which probably could be counteracted with suitable interventions such as administration of antioxidant vitamins during the course of pregnancy.

Keywords: Oxidative stress (OS), Antioxidant Enzymes (AOE), Thiobarbituric acid reactive substances (TBARS), advanced oxidation protein products (AOPP), Superoxide dismutase (SOD), Glutathione reductase (GR), and Glutathione peroxidase (GPx)

Acknowledgement: The authors wish to thank management, mLAC for providing facilities.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Role of ERK1/2 in tumour progression of N-Ethyl N-Nitrosourea (ENU) induced transplacental wistar rats glioma models

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Abstract
Gliomas are the common form of brain cancers amongst which astrocytomas are the predominant forms. Glioblastoma multiforme (GBM) represent the high grade glioma which may occur either directly (Primary or *de novo*) or may recur from low grade astrocytomas (secondary GBM). The *Wistar* rats were administered with n-Ethyl n-Nitrosourea (ENU) transplacentally during the critical days of gestation. The pups with glioma were examined for the role of Extra-cellular signal Regulated Kinase (ERK1/2) on cell proliferation during early (90 days of post neonatal age) and later stages (180 days of post neonatal age) of glioma tumor progression. This study is carried out to understand the role of Extra-cellular signal Regulated Kinase (ERK1/2) in unregulated cell proliferation of early and later stages of ENU induced glioma rats. Pregnant *Wistar* rats were administered with ENU (75 mg/Kg Body Weight) through intra-peritoneal administrations. Pups after 90 days (Early) and 180 days (Later) of post neonatal age were decapitated and their brain tissues were used for morphological, immunohistochemical and western blot analyses. The early stage gliomas developed early neoplastic cell proliferation centers which developed into highly vascularized tumor phenotypes in later stage. The later stage tumors have shown higher (30%) Ki67 index compared to early stage (10%). Increased expression levels of GFAP, pERK1/2, pBad and Bcl-2 proteins were found in later stage tumors. Our results have clearly shown that in ENU induced transplacental Wistar rats, tumor progression is mediated through increased rates of cell proliferation, pERK1/2 activation and anti-apoptotic characteristics.

Keywords: Glioma, Immuno-histochemistry, Tumor, GFAP, pBAD, Bcl-2

Acknowledgement: The authors wish to thank management, MSR for providing facilities.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Development of modified method for preparation of full and low calorie rasomalai with enhanced sensory attributes

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Abstract
The flavour of the new millennium is confined largely in varieties of indigenous milk based sweets. Each sweet product has its distinctive taste and flavour which has been evolved through ages. This concept of consuming nutritionally rich milk based sweet with exceptional taste as with stood test of time not withstanding cholesterol scare of the west. One of the milk chhana based sweet known for its unique based taste gaining popularity is rasomalai, Much of the processing involved in this preparation is done on a small scale by traditional confectionaries. To prepare sweetened condensed milk adjusting the fat content to 6 percent. In this investigation an alternate method was developed to prepare rasomalai with attractive flavour and taste. Rasomalai liquid base. The standardised sweetened condensed milk was flavoured with saffron and permitted colour and was subjected to chemical, microbiological and sensory qualities by adopting standard procedure. Similarly rasomalai was prepared by using combination of cream and skim milk liquid base followed with addition of flavour and colour. Rasomalai obtained using sweetened condensed milk and flattened rosogolla gave a unique taste with very good flavour and taste with high sensory attributes better than the normal conventional rasomalai. Rasomalai prepared by using cream and skim milk also gave similar sensory attributes to that of usual rasomalai. The liquid base of rasomalai was fortified with functionally ingredients namely green tea extract, phytosterol, vitamin A, E, C and iron to impart health benefits. Apart from this low calorie rasomalai was standardised by replacing fat with maltodextrin and sugar with sucralose for the benefits of diabetic and diet conscious consumers. Development of value added rasomalai with health providing functional ingredients would offer good market demand.

Keywords: Rasomalai, maltodextrin, sucralose, skim milk, chhana, fortification

Acknowledgement: KC Das Pvt. Ltd. for providing laboratory facility for the research work

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Significance of [-2] proPSA as a novel and early diagnostic marker for prostate cancer

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Abstract

Prostate cancer (PCa) continues to be a leading cause of cancer mortality in men, Prostate specific antigen (PSA) which is a glycoprotein is the most widely used serum marker for early PCa detection. Use of PSA in PCa screening has revolutionized the clinical practice of PCa detection. Under normal conditions, PSA is produced as a pro-enzyme (proPSA) by the secretary cells that line the prostate glands (acini) and secreted into the lumen where the pro-peptide is removed to generate active PSA. The active PSA can then undergo proteolysis to generate inactive PSA. Of which a small portion then enters the bloodstream and circulates in an unbound state (free PSA). Alternatively, Active PSA can diffuse directly into the circulation where it is rapidly bound by protease inhibitors including alpha-1-antichymotrypsin (ACT) and alpha-2 macroglobulin. Although generating less PSA per cell than normal tissue, prostate cancer cells lacks basal cells, resulting in the disruption of the basement membrane and normal lumen architecture. As a result, the secreted proPSA have direct access to the circulation resulting in "leakage" of PSA into the blood stream. The majority of free PSA (fPSA) in the serum reflects the mature protein that has been inactivated by internal proteolytic cleavage. In contrast, this cleaved fraction is relatively decreased in prostate cancer. Typically, from 70-90% of the PSA in serum is combined PSA (cPSA), with the remainder being fPSA. The % fPSA (ratio of fPSA to tPSA) in serum has been demonstrated to significantly improve the discrimination of prostate cancer from benign prostatic conditions, especially in patients with PSA levels in the$\geq$ 4 to $\leq$ 10 ng/ml range. A higher % fPSA in serum is correlated with a lower risk of prostate cancer, while % fPSA values below 10% are more highly associated with cancer.

Amino acid sequencing of whole purified PSA isolated from prostate tissues showed that the proPSA in peripheral zone cancer consisted mainly of [-2]proPSA (p2PSA) rather than other 4 isoforms present in the serum of proPSA. The [-2] proPSA test is particularly useful for patients with a normal prostate, whose PSA levels is between the range 4 to 10ng/ml, a range considered the "diagnostic gray zone" because most men with higher levels have prostate cancer and most men with lower levels do not . Therefore, serum p2PSA emerged as a promising marker for PCa detection. The current study indicates that p2PSA is a promising screening tool with enhanced accuracy reducing number of unnecessary biopsies and thus the cost.

Keywords: Prostate Cancer, Serum, PCa Markers

Acknowledgement: The authors wish to thank the management, T. John College for providing facilities.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Study of the electrochemical redox characteristics of Quinoline Carboxamide Derivatives and their derivatives

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Abstract
A series of novel Quinoline-6-carboxamides and 2-Chloroquinoline-4-carboxamides were synthesized by the reaction of their analogous carboxylic acids with various amine derivatives in the presence of base TEA and protecting agent BOP at room temperature. Synthesized compounds were confirmed by spectral characterization viz IR, ^{1}H-NMR, and MS. The electrochemical behaviour of anticancer carboxamide and its derivates was studied at a glassy carbon electrode using cyclic and differential-pulse voltammetric techniques. The various parameters such as effects of anodic peak potential (E_p), anodic peak current (I_{pa}), scan rate, effect of substituent, heterogeneous rate constant (k^0), etc have been discussed. The shifts in peak potential were observed with the various in substituent's.

Keywords: Quinoline-6-carboxamides, 2-chloro quinoline-4-carboxamides, antibacterial activity

Acknowledgement: The authors wish to thank management, Govt Sci. College for providing facilities.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Myricetin: A Natural Anti-Cancerous Dietary Agent

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Abstract
Flavonoids comprise the most common group of plant polyphenols and provide much of the flavor and color to fruits and vegetables. More than 5000 different flavonoids have been described. Myricetin belonging to the subclass of flavonol shows possible health benefits by their potent antioxidant and free-radical scavenging activities observed *in vitro*. Myricetin treatment on cancer cells exhibited anti-proliferative effects by inducing apoptosis and cell cycle arrest. Apoptosis of pancreatic cancer cells *via* the activation of caspase-3 and 9 is observed. It induces apoptosis of human bladder carcinoma cell line T-24 with activation of caspase-3 after DNA cleavage and cell cycle arrest in G2/ M phase by a down-regulation of Cyclin B1 and cdc2. It inhibits the phosphorylation of Akt but increases the phosphorylation of p38 and decreases MMP-9 expression. The above mechanisms prove the potentiality of myricetin as a natural apoptotic & anti-cancerous dietary agent.

Keywords: Flavonoids; Myricetin; Apoptosis; Caspase; Anti-cancer

Acknowledgement: The authors wish to thank management, Department of Biotechnology, Sapthagiri College of Engineering, Bangalore

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Development of full and low calorie mysore pak fortified with effective functional ingredients to enhance its nutritive and therapeutic value

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Abstract

Traditional dairy products in India have a very long history and have been the nucleus of a vast variety of delicacies prepared by our ancestor. Among the indigenous sweets delicious mysore pak (ghee based sweet) occupies an important place of preference by virtue of its unique taste. So far very little improvement in the ghee based mysore pak have been noticed. Further mysore pak occupies a special place since it is made out of ghee being the dairy product. In this investigation attempts have been made to enhance its nutritive and therapeutic value since these sweet are popular among all sections of society. Enhancement by fortifying the base ingredients with functional ingredients namely oats, barley (anticholesterol), fibre control for diabetic and improved digestion. Green tea extract and grape seed extract (source of polyphenols and antioxidant) wheat fibre, mulberry leaves extract (natural calcium, antioxidant, antimicrobial activity), Ginger extract (to provide good flavour, anti-inflammatory effect, gastro intestinal relief). A method for standardization for low calorie mysore pak using appropriate low calorie fat substitute and synthetic sugar, a premix was compounded for fortification containing vital micronutrients and calcium and iron. All the experimental mysore pak were subjected to chemical, microbiological, and sensory qualities adopting standard procedures showing high level of acceptability. Indian delicacies from indigenous sweets have been a source of joy for ages. Each delicacy involves a presenting and modified one as its distinctive charms and continuous to surprise and benefit the connoisseurs even today. The tenfold growth in demand for this delicacy mysore pak with enhanced nutritive and therapeutic value will provide a good opportunity in related industry to market value added mysore pak with enriched health attributes to benefit the consumers at large and thus provide health for all in the current millennium through consumption of this health oriented indigenous sweet.

Keywords: Mysore pak, functional ingredients, sensory evaluation, therapeutic value

Acknowledgement: The authors thanks KC Das Pvt. Ltd. for providing laboratory facility for the research work.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Development of full and low calorie probiotic along with yakult cultured mishti dahi fortified with functional nutrients, enhancing its nutritive and therapeutic value

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Abstract
Burning issues like obesity, malnutrition, micronutrient deficiencies, lifestyle impacts throw considerable opportunities for food industry to address these health concerns. Industry and product related concerns cannot be addressed in isolation. To develop products like misti dahi with enhanced nutritive and therapeutic value. Yakult is fermented milk known to impart high therapeutic value such as modification of intestinal function, cancer prevention, restores impaired immune function, corrects sodium imbalance, antienterocolitis, preoperative symbiotic therapy which is prepared using health providing strain Shirota of *L. Casei* and is being marketed widely. Misti dahi preparation is standardized using concentrated milk with high sugar content. In this investigation a combination of probiotic cultures along with *L.Casei* Shirota strain were used in the preparation of Mishti dahi to further enhance the therapeutic value. There are a number of factors introduced to obtain a rich harvest of both probiotic and yakult cultures, fortifying with functional ingredients along with micronutrients which will be highlighted. Preparation of low calorie Mishti dahi possessing high nutritive and therapeutic value was standardized using appropriate fat replacer (maltodextrin) and sugar replacers (sucralose). All the experimental Mishti dahi were examined for chemical, microbiological, sensory quality parameters adopting standard procedures. Therapeutically and nutritionally enriched Mishti dahi recorded a high incidence of probiotic yakult lactic cultures with high growth density exceeding 1×10^{7}cfu per ml with almost equal proportion of *ST:LA:Bi:Lc* organisms. Development of full and low calorie Mishti dahi with enhanced therapeutic value using combination of probiotic along with yakult lactic cultures would provide immense opportunity to market health oriented popular fermented milk to benefit both diabetic and diet conscious subjects in particular.

Keywords: Mishti dahi, Probiotic culture, therapeutic value, standardization

Acknowledgement: The authors thanks KC Das Pvt. Ltd. for providing laboratory facility for the research work.

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Open Access

ISSN 2278-1404

International Journal of Fundamental & Applied Sciences

Phytochemicals and Cancer

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Abstract

Cancer remains to one of the leading causes of death around the world. Epidemiological studies showing a protective effect of diets rich in fruits and vegetables against cancer have focused attention on the possibility that biologically-active plant secondary metabolites exert anti-carcinogenic activity. This huge group of compounds, now collectively termed 'phytochemicals', provides much of the flavor and color of edible plants and the beverages derived from them. Many of these compounds also exert anti-carcinogenic effects in animal models of cancer, and much progress has been made in defining their many biological activities at the molecular level. Cancer chemoprevention with natural phytochemical compounds is an emerging strategy to prevent, impede,. delay, or cure cancer. Phytochemicals are compounds found in the plants, which protects us from environmental and ingested carcinogens by arming our antioxidant enzymes, enhancing DNA repair pathways and have direct effects on the fundamental hallmarks of cancer progression and metastasis. However, much of the research on phytochemicals has been conducted which shows that many phytochemicals present in plant foods are poorly absorbed by human subjects, and this fraction usually undergoes metabolism and rapid excretion.

Keywords: Phytochemicals, anti-carcinogenic activity, secondary metabolites, chemopreservation.

Acknowledgement: The authors wish to thank management, ABBS, Bangalore for providing facilities.

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