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ARJYOPA
HEALTHCARE

CONTENTS

CONTENTS

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Sex and Relationship After Cancer

"There is life after Cancer"

As more people are living for a long period after cancer, sexual dysfunction and infertility have increasingly been recognized as negative consequences that impact quality of life.

Sexual dysfunction is a frequent long term side effect of cancer treatment.Although not every cancer survivor cares about remaining sexually active, long term sexual dysfunction will be present in at least 50% of patients treated for cancer of breast, prostate, colorectal or gynaecological cancer. Only 20% of them seek medical help.

Sexual rehabilitation and treatment of organic problems, behaviour treatment and relationship require counseling of both partners.

According to Gina Maisano, a two-time breast cancer survivor and the author of "Intimacy after breast Cancer", "It is not the kind of issue many doctors address. They think we have saved your life and we are done, you should be happy, But you want your life back, you did not fight this hard to live half a life, you want everything and that includes sex".

One can start a beautiful new relationship with some one you have been with for years after cancer diagnosis. Doctors should to address physical, mental, emotional and relationship issues of the patient.

Cancer treatment can cause damage to hormonal, vascular, neurologic and psychological elements of sexual function. Cancer treatment through surgery, radiation and chemotherapy can have profound effect on sex and relationship.

The various sexual dysfunctions in men include decrease in libido, erectile dysfunction and ejaculatory disturbances. In women, cancer treatment can cause decreased desire, dyspareunea (painful intercourse) and lack of arousal and orgasm.

Various treatment options are available to treat sexual problems in both men and women.

Hence sexual function and fertility after cancer can no longer be regarded as frivolons or irrelevant issues. Counseling, prevention and treatment of sexual and relationship issues should be a part of overall treatment of cancer in both men and women.

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CANscript™: A Patient Driven Multiplex Phenotypic Platform for the Selection of Optimal Therapy

Cancer discovery and research has led to significant translational progress. The success rate of treatments, however, has not met our larger expectations. In fact, overall survival (OS) for many cancers remains static for last few decades. This trend prevails despite our intense efforts to validate biomarker guided response prediction tools and, in more recent times, vouching for Next Generation Sequencing (NGS) to identify new actionable molecular targets. As cancer therapy enters an era of individualized medicine, one important realization that has changed the focus and direction of our strategic thinking is the value of considering tumor as a complex and dynamic phenotypic entity.It is apprehended that the fate of an intended therapy is not solely guided by molecular mechanisms of action (MMOA) of a particular drug for a particular patient, rather orchestrated by the diverse phenotypic context and its functional modulation within tumor microenvironment (TME) during and after therapy. This asserts a new paradigm for patient driven individualized medicine when considering the personalization of informed treatment decision.

CANscript™ is a systems biology driven 3rd generation multiplex phenotypic assay platform that was engineered and subsequently validated for multiple cancer indications using drugs which have diverse mechanisms of action. In this platform, patient derived tumor matrix proteins and autologous ligands support stable growth, heterogeneity of the signaling networks, transcriptomic profiles and active balance of diverse phenotypes at the tumor-immune interface in a personalized ex vivo 3D setting (Majumder B et al, Nature Commun, 2015, Goldman A et al., Nature Commun, 2015). The phenotypic diversity of tumors at baseline and the systems level complexity that this platform recreates in live tumor explant culture along with contextual multiplexing of kinetic and functional modulation of response markers comprehensively allows it to offer enormous scope of interrogating the comparative efficacy of drugs ranging from cytotoxics, targeted, metabolic inhibitors and, more encouragingly, immune checkpoint inhibitors for clinically defined individual patients. The rapid readouts (both pathological and biochemical) of CANscript™ are integrated into a single predictive score evolved from a novel machine learning algorithm and it demonstrates high negative and positive predictive value for multiple cancer indications. Collectively, CANscript™ represents a new frontier in the next generation phenotypic assay platforms that are emerging as game changing technologies, to shift the global landscape of individualized cancer therapy and underpin newer opportunities in the premise of rational selection of treatments.

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Gamma Tocotrienol as novel radiation countermeasure

Currently there is no drug for countering acute injuries resulting from external penetrating ionizing radiation exposures approved by the Food and Drug Administration (FDA) to protect first responders deployed in a radiation field for military operations, which is a likely event. This is a serious capability shortfall. In this regard, we have been studying the radioprotective efficacy of various tocol isomers for the last several years. We demonstrated that a single subcutaneous injection of gamma-tocotrienol (GT3) to mice 24 h prior to whole body gamma-radiation confers a striking survival benefit. We have shown that GT3 protect (1) animals exposed to lethal radiation and (2) against radiation-induced hematopoietic and gastrointestinal injury. GT3 also protected animals from vascular damage. Survival was partly dependent on inhibition of the enzyme hydroxyl-methyl-glutaryl coenzyme A reductase and involves biosynthesis of tetrahydrobiopterin. GT3 induces thrombomodulin (TM) and endothelial TM enhances GT3-mediated recovery post-TBI and hematopoietic cell recovery. GT3 attenuates radiation-induced cytogenetic damage, possibly by modulating RAD50 expression.

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An Evidence Based Approach to Complementary and Alternative Medicine in Cancer

Cancer death rates have declined across all age groups worldwide. Consequently, the number of cancer survivors is increasing. The use of complementary and alternative medicine (CAM) by cancer patients is widespread. It is estimated that as many as 75-80 % of cancer patients use CAM therapies, and a large percentage of them combine conventional therapies with CAM. CAM use in the Indian Subcontinent is also common.

Patients seeking integrated cancer care, and health care providers wishing to provide such care, face confusing information about CAM. This current position concerning cancer CAM education is unsatisfactory and must change. The challenge for the future is to match CAM's popularity for cancer prevention and treatment, and demand with an evidence-based information.

This seminar will provide evidence based CAM information to practitioners. This will enable them to engage in meaningful discussions with patients concerning CAM benefits, limitations and risks in the treatment and prevention of cancer. Evidence from randomized control studies is sufficiently significant to justify complementary (adjunctive) use of CAM therapies for a variety of clinical problems and troublesome symptoms associated with cancer and other chronic diseases. For example, there is sufficient evidence to support the use of: (a) acupuncture for nausea and vomiting associated with chemotherapy, and chronic pain; (b) mind -body techniques such as meditation and biofeedback for pain and anxiety associated with cancer. and c) certain dietary practices and nutrients for cancer prevention. Physicians who utilize these treatments in their practice report benefits both for their patients and themselves. Several studies have repeatedly confirmed that patient satisfaction with CAM is very high.

There are many CAM therapies, however, that have yet to show a benefit or might even present an unjustifiable risk to cancer patients. Those therapies include coffee enemas, chelation, Laetrile, ozone therapy, megadoses of vitamins and shark cartilage, Herbal therapies may pose risks as well. Use of these unproven and or disproven therapies may also result in loss of valuable time and the opportunity to receive potentially beneficial therapies.

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Ultrasound as a diagnostic tool in Oral Cancer - A Review

Ultrasonography (US) is one among the more commonly used imaging modalities for diagnosing maxillofacial diseases and disorders. It's an inexpansive, easy to use and non-invasive technique when we compare it with other maxillofacial imaging modalities like Computed Tomography, Magnetic Resonance Imaging, Positron Emitting Tomography etc. Use of USG in maxillofacial region imaging has been explored much in recent years and found to be important in diagnosing solid and cystic swellings of head and neck region, space infections, intra-osseous lesion of jaw etc. Development of high-resolution US and US-elastography has stretched its uses in diagnosis of TMJ disorders, carcinoma of tongue, cervical lymph node metastasis etc. Other than these USG have also been of use for Guided fine needle aspiration. Though in present scenario USG is being used to diagnose multiple numbers of maxillofacial diseases but it is yet to have its share in maxillofacial imaging as a routine diagnostic aid.

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Herbal Medicine offers great potential in support of Metronomic Cancer Therapy

Background: In spite of the advances in Cancer treatment, limitations exist. Refractory cases and late presentations are particularly worrying. The uncertainty of cure and the high costs have led to the popularly of complementary and alternative medicine in cancer treatment. Herbal medicine has particular attraction because it has been shown to be working on a multi-targets direction: promoting apoptosis of cancer cells, anti-angiogenic and immunomodulating.
Research on creating a simple herbal formula with multiple effects of cancer control has started and showed in laboratory platforms promising results.

Metronomic Chemotherapy: Attention on the use of old oral cytotoxic drugs in small doses for refractory and late cancer cases has started more than a decade. Satisfactory and good results have been found to be related to anti-angiogenesis, immunomodulations and cancer all apoptosis. These findings are comparable to the use of multiple targets herbal medicine.

Research on Anti-Cancer Medicinal Herbs
5 medicinal herbs have been screened out from a collection of reported records for platform research studies. These herbs were found to possess multiple effects of pro-apoptosis, anti-angiogenesis, immunolo-modulating and anti-metastases. The combination would make an ideal anti-cancer supplement to be used as adjuvant in metronomic cancer therapy.

Conclusion: Assumption is made that metronomic chemotherapy, combined with herbal medicine could be achieving synergistic effects and would be affordable to all patients.

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Role of cytochrome P4501A enzymes in polycyclic aromatic hydrocarbon (PAH)-mediated pulmonary carcinogenesis in mice, and attenuation of carcinogenesis and tumorigenesis by omega 3-fatty acids.

Methylcholanthrene (MC) and benzo[a]pyrene (BP) are potent polycyclic aromatic hydrocarbons (PAHs) carcinogens. PAHs are present in cigarette smoke, diesel exhausts, and charcoal broiled meats, etc. Cytochrome P450 (CYP) 1A/1B1 enzymes play key roles in the activation of PAHs to carcinogenic metabolites, which initiate carcinogenesis by binding covalently to DNA, and these adducts, if not repaired, could lead to tumorigenesis. In this study we tested the hypothesis that pre-treatment of mice with omega-3-fatty acids, i.e. [eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) will lead to attenuation of PAH-mediated pulmonary DNA adduct formation and pulmonary tumorigenesis. Twelve week old male and female A/J mice received EPA (60 mg/kg) and DHA (40 mg/kg) from day 1 to day 24. Control mice were treated with vehicle corn oil. On day 3, mice were treated with BP (40 µmol/kg) or 3-methylcholanthrene (MC, 40 µmol/kg) by i.p. In the short-term experiment (DNA adduct studies), 3-5 mice from each group were terminated at day 10 (7 days after BP or MC treatment). EPA/DHA significantly suppressed formation of BP-DNA and MC-DNA adducts in lung and liver of both male and female mice. In the long-term experiment (tumor studies), 8 mice for each group continued to receive EPA/DHA twice per week till end of experiment (16 weeks). Pulmonary tumor incidence and multiplicity was significantly suppressed in mice given EPA+DHA, compared to those given the PAHs, BP or MC alone. These studies suggest that the omega 3-fatty acids are potential candidates for the prevention of PAH-mediated lung cancers in humans

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Nitric Oxide in Cancer Drug Resistance

Topoisomerase poisons (Camptothecins, Etoposide and Doxorubicin) are important drugs for the treatment of human tumors in the clinic. Nitric oxide (˙NO), a physiological signaling molecule, is involved in many cellular functions, including cell proliferation, survival, and death. Topoisomerases contain several free sulfhydryl groups which are important for their activity and are also potential targets for nitric oxide (NO)-induced nitrosation. NO nitrosates many cellular proteins, causing altered protein and cellular functions. NO/˙NO-derived species induced a significant down-regulation of topoisomerase I protein via the ubiquitin/26S proteasome pathway in human colon (HT-29) and breast (MCF-7) cancer cell lines. Importantly, ˙NO treatment induced a significant resistance to CPT only in MCF-7 cells. Treatment of purified topo IIα and β with propylamine propylamine nonoate (PPNO), an NO donor, resulted in inhibition of the catalytic activity of topoisomerase II. Furthermore, PPNO significantly inhibited topoisomerase II-dependent ATP hydrolysis. NO-induced inhibition of these topoisomerase II (α and β) functions resulted in a decrease in cleavable complex formation in MCF-7 cells in the presence of VP-16, m-AMSA and XK469 and induced significant resistance to these drugs in MCF-7 cells. As tumors express nitric oxide synthase and generate NO, inhibition of topoisomerase functions by NO/NO-derived species could render tumors resistant to certain topoisomerase poisons in the clinic.

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Mesenchymal stem cells and pericytes: New challenge for cancer immunotherapy

In spite of escalating significance of immunotherapy for cancer management, desired success is yet to be achieved. Presence and participation of non-hematopoetic stromal cells (NHSCs) within tumor microenvironment (TME) in tuning and defining the immune evasion strategies of tumor is poorly understood and thus needs special evaluation. In this context we have studied the immune-regulatory mechanisms imparted by two closely-related NHSCs, mesenchymal stem cells (MSC) and pericytes. We are reporting that tumor-MSCs in contact independent way prevent the ability of dendritic cells to promote naïve T cell expansion and late-phase effector functions without affecting activation. Tumor-MSCs secret IL-10 and facilitate binding of STAT3 to a GAS-like motif within cystathionase promoter leading to repression of cystathionase transcription, which generate scarcity of cysteine (required for T cell function). Whereas, tumor-pericytes prevent activation and effector functions of T cells in contact dependent way. IL-6 orchestrates nod-like receptor family member to help tumor-pericytes to acquire 'regulatory antigen presenting cell' like feature and thereby promote antigen specific T cell anergy or deletional tolerance. Therefore, our study first time demonstrated that MSCs and pericytes employed completely different mechanisms to suppress T cell immunity within TME. Given the important contribution of NHSCs in immune evasion this study help in better understanding of tumor biology as well as in crafting more successful immune-based therapy.

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Tumor-treating fields elicit a conditional vulnerability to ionizing radiation via the down regulation of BRCA1 signaling and reduced DNA double-strand break repair capacity in non-small cell lung cancer cell lines

The use of tumor-treating fields (TTFields) has revolutionized the treatment of recurrent and newly diagnosed glioblastoma (GBM). TTFields are low-intensity, intermediate frequency, alternating electric fields that are applied to tumor regions and cells using non-invasive arrays. The predominant mechanism by which TTFields are thought to kill tumor cells is the disruption of mitosis. Using five non-small cell lung cancer (NSCLC) cell lines we found that there is a variable response in cell proliferation and cell killing between these NSCLC cell lines that was independent of p53 status. TTFields treatment increased the G2/M population, with a concomitant reduction in S-phase cells followed by the appearance of a sub-G1 population indicative of apoptosis. Temporal changes in gene expression during TTFields exposure was evaluated to identify molecular signaling changes underlying the differential TTFields response. The most differentially expressed genes were associated with the cell cycle and cell proliferation pathways. However, the expression of genes found within the BRCA1 DNA-damage response were significantly downregulated (Po0.05) during TTFields treatment. DNA double-strand break (DSB) repair foci increased when cells were exposed to TTFields as did the appearance of chromatid-type aberrations, suggesting an interphase mechanism responsible for cell death involving DNArepair. Exposing cells to TTFields immediately following ionizing radiation resulted in increased chromatid aberrations and a reduced capacity to repair DNA DSBs, which were likely responsible for at least a portion of the enhanced cell killing seen with the combination. These findings suggest that TTFields induce a state of 'BRCAness' leading to a conditional susceptibility resulting in enhanced sensitivity to ionizing radiation and provides a strong rationale for the use of TTFields as a combined modality therapy with radiation or other DNA-damaging agents.

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Emerging Trends in Diagnostic and Theranostic Nanoprobe for Cancer Treatment

Drug-development is the most challenging foot-step in modern pharma and biotech research. After finding the therapeutic efficacy of a drug or drug candidate successful implementation depends on the right developmental team work among chemists, biologists, bioinformatics, and medical doctors. However, therapeutic efficacy of a drug depends on its ability to overcome the biological barriers and reach the desired tissue and intracellular target sites. The biological barriers includes, for example cellular plasma membranes, blood-brain barriers (BBB), and nuclear membranes. It is generally known that the plasma membrane allows entrance only those molecules with an appropriate range of molecular size, polarity, and charge. Therefore, many well developed drug with promising *in vitro* activities fail to come up as a successful pharmaceutical agents. In the present scenario production of suitable drug delivery vehicle or molecular transporters or nano-carrier to overcome the biological barriers would highly desirable in drug development. In this context, a number of cell-penetrating peptides (CPPs) derived from HIV-1 Tat protein have been extensively studied to improve the absorption, distribution, metabolism and elimination (ADME) properties of poorly bio available drugs including small molecules. Drug delivery system particularly targeted drug delivery vector development towards diseased cells or tissues is an important and attractive area in biomedical of research. Next, exploration of a sensitive diagnostic nanoprobe especially towards the aim of point of care treatment is another challenging task for early and accurate diagnosis of malignant cells and tissues which facilitates efficacious therapy and monitoring of therapeutic progression to reduce mortality and morbidity. In this regard, optical imaging technologies using nanomaterials such as gold or silver nanoparticles, iron oxide nanocrystals and quantum dots have successfully been applied for molecular diagnosis, *in vivo* imaging and drug delivery. In recent years, surface-enhanced Raman scattering (SERS) technology invented to be most sensitive techniques among other optical imaging modalities as the signal intensity of molecular vibration enhanced 10^{8} –10^{14} folds compare to simple Raman spectra. Our group has revealed a systematic and comprehensive screening and selection process to identify ultra sensitive and potential multiplexing-capable novel SERS nanotags for *in vitro* and *in vivo* imaging. As a practical application of the novel probes, we have successfully demonstrated the recognition of targeting specific cancer biomarkers e.g. EGFR and Her2, which are important targets for cancer detection and therapy, e.g. breast, lung and cervical and prostate.

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Delivery of Vitamin D3 Topically: Is it possible; A Randomized controlled Trial (RCT)

The IRB of University of Dammam was obtained and informed consent from 550 healthy patients, with vitamin D deficiency and vitamin D insufficiency and deficiency were recruited. Age, weight and height was taken, a detailed history, meticulous clinical examination was performed to rule out any diseases and complete blood picture, serum calcium, phosphorous, alkaline phosphatase, Parathormone and 25 Hydroxy-vitamin D (25OHD) will be done. 25-Hydroxy Vitamin D3 was measured in house by chemiluminescence immunoassay (CLIA) and 30ng/mL was taken as normal, 21-29ng/mL as insufficiency and 20 ng/mL as deficiency. The participants were divided into two groups of 350 in study arm and 200 in control arm. All participants were instructed not to change their dietary habits and life style till the study was over. The study group of women were instructed to apply to apply Top-D (Proniosomal Delivered- Vitamin D3) 1 gram containing 5000 IU of vitamin D3. The second group used 1 gram of Aloe vera gel. The participants had no knowledge to which group they belong. A second blood sample was taken at the end of 4 months and the data was entered in the data base and analyzed using SPSS Inc version 19.

Results: Three hundred and forty five patients in study group and 192 in control group completed the study . The average age of the patients in the study group waszwere 65 males and 280 females whereas in control group males were 55 and 137 females. The pretreatment vitamin D3 level in the study group was 11.03±4.57 (2-12) ng/l compared to the study control group patients 10.36±4.09 (2-21) ($p<0.9$) and post treatment the levels were 37.17±6.04 (12-54) ng/ml and 10.51±3.5 (2-19) ng/ml ($p <0.001$). In the study group 36 (10.28%) patients there was failure of vitaminD3 levels to reach above normal. In the study group 11 patients complained of initial irritation but decided to continue to be in study. In the control group 7 patients had itching which subsided with time (Aloe-Vera).

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Cancer Diagnosis and Margin Analysis by Molecular Assessment of Biopsy Specimens using Mass Spectrometric Imaging

Global changes in metabolism are hallmark features of neoplasia. Cancer exhibits alterations in lipid metabolism caused by the dysregulation of lipogenic enzymes. Metabolic defects also originate by the plethora of the dysregulation of a number of Krebs cycle enzymes, showing significant changes in production of small metabolites. Desorption electrospray ionization mass spectrometric imaging (DESI-MSI) is a powerful emerging analytical technique that enables simultaneous visualization of the distribution of hundreds of metabolites/lipids in biologic tissues. Together with a team of surgeons, pathologists, statisticians, and chemists led by Prof. Richard N. Zare at Stanford University, we are currently exploring DESI-MSI as a rapid diagnostic technique for cancer margin assessment by pixel-to-pixel mapping of metabolites/lipids or ratio of two metabolites. Our success of cancer margin evaluation by DESI-MSI on different cancers, *e.g.,* prostate, pancreatic, and gastric[3] cancers, will be discussed in this presentation with a hope of invoking this technique as a rapid, accurate, sensitive, and intraoperative diagnostic method. The results based on DESI-MSI followed by the statistical method of least absolute shrinkage and selection operator (Lasso) showed 90-98 % agreement with the conventional histopathological evaluation for cancer detection. Mapping the differential distribution of lipids and metabolites on benign and cancer specimens by this technique may also potentially inform us the biochemistry of some unknown behavior of cancer cells, aiding the development of new therapeutic targets for cancer. There are more than a hundred different known cancers that affect humans. The

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Effects of melatonin and vitamin E on oxidative-antioxidative status in rats exposed to irradiation

In this study, the effects of treatment with Vitamin E and melatonin and irradiation-induced lipid peroxidation and its association with antioxidant enzymes in the total bone (bone and
bone marrow) and skeletal muscle of rats subjected to total body irradiation was investigated. Wistar-Albino rats were intraperitoneally treated with 100 mg/kg Vitamin E or melatonin before exposure to 720 cGy irradiation. Control, irradiation, Vitamin E plus irradiation, melatonin plus irradiation groups were sacrificed on the 10^{th} day after irradiation exposure. Application of total body irradiation elevated malondialdehyde (MDA) levels in rat skeletal muscle ($p < 0.001$), but glutathione peroxidase (GSH-Px) and catalase activities remained unchanged. Application of Vitamin E with irradiation or melatonin decreased the MDA levels in skeletal muscle ($p < 0.01$), but did not affect the GSH-Px and catalase activity. MDA levels were found elevated in total bone ($p < 0.001$), GSH-Px activity decreased ($p < 0.001$) and catalase activity remained unchanged in the group treated with irradiation. Application of Vitamin E with irradiation increased the GSH-Px activity intotal bone ($p < 0.01$), but the activity of MDA and catalase remained unchanged. Treatment of the animals with melatonin concurrent with total body irradiation reduced the degree of lipid peroxidation and elevation in antioxidant enzymes in total bone($p < 0.01$).

We conclude that melatonin may protect the total bone from oxidative stress of irradiation exposure. However, the protective effects of Vitamin E were not observed in this study.

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Anticancer effect of Protein A from Staphylococcus aureus Cowan I

Protein A (PA) is a 42kDa glycoprotein present on the surface of *Staphylococcus aureus* Cowan-I (SAC). PA from SAC is well established as one of the immunomodulators with its anti-tumor and immunomodulatory properties. The anti-tumor properties of PA has been successfully demonstrated in different animal models in different types of cancers like chemically induced tumors as well as various transplantable tumors like Dalton's Lymphoma, Ehrlic's Ascities Tumor, *etc.* PA is known to potentiate the cell mediated immunity as well as humoral immunity. PA has been shown to induce natural killer cells in tumor bearing host, which could be a very effective means to control the tumor growth and progression in tumor bearing host.

PA is well known for its unique property to bind with Fc portion of immunoglobulin G (IgG). More interestingly, PA binding affinity at Fc portion has been observed more with immune-complexes as compared to IgG. This unique characteristic of PA makes PA a pertinent and effective tool to alter the balance between tumor antigens, antibodies against tumor antigens and immune complexes in tumor bearing host. As tumor progresses and increase in tumor load leads to complete or incomplete immune-complexes (ICs) are formation which circulates in the hosts' blood-circulation.

Tumor Antigens + Anti-tumor Antibodies $\rightleftharpoons$ **Immune Complexes (ICs)**

Due to the large configuration of ICs they cannot be removed efficiently and effectively from the circulation. Removal of circulating ICs makes a shift in the equilibrium as mentioned in above-mentioned equation leading to immune-potentiation. This strategy can be especially useful for treating those tumors which produce huge amount of immune-complexes like ascites tumor. Further studies in this area could lead to development of new and novel therapeutic strategies to treat fast progressing tumors by removing immunosuppressive immune-complexes using PA from SAC.

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Solubility and Physicochemical Stability Enhancement of Artemisinin and Mefloquine Co-Formulation via Nano-Confinement with Mesoporous SBA-15

The objective of this study is to enhance the dissolution rate, supersaturation and physicochemical stability of combination of two poorly water-soluble anti-malarial drugs, artemisinin (ART) and mefloquine (MFQ), by encapsulating them inside mesoporous silica (SBA-15) via co-spray drying. Characteristic studies such as powder X-ray diffraction (PXRD), transmission electron microscopy (TEM) and scanning electron microscope (SEM) clearly indicate the amorphization of the crystalline drugs. ART/MQF/SBA-15 formulations show a superior dissolution enhancement with a burst release of more than 80% of drugs within 30 min. In addition, the combination formulation exhibits a stable supersaturation enhancement by 2-fold higher than that of the untreated crystalline counterparts. ART/MQF/SBA-15 samples possess excellent physicochemical stability under 2 different moderate storage conditions for 6 months. The amorphization of ART and MFQ via nano-confinement using mesoporous SBA-15 is a potentially promising approach to enhance the solubility of poorly water-soluble anti-malarial drugs that co-formulated into a single dosage

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Race between Cancer and Life - Deuterium Depleted Water (DDW)

Deuterium is a stable isotope of hydrogen. Natural water contains nearly 150 ppm Deuterium. Water containing less than natural abundance of deuterium, is known as Deuterium Depleted Water (DDW). Recent literature survey indicates that DDW of 25 ppm to 120 ppm has many positive health applications like anti-cancer/tumor, antidiabetic, nonspecific immune defense of the body, anti-ageing, and Radio-protective effects. International papers reveal that insulin resistance has been treated with DDW. These are available in international markets to the common public on prescription by authorized persons. Reports of few clinical trials involving human beings have also been published.

DDW is being used abroad for more than a decade for treatment of cancer (adjuvant therapy) fight against side effects of chemotherapy and radiotherapy, fighting ageing for skin treatment, removing the DNA errors and getting rid of hereditary diseases like diabetes, heart diseases, thalassemia, etc. Some of the experts feel that continuous consumption of DDW for 3 months daily as per the prescribed dose increases survival rates of cancer patients and rejuvenates healthy people by eradicating DNA error.

As mentioned in the literature, presence of natural concentration of deuterium is vital for cell proliferation and that the cell division is triggered by the change of the D/H ratio (the ratio of D/H temporarily increases during the process of cell division). Basically hydrogen gets pumped out from the cell during cell division, therefore, deuterium concentration increases within the cell. As a result when D concentrations decreases in the body by deuterium depletion, cell division gets hindered and this effect is more prominent in tumor cell (rate of proliferation is high for tumor cell compare to normal cell) compare to the normal cells.

This, in the majority of cases, resulted in the destruction of the malignant cells, a decrease in tumor mass or its total regression. It is also noted that, Pharmaceutical firm like, HYD pharma, Hungary has already received GMP certification for DDW production facility for clinical trials and will soon apply for ethical approval to start phase 2 clinical trial in chronic lymphocytic leukemia. Based on his findings, various concentrations of DDW are used for therapy and prevention as a dietary supplement e.g. in Hungary as PREVENTA®105, anti-cancer veterinary drug (VETERA® DDW-25 A.U.V), cosmetic product for rejuvenating skin (YUVAN DDW-) etc. Similar products of 25, 50, 90, 120 ppm DDW are also marketed in Japan, UK and USA. Romanian heavy water plants are generating and supplying DDW of various concentrations up to 80 ppm. M/s Cambridge Isotope Laboratories, USA M/s Sigma-Aldrich, USA have catalogued DDW of 2-3 ppm for R&D purpose. Clinical trials by Russian researchers indicate that use of DDW in breast cancer patients removed the toxicity of chemotherapy.

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Protective Effect of Artichoke against Cyclophosphamide Induced Toxicity in Experimental Rats

Cyclophosphamide (CYP) is a widely used antineoplastic drug, which could cause toxicity of the normal cells due to its toxic metabolites. The purpose of this study is to investigate the possible protective role of artichoke towards the tissue defense system on CYP toxicity. Adult male Wistar-Albino rats were used for the study. Rats were divided into four groups as follows; control group, artichoke group (artichoke was administered), CYP group (CYP was administered), CYP with artichoke group (CYP and artichoke were administered). The rats were administered orally of artichoke at the dose of 1 g/kg for 7 days before and 5 day after CYP injection. The rats were administered a single injection dose of CYP in the dose of 150 mg/kg and sacrificed at 5th day after the dose of CYP. The effects of artichoke on CYP induced tissue toxicity were evaluated by using malondialdehyde (MDA), reduced glutathione (GSH) levels, catalase (CAT), glutathione peroxidase (GSH-Px), glutathione-S-transferase (GST), superoxide dismutase (SOD), glucose-6-phosphate dehydrogenase (G6PD) activities and histopathological examination in liver tissues. CYP caused the oxidative stress by the increased MDA level and the reduced GSH level, CAT, GSH-Px, SOD, GST and G6PD activities in liver ($p<0.05$). MDA, GSH levels and CAT, GSH-Px, SOD, G6PD enzyme

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The Role of Calreticulin Transacetylase Mediated Epigenetic Modulation by Polyphenolic Acetates in Lung Tumor suppression

Background: Cancer, also called malignancy, a genetic disease initiated either by mutation or epigenetics. We are targeting lung carcinoma, most common cause of cancer-related death in men and women. This work aims new drug discovery for targeted mechanism comprising *Calreticulin Transacetylase* (CRTAase). Target oriented drugs for treating lung cancer by inducing hyperacetylation and upregulating the expression of genes important in tumor suppression. The polyphenolic acetates in combination with HDAC inhibitors are known to promote hyperacetylation, leading to apoptosis in cancer cells.

Aim: To determine the efficacy of Polyphenolic acetates as an anti-cancer drug targeting acetylated histone interaction.

Methodology: The transacetylation activity of CRTAase was established in A549 cells by transfection of CRTAase gene, additionally the DAMC (7, 8-Diacetoxy-4-Methyl Coumarin) was screened for their anticancer activity. On confirmation of the transacetylation activity of CRTAase in A549 cells, hyperacetylation activity of DAMC was assessed followed by validation of apoptosis. Specific target based anticancer property of DAMC was evaluated using microarray and RTPCR prior and after demethylation.

Results: Highest transfection efficiency was obtained at 72 hrs. Significant increase ($p<0.01$) in expression of H3 (2.67±0.02) and H4 2.755±0.016) was observed in DAMC treated CRTAase gene transfected A549 cells as compared to non-transfected A549 cells treated with DAMC (2.14±0.023) and (2.161±0.011) respectively. The RNA having RIN (RNA Integrity) values between 8.5 - 9.8 on electropherogram were subjected to microarray and RTPCR. The cells treated with DAMC and Valproic acid(VA) were suggestive of synergistic upregulation of tumor suppressor genes viz. ING4, TCF21, MFSD2A, FHIT and metalloproteinase inhibitor 3 i.e.TIMP3 and downregulating the oncogene Skp2.

Conclusion: The findings suggest that DAMC and VA can potentiate the apoptotic pathway via CRTAase and thus can be a very promising anticancer drug candidate. In further studies we will be screening more drugs targeting similar/more molecular targets and extending similar studies *in-vivo* with clinical applications.

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Complex Genetic Heterogeneity Increases "Risk Factor" During Organogenesis in Wilms' Tumor

Wilms' Tumor (WT1) is one of the rare tumor among all associated to the early embryogenesis of developmental life in children. Genetic factors play an important role during organogenesis due to heterogeneous cell population. Interestingly, WT has been reported in association with a variety of different unconstitutional abnormal karyotypes such as XY/XO and break points. The loss of Y- chromosome seems to be closely associated to tumorigenesis and their role either in development of germ line tumour progression or in association to testicular differentiation. Hence, the curiosity has been developed to evaluate WT1 gene mutation and their correlation with MTHFR C677T gene polymorphism to assess the genetic heterogeneity in Paediatric tumor with special reference to WT. In the present study, blood samples (1.0 ml) of WT were collected for lymphocytes culture to develop Karyotypic analysis, evaluate WT 2 gene mutation by PCR and MTHFR (C677T allele) gene polymorphism by ARMS - PCR in WT cases. These DNA samples were further characterized by DNA sequencing (Sanger method) for SNP analysis and involvement of "novel mutation". However, WT 1 missense mutation was detected in one male case out of n=15 samples, and mutation of 226bp was observed along with appearance of isoforms of approximate 190 bp isoforms. Further, MTHFR gene polymorphism identified MTHFR C677T gene polymorphism where C→T increases "Risk factor for development of disease..Further, stem cell study showed down regulation of Oct, Sox in one case of WT and lack of changes was observed in rest of the cases. However, further characterization of stem cells SOX2, OCT4 & NANOG were also assess to find their association between WT1 gene mutation & pluripotency during organogenesis in population of Bihar

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Effect of Reactive Oxygen Species in p16 protein expression and its modulation by curcumin in MCF-7 breast cancer cell line.

Background: Breast cancer is the leading cause of cancer-related death in women worldwide. Cancer is a hyperproliferative disorder that is usually treated by chemotherapeutic agents that are toxic not only to tumor cells but also to normal cells, so these agents produce major side effects. In addition, these agents are highly expensive and thus not affordable for most. Moreover, such agents cannot be used for cancer prevention. Traditional medicines are generally free of the deleterious side effects and usually inexpensive. Curcumin, a component of turmeric (Curcuma longa), is one such agent that is safe, affordable, and efficacious.

Aim: To investigate the role of p16 protein expression and to see the effect of curcumin in ROS affected MCF-7 cells by western blotting.

Materials & Methods: MCF-7 cells were grow in DMEM with penicillin/streptomycin media and MTT assay were done to see the cell viability followed by UV exposure, ROS and the cells treated with curcumin followed by western blotting.
Results: We checked the p16 protein expression in UV exposed cells at different time interval that showed the expression of p16 protein is increased in higher exposure as compared to lower time interval and ROS expression is decreased. Further we checked the p16 protein expression in UV exposed MCF-7 cells and treated with curcumin anti cancer drug that showed p16 protein expression is increasing in lower concentration of drug and ROS level was increased. Statistical analysis was done between treated cells with curcumin and p16 protein expression it was statistical significant $p<0.001$.
Conclusion: p16 protein expression in UV exposed MCF-7 cells and treated with curcumin showed expression is increasing in lower concentration of drug and ROS level also increased.

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Targeting GSK-3beta for Oral Cancer Treatment

Background: Cancers of oral cavity is one of the most common cancer types in Indian subcontinent. Glycogen synthase kinase (GSK3) is a novel tumor suppressor, and emerging evidence has suggested its role in oral cancer progression, pathogenesis and drug resistance. Hence targeting this key molecule may lead to control this devastating disease.

Methods: The expression, activity and regulation of GSK3 beta were assessed in human oral cancer tissue samples (including apparently normal adjacent tissues, benign tumor samples, premalignant lesions healthy normal tissues) and oral cancer cell line (SCC4/-9) and this was correlated with the expression of various markers of the cell division, cell survival, cell death and cell invasion regulators. These were performed by using various biochemical and statistical methods.

Results: The high expression and inactivation of GSK3 beta was observed in most of the tumor samples compared to normal oral mucosa [1,2,3]. Further, the ectopic over-expression of active GSK3 beta in SCC9 cells increased the cell death and negatively affects growth, compared to vector alone and these anti cancer effects were further enhanced by use of cisplatin, taxal and natural compounds like nimbolide (a limonoid isolated from the leaves and flowers of the neem tree (Azadirachta indica A.Juss)) in cell culture.

Conclusions: These studies demonstrated that, combination of activating GSK3 beta along with application of chemotherapeutic drugs, natural compounds might be a potential strategy for the treatment of human oral cancer.

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Impact of host immunogenetics in cervical cancer: A study in Indian women

High risk Human papillomavirus (HPV) infection, the etiological factor of cervical cancer (CaCx), is mostly transient. However, in few infected women it persists and leads to CaCx . To understand this differential outcome of HPV infection, we aimed to identify possible association of host immunogenetics with this infection that leads to such complication. Women were recruited from the Tata Memorial Hospital and KEM Hospital, Mumbai. They were divided in three groups on the basis of their cervical abnormalities and infection status. HPV typing, HLA analysis and polymorphism in a specific T cell receptor was done using standardized methods. Results revealed, multiple HPV types along with HPV type 16 is the major cause of CaCx. The European T350G variant of E6 gene of HPV 16 was the most prevalent type. This variant is known to cause a persistence infection thus, increasing the risk. Three novel variants of E6 gene of HPV 16 was reported in the study population. Specific HLA alleles are observed to be associated with CaCx or with its prevention. Study highlighted for the first time significant association of a specific SNP +49A/G of CTLA-4 gene with CaCx. Type of HPV infection and presence of specific host factors may predict infection outcomes. Hence, they may be useful in cancer screening programs or in successful implementation of HPV based immunization programs.

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MicroRNA-183 cluster in hepatocellular carcinoma (HCC): Potential as a biomarker

Hepatocellular carcinoma (HCC) a primary liver cancer is the second leading cause of cancer related deaths worldwide.Molecular mechanisms of HCC pathogenesis are complex involving epigenetic alterations including miRNAs. MiR-183-96-182 cluster is consistently reported to be up regulated in HCC. Hence, the present study evaluated the role of miR-183-96-182 cluster and its diagnostic potential in HCC.

Expression of miR-183-96-182 cluster in cells and tissues of HCC was determined and its functional characterization carried out in HCC cells. Target genes for miR-183-96-182 cluster were identified and validated. Temporal analysis of 183-96-182 cluster in liver and plasma of diethylnitrosamine induced HCC rat model was done. Serum levels of 183-96-182 cluster in different categories of HBV infected patients during the progression of liver disease to HCC were determined.

Our results showed up regulation of miR-183-96-182 cluster in various cell lines and tumor tissues of HCC. Molecular mechanism behind functional role of miR-183-96-182 cluster in cell viability, migration and invasion involved regulation of *ETS2* and *EGR1* expression by hsa-miR-182-5p and hsa-miR-183-5p in Hep3B cells respectively. miR-183-96-182 cluster was found to be significantly up regulated in liver tissues and plasma of DEN treated Wistar rats. Interestingly, levels of hsa-miR-182 and hsa-miR-96 were found to distinguish between HCC and normal subjects whereas levels of miR-96 could distinguish CHB and control subjects as determined by ROC curve indicating their diagnostic potential.

The present study suggested that up regulated miR-183-96-182 cluster has a role in liver disease progression and elevated levels of plasma of miR-183 and miR-96 indicated their biomarker potential.

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Renoprotective and Antihyperglycemic Effects of Tinospora Cordifolia Stem on Alloxan Induced Diabetic Mice

Tinospora cordifolia commonly called Guduchi has been extensively used for its various medicinal properties. The effects of methanolic stem extract of this plant on blood glucose concentration and histopathology of kidneys was assessed. Mice were given intraperitoneal injection of alloxan monohydrate to a dose of 120 mg/kg body weight and divided into two groups with three mice in each group. First group served as control and were given distilled water. Second group were given Tinospora stem extract orally to a dose of 300 mg/kg body weight for a period of 28 days. Fasting blood sugar levels were determined after regular intervals and prior to dissection. A significant decrease in blood glucose levels with value 114.00±8.71 mg/dl in extract administered groups was observed as compared to diabetic mice with value 183.00±6.24 during the period of experiment up to 28 days stage. The histopathological studies of kidneys of diabetic mice revealed degeneration of renal architecture, but with restoration after treatment with administration of Tinospora extract was observed.

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Understanding of Molecular Mechanism of Colorectal Cancer in Indian Population

Colorectal cancer (CRC) is the third most common cancer in men and the second in women worldwide, making it the fourth most common cause of death from cancer. In India, the estimated incidence and mortality from CRC is 36476 cases and 25690 cases, respectively. CRC rates are about 2 to 5 times higher in the developed countries in comparison to the developing countries which may be attributable to a range of variations in a disparate set of risk factors and diagnostic practices. Lifestyle related predisposing modifiable risk factors for CRC include physical inactivity, overweight and obesity, red and processed meat consumption, smoking and excessive alcohol consumption.Colorectal cancer (CRC) development involves underlying modifications at genetic/ epigenetic level. This study evaluated the role of Kras gene mutation and RASSF1A, FHIT and MGMT gene promoter hypermethylation together/ independently in sporadic CRC in Indian population and correlation with clinicopathological variables of the disease.

One hundred and twenty four consecutive surgically resected tissues (62 tumor and equal number of normal adjacent controls) of primary sporadic CRC were included and patient details including demographic characteristics, lifestyle/ food or drinking habits, clinical and histopathological profile was recorded. Kras gene mutation at codon 12 & 13 and methylated RASSF1A, FHIT and MGMT gene was observed in 47%, 19%, 47%, 37% and 47% cases, respectively. Alcohol intake and smoking were significantly associated with presence of Kras mutation (codon 12) and MGMT methylation (p-value <0.049). Tumor stage and metastasis correlated with presence of mutant Kras codon 12 (p-values 0.018, 0.044) and methylated RASSF1A (p-values 0.034, 0.044), FHIT (p-values 0.001, 0.047) and MGMT (p-values 0.018, 0.044) genes. Combinatorial effect of gene mutation/ methylation was also observed (p-value <0.025). Overall, tumor stage 3, moderately differentiated tumors, presence of lymphatic invasion and absence of metastasis was more frequently observed in tumors with mutated Kras and/ or methylated RASSF1A, FHIT and MGMT genes. Synergistic interrelationship between these genes in sporadic CRC may be used as diagnostic/ prognostic markers in assessing the overall pathological status of CRC. Oncogenic human papilloma virus (HPV) is the major viral etiology in cervical cancer, oral cancer.Cancer of uterine cervix is the second most common cancer among women worldwide but it is the leading cancer in Indian women. Infection with high risk-HPVs (HR-HPV) is associated with precancerous lesions and cancer, with type HPV-16 being the most prevalent, followed by types 18, 31, 33, and 45 in India. Though persistent HPV infection is needed for development

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Personalized Medicine: An Ayurvedic Perspective

The Ayurvedic system of diagnosing *Prakriti* offers a unique approach in understanding and assessing one's health. *Prakriti* of a person is individual as a genome sequence. It is comprehensive in scope, spanning both physical and mental aspect. It is not merely a diagnostic tool but also a guide to action for good health. *Prakriti* plays an important role to predict the susceptibility of the manifestation of disease, and it is also possible to predict the probable clinical features of each *Prakriti* type. This would give us an opportunity to predict clinical features and will be helpful in taking preventive measures on how they should be avoided and cured. This kind of study would further help in selecting the drugs and treatment modalities and also be helpful in the prevention and progression of the disease. *Prakriti* theory is unique in terms of multi-faceted approach, however it is not been fully utilized to its potential. Contemporary studies confirm and establish the *Prakriti* as genetic theory of modern science. However, the Ayurvedic hypothesize give us a clear cut indication and a material for research to the scientists of today, which if proved may provide a revolutionary instrument to the mankind in the field of development of human organism and its personality in the field of personalized medicine.

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High Throughput Screening in Drug Discovery

Nanomedicines, the medical applications of nanotechnology, are promising candidates for targeted drug delivery. Novel targeted drug-delivery approaches using nanomedicines are changing the future of therapy. The nanomedicine field has devoted significant effort towards developing insight into the technological and biopharmaceutical advantages and disadvantages of different nanomedicine systems. Many different nanomedicines have been developed that improve the stability, solubility, pharmacokinetics/biodistribution, toxicity, and/or efficacy of cytotoxics and other classes of payloads Delivery system characteristics like size, charge, shape, type of surfacemodification, and biocompatibility have an important influence on the biodistribution and clearance of the nanomedicine. This industry perspective focusses on oncology-based nanomedicinal therapeutics only, as they receive about two-thirds of the research attention.The concept that nanomedicines aim to improve the therapeutic index of anticancer drugs by modifying their pharmacokinetics and tissue distribution to improve delivery to the site of action is well known.Anti-cancer nanomedicines in clinical development can be broadly divided into five main types: liposomes, polymeric conjugates, polymeric nanoparticles, polymeric micelles, and others. Although human clinical studies to assess the efficacy and safety of nanomedicine agents have started to emerge, there are many challenges to address before further commercialization or widespread implementation and clinical acceptance can occur. These barriers include the need for long-term material/ therapeutic storage, the availability of substantial clinical trial funding, social and ethical issues, potential health and environmental impacts, regulatory requirements (e.g., manufacturing and controls, safety and toxicity validation, etc.), and a continually evolving intellectual property landscape. Thus the herbal/marine resources having rich anticancer activities are targeted by conversion into nanomaterials as drug targets towards global cancer.

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Relationship of Blood Groups with Oral Precancers and Oral Cancer

Aim: To evaluate whether any of the ABO blood groups are associated with an increased risk for oral cancer.

Materials and Methods: The present study was conducted at Department of Oral & Maxillofacial Pathology, after obtaining permission from the Institutional review board. The study sample comprised 60 patients of each histologically diagnosed Oral Squamous Cell carcinoma (OSCC, n=30), clinically diagnosed oral Submucous Fibrosis (OSMF n=30) and 30 control groups. For statistical analysis, Chi-square
Test using Graph Pad prism 5 software to assess the relationship between ABO blood groups and OSCC, OSMF and control group.

Results: It was found that people with blood group A had almost 60-70 % increased risk of developing OSCC with most prevalant being Well Differentiated OSCC as compared to people of other blood groups. Similarly blood group A was also found to be more prevalant for cases of stage II OSMF.

Conclusion: By employing a simple blood grouping test during community field programs,
people with blood group A in the age group of 40–59 years having tobacco chewing habits can be apprised that they are more at risk to develop oral cancer than people with other blood groups.

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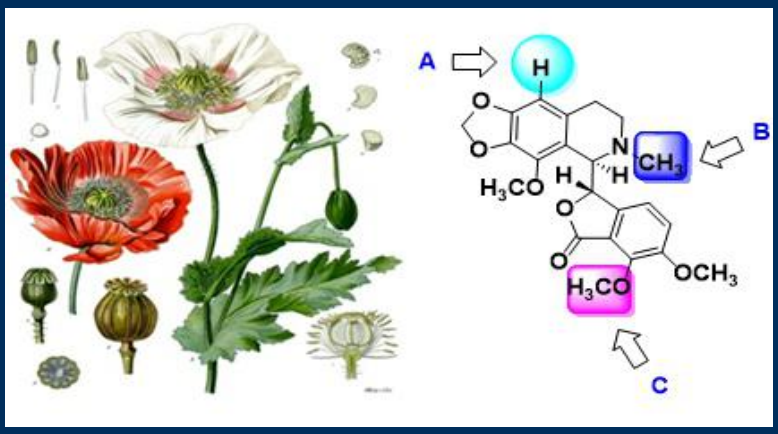
Design, synthesis and evaluation of novel noscapinoids as anticancer agents

α-Noscapine (also known as Narcotine, Nectodon, Nospen, and Anarcotine) is a naturally occurring phthalide isoquinoline alkaloid isolated from plants of the Papaveraceae family.[1] It has been used orally as antitussive agent and displays a favorable toxicity profile. It has also been known for some time that α-noscapine can act as anticancer agent through the disruption of tubulin steady state dynamics. Although it is weak inhibitor of microtubule polymerization, it is not toxic at tumor suppressive doses. With excellentoral bioavailability and low cost, allow this natural product for further exploratory medicinal chemistry.[2] Derivatives of noscapine (also called as noscapinoids) such as 9-fluoro, 9-bromo, 9-chloro, 9-iodo, 9-amino and 9-azido noscapines have shown to increase anticancer activity than the parent α-noscapine..

we herein discuss synthesis of various new α-noscapine congeners designed by adding various functional substituents at positions designated as A, B and C on noscapine core. The anticancer activity profile of new noscapinoids will also be described.



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Molecular Mechanism of DNA Repair in Plant Genome

Plant cells are subject to high levels of DNA damage resulting from plant's obligatory dependence on sunlight and the associated exposure to environmental stresses like solar UV radiation, high soil salinity, drought, chilling injury and other air and soil pollutants including heavy metals and metabolic byproducts from endogenous processes. The irreversible DNA damages, generated by the environmental and genotoxic stresses affect plant growth and development, reproduction and crop productivity. Thus, for maintaining genome stability, plants have developed an extensive array of mechanisms for the detection and repair of DNA damages. DNA polymerase I (Pol I) is the sole member of family X DNA polymerase in plants and plays crucial role in nuclear DNA damage repair. transcriptional up-regulation of *Arabidopsis thaliana* DNA polymerase I (*AtPol*I) in response to abiotic and genotoxic stress including salinity and DNA cross-linking agent mitomycin C (MMC). The increased sensitivity of *atpol*I knockout mutants towards high salinity and MMC treatments with high levels of accumulation of double strand breaks (DSBs) than wild-type plants and delayed repair of DSBs have suggested requirement of Pol I in DSB repair in plants. This work focuses on the recent advances in our understanding of mechanisms regulating plant genome stability in the context of role

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Alteration of Gut Microflora by Anti-Cancer Drugs

Introduction: Hepatocellular carcinoma (HCC) is the third most common cause of cancer death, the most recurrent primary liver cancer and fifth most common malignant worldwide with over 7-8 lakhs new cases each year[1]. HCC can develop at any stage of liver cirrhosis

Materials & Methods: Diethylnitrosamine (DEN) and 2-acetylaminofluorene (AAF) were used for liver cancer induction in male Wistar rats[11]. 5-Fluorouracil (20mg/kg bw) and Doxorubicin (1 mg/kg bw) were two chemotherapeutic agents selected in the study and were administered intraperitoneally. Upon completion of the the induction and treatment, the tissues i.e., liver, small intestine and large intestine were used for expression studies as well as for the histophological analysis. The fresh fecal sample were collected just before the autopsy and used for the stool DNA isolation to study different phyla and bacterial sps.

Results: Induction of apoptosis is one of the most important characteristics which differentiates a cancerous cell from a normal cells. The liver showed an increased proliferation of hepatocytes following DEN-AAF induced hepatocellular carcinoma as compared to the control group. Following the treatment with 5-F and Dox the proliferative characteristics reduced significantly and more profound results were obtained in 5-F treated group. The expression studies carried for the analysis of NF-kB, TLR-2, TLR-4, MMP2 and MMP9 revealed that MMP2 and MMP9 expression in the liver which was up-regulated in cancer induced groups was down regulated in both the reversal groups. In contrast, there was no change in the NF-kB expression but the TLR-2 and 4 expressions increased significantly in both 5-F and Dox treated groups. The NF-kB, TLR-2 and TLR-4 expressions in the liver were at par to that found in small and large intestine with large intestine majorly affected.

Conclusion: Although the currently used chemotherapeutic agents show most efficient anti-cancer efficacy but they are also a potent agent to cause severe gut microfloral dysbiosis. In the present scenario, the liver cancer characteristics are reversed but there is a permanent irreplaceable damage caused on the microbiome which by itself may lead to other complications. The need of the hour would be targeting the microbiome for the treatment of cancer

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Targeted Nanomedicine - Challenges and Strategies against Global Cancer

Nanomedicines, the medical applications of nanotechnology, are promising candidates for targeted drug delivery. Novel targeted drug-delivery approaches using nanomedicines are changing the future of therapy. The nanomedicine field has devoted significant effort towards developing insight into the technological and biopharmaceutical advantages and disadvantages of different nanomedicine systems. Many different nanomedicines have been developed that improve the stability, solubility, pharmacokinetics/biodistribution, toxicity, and/or efficacy of cytotoxics and other classes of payloads Delivery system characteristics like size, charge, shape, type of surfacemodification, and biocompatibility have an important influence on the biodistribution and clearance of the nanomedicine. This industry perspective focusses on oncology-based nanomedicinal therapeutics only, as they receive about two-thirds of the research attention.The concept that nanomedicines aim to improve the therapeutic index of anticancer drugs by modifying their pharmacokinetics and tissue distribution to improve delivery to the site of action is well known.Anti-cancer nanomedicines in clinical development can be broadly divided into five main types: liposomes, polymeric conjugates, polymeric nanoparticles, polymeric micelles, and others. Although human clinical studies to assess the efficacy and safety of nanomedicine agents have started to emerge, there are many challenges to address before further commercialization or widespread implementation and clinical acceptance can occur. These barriers include the need for long-term material/ therapeutic storage, the availability of substantial clinical trial funding, social and ethical issues, potential health and environmental impacts, regulatory requirements (e.g., manufacturing and controls, safety and toxicity validation, etc.), and a continually evolving intellectual property landscape.

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Characteristics and treatment outcomes of male breast cancer reported to Regional Cancer Centre, India

Introduction: Breast cancer in men is a rare disease that accounts for less than 1% of all cancers in men and less than 1% of all diagnosed breast cancers1. The mean age at diagnosis is between 60 and 70 years, though men of all ages can be affected with the disease.
Research methodology: This retrospective study was carried out in the department of radiation oncology Regional Cancer Centre, Kamala Nehru Memorial Hospital, Allahabad, India. The institute is recognized by Ministry of Health and Family Welfare, Department of Science and Technology, and Department of Atomic Energy of Regulatory Board, Government of India as research institute. The institute provides comprehensive facilities for cancer diagnosis, treatment and patient monitoring under one roof.

Results: During the study period, male breast cancer accounts for 2.5% of all breast cancer cases reported to the hospital. The mean age at diagnosis was 52.17±12.4 years. Right and left breasts were affected in 17(74%) and 6(26%) patients respectively. The most common symptoms were breast lump (52%), skin ulceration (22%), nipple discharge (17%) and others (9%). The most common location of the tumor was retroareolar (65%). Histologically, all the patients were infiltrating ductal carcinoma (IDC). Most of the patients were presented in stage III (87%) of which 39% in stage IIIB, 26% in stage IIIC, 22% in stage IIIA. Based on IHC, breast cancer was grouped into TNBC (22%) and non- TNBC (61%). IHC status was unavailable in 17%. At the end of last follow up, loco-regional failures, disease free survival and overall survival analysis showed 1(4%), 10(43%) and 17(74%) patients respectively. Distant metastasis was observed in 5 patients (22%). Liver (60%), followed by lungs (40%) were the sites of metastasis. 1 patient (4%) during the last follow up, reported to have 2nd primary malignancy in gall bladder, 4 patients (17%) lost to follow up and 2 patients (9%) encountered death.

Discussion: The expressions of oestrogen and progesterone receptor in male breast cancer are higher than in females5 and it is consistent with our study (68.4%). Distant metastasis observed in patients with higher grade and advanced stage.The most common treatment for male breast cancer employed was modified radical mastectomy (unlike in females where lumpectomy is one of the options), followed by radiotherapy. Adjuvant chemotherapy in male breast cancer can usually be decided by assessing the risks and benefits in the same manner as in female breast cancer. Because of high expression rates of hormone receptor positivity in male breast cancer, adjuvant hormone therapy with tamoxifen is theoretically the rational therapeutic strategy and should be considered in men with breast cancer

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Cytotoxicity and kinetic studies of potential anticancer agents resistant to deactivation by glutathione

The effect of steric hindrance on reactivity towards biomolecules while designing Ru^{II}*p*-cymene and Pt- based anticancer agents seems to be an important parameter in improving the activity under glutathione (GSH) resistance. Our studies show that the structure, hydrolysis, anticancer activity and the effect on steric hindrance on deactivation by glutathione for a series of Ru(II)–arene complexes of formulation $[Ru^{II}$(p-cymene)(L1)$](PF_6)$ (where L1 is a bis chelate) are very encouraging.[1] The complex with highest steric hindrance has the lowest inhibition by GSH and is more active under hypoxic conditions. In addition, Pt(II) complexes of the type $[Pt(L2)Cl_2]$, where L2 is a bis chelate and a nitrogen mustard, shows that in presence of metal chelation the stability of the mustard may be enhanced and the cellular toxicity under hypoxia exhibits better traits than cisplatin. The cytotoxicity results strongly suggest that controlling rate of hydrolysis through tuning steric hindrance may be a feasible pathway to derive GSH resistant anticancer agents.[2] The cellular studies show that all the complexes show good blood compatibility (haemolysis <3%), cellular death through caspase activation via mitochondrial pathway. On the other hand, we have been able to derive fluorescent cyclic phosphoramides which preferentially localize in the endoplasmic reticulum, have similar or more toxicity in hypoxia and may be tracked due to their fluorescent nature. These phosphoramides are more toxic to HepG2 cancer cells and follow both intrinsic and extrinsic pathways of apoptosis. The phosphoramides are able to inhibit spheroid formation by cancer

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Keratinophilic fungi –Their role in Environmental Ecology

Keratinophilic fungi are natural colonizers on keratinic substrates. Some are keratinolytic and play an important ecological role in decomposing a-keratins, the insoluble fibrous proteins. Because of the tight packing of their polypeptide chains in a-helix structures and their linkage by disulphide bridges, they are hardly biodegradable. Two main ways of attack have been identified: surface erosion and radial penetration. In surface erosion, the sequence of degradation proceeds as the level of keratinization (the cystine crosslinks) of the components of the keratinic matrix increases. In radial penetration, on the other hand, specialized hyphae can penetrate through the matrix, irrespective of the degree of keratinization. This may illustrate how the growth can change direction and how secretory activity may concentrate at the tips of the penetrating hyphae.

Fungi are the second largest group of organisms after insects. Their unusually wide morphological diversity is matched by a singular behavioral diversity, while the many life strategies they have evolved explain their enormous importance in evolution, the ecosystem, human progress, and most of the processes that take place on the Earth considered as a whole, the atmosphere, the oceans, biota and lithosphere.

Diversity is also a feature of fungal nutrition. Moreover, many fungi do not confine themselves to a single mode but display varying degrees of flexibility in response to changes in their environment.

The ability of fungi to adapt quickly to such changes primarily stems from the ease with which they acquire and store genetic information through special hyphae fusion mechanisms that result in the coexistence of different nuclear types, known as heterokaryosis. Differential gene expression rather than selection of nuclei appropriate for a particular way of life seems the mechanism of choice. The direction of nutritional evolution may therefore be assumed to be determined by the options imposed on a fungus by its environment, including, where appropriate the narrowing of specialism within a single mode.

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Proteomics profiling of plasma and synovial fluid for the diagnosis and treatment of Rheumatoid Arthritis

Rheumatoid arthritis (RA) is known to be a chronic, systemic inflammatory and pathologically complex autoimmune disorders of joints. The process of joint damage begins much before the clinical onset of disease. The etiology of this disease is not well characterized, pathophysiology are not well understood and early diagnosis is still remaining a challenge. It is characterized by inflammatory cell infiltration, swollen cartilage, destruction of cartilage and aberrant post-translational modifications of self-proteins. Present study was therefore, planned to identify differential protein using plasma and synovial fluid sample of RA patients along with their control sample. The screening of proteins were carried out using proteomic technique such as 2-dimensional gel electrophoresis followed by identification of differentially expressed protein by matrix-assisted laser desorption/ionization- time of flight mass spectrometer (MALDI-TOF MS/MS) and validation by Western blot, enzyme-linked immunosorbent assay (ELISA), fluorescence-activated cell sorting (FACS) etc. Among several differentially expressed proteins, glial fibrillary acidic protein (GFAP) and α1B-glycoprotein (A1BG) from synovial fluid and transthyretin (TTR) from plasma has been identified as significantly up regulated protein in RA. Further, functional significance of differentially expressed protein (GFAP) in RA has been predicted by making 3D model using *in-silico* methods. The model was subjected to Molecular Dynamic (MD) simulation and protein quality analysis using Gromacs 4.5. These results provided the insights in understanding its molecular structural features towards drug discovery. In addition to this, we used natural extract as a drug to investigate the effect on proteomic profile using *in-vivo* and *in-vitro* studies. Both the studies showed the significant decrease in the level of inflammatory cytokines in RA. The above identified protein may thus can be used as a serum diagnostic marker along with other biochemical parameters and clinical symptoms for screening and diagnosis of RA.

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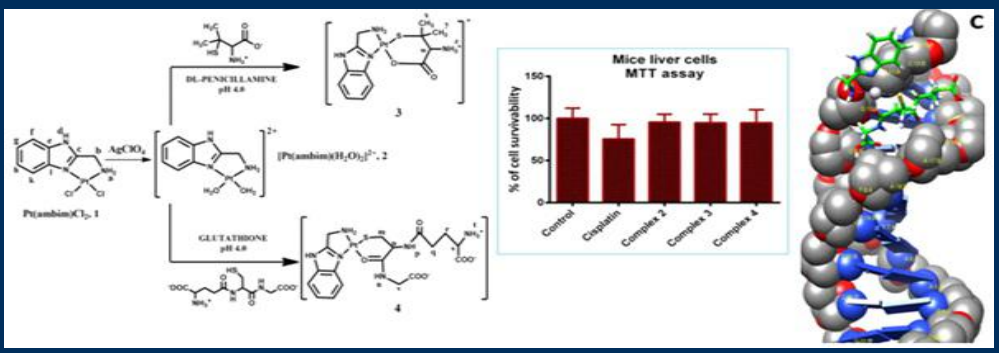
Superior normal cell viability of Pt(II) complexes than cisplatin with benzimidazole as carrier ligand: Synthesis, DNA binding, anticancer property and computational study

The transformations of Pt(II)-Sulfur adduct formation from labile Pt(II) complexes with biologically relevant agents provide a fundamental basis for understanding toxicity and development of resistance in biological systems and hence, is of special concern for pharmaceutical and biomedical research. *cis*-[Pt(ambim)Cl_2] **1** (where, ambim= 2-aminomethylbenzimidazole) was synthesized and characterized by spectroscopic methods. Reaction kinetics between the hydrolyzed product, cis-[Pt(ambim)$(H_2O)_2]^{2+}$ **2** with DL-penicillamine(DL-pen) and Glutathione(GSH) were studied spectrophotometrically in aqueous medium as model reaction of Pt(II)-sulfur adduct. The interactions of **2** with the ligands at pH 4.0 show two distinct consecutive steps. Activation parameters ($\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$) were calculated using Eyring equation and an associative mechanism is proposed for both the reactions. Computational studies using Density Functional Theory (DFT) were carried out to know the electronic structure of the complexes. DNA binding property of the complexes **2-4** was evaluated by spectroscopic titrations, fluorescence indicator displacement experiments and electrophoresis measurements. The complexes effectively bind to calf-thymus DNA via different binding modes with intrinsic binding constants (K_b) in the range of 2.22×10^4–4.76×10^4 M^{-1}, which was supported by molecular docking studies. Antiproliferative properties of **2-4** were probed in vitro against human cervical cancer, non-small cell lung carcinoma and hepatocellular liver carcinoma cell lines and **2** was found to be most effective in growth inhibition in all the cell lines. Remarkably, the complexes also generate lower levels of reactive oxygen species (ROS) than *cis*platin and have almost no adverse effects on normal cells.



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Clomiphene citrate and oocyte quality

The clomiphene citrate (CC) is a first line of medicine used for ovulation induction in women worldwide. CC has good ovulation induction ability in anovulatory women but the pregnancy rate is very poor. This discrepancy might be due to the anti-estrogenic effect of CC at various level including ovary and oocytes. The hypoestrogenic conditions due to CC treatment inhibit follicular growth and development, induce susceptibility of oocytes towards apoptosis and deteriorate oocyte quality after ovulation. Animal studies suggest that the CC induces apoptosis in granulosa cells and results hypoestrogenic state in the ovary. Reduced estradiol 17β level in the ovary affects development and maturation of oocyte leading to oocyte apoptosis. Further, CC increases hydrogen peroxide (H_2O_2) level and thereby bax protein expression and DNA fragmentation in cumulus-granulosa cells as well as in oocytes. Apoptosis deteriorates oocyte quality and thereby reproductive outcome. The exogenous supplementation of either estradiol 17β or melatonin reduces H_2O_2 level in ovary, delays meiotic cell cycle progression in oocyte and protects oocyte apoptosis. Hence, supplementation of estradiol 17β or melatonin along with CC could be beneficial to protect granulosa cell as well as oocyte apoptosis and inhibit deterioration of oocyte quality. Thus, maintenance of oocyte quality may overcome the adverse effect caused due to CC treatment during infertility management.

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New Laws of Health and Health Improvement: Deeper Understanding of Medicine

Lectins are a group of proteins found in all types of living organisms, either in soluble or in membrane-bound form that recognizes specific carbohydrate structures and thereby agglutinate cells by binding to cell-surface glycoproteins and glycoconjugates. Lectin plays potential roles for the prevention and treatment of a wide range of diseases. They occur in foods like wheat, corn, tomato, potato, peanut, kidney bean, banana, pea, lentil, soybean, mushroom, rice etc. Recently, some novel and known lectins were isolated in our laboratory from edible plant sources. Recently, several lectins were isolated at our laboratory from the edible plant sources (*K. rotunda*, *M. oleifera*, *P. sativum*, *N. nouchali*, *S. tuberosum*, *T. dioica*, *S. lycopersicum* etc.) by using different chromatographic methods and their anticancer properties were studied against rapidly growing Ehrlich ascites carcinoma cells (EAC) *in vitro* and *in vivo* in mice as well as against human cancer cell lines. The lectins showed antiproliferative activities with the 10 to 40% cell growth inhibition against EAC cells *in vitro* after incubation for 24 h at 37°C with 5% CO_2. Most effective lectins were then injected (i.p.) in EAC-bearing Swiss albino mice at doses ranging from 0.5 to 6 mg/kg/day for five consequence days. At the 7th day of the EAC cells inoculation, the mice were sacrificed and 30 to 88 % of EAC cell growth inhibition was observed by trypan blue exclusive assay. For the antitumor mechanism study cell morphological changes were studied by florescence microscopy. Effects of caspases were checked by caspase inhibitors and several genes expressions were observed by RT PCR. The results were varied with the change of lectin. Some lectins caused apoptosis by condensing only DNA, while others caused cell morphological changes, fragmentation of DNA and cell blebbing. Moreover few lectins caused cell growth inhibition without triggering apoptosis. The expression of apoptosis-related Bcl-2, Bcl-X, p53, Bax, Bak, NFkB, Cytochrome-c, caspase-3 genes/proteins were obtained for the most of the apoptosis-causing lectins whereas most of them failed to exert their effects in the presence of caspase-3, caspase-9 and/or caspase-8 inhibitors. In most cases, after treating of EAC cells with different lectins, the expression of p53, Bax, Bak, NFkB, Cytochrome-c, caspase-3 gene expressions were increased with the decrease of Bcl-X and Bcl-2 genes expression. Most of the lectins agglutinated EAC cells at different levels where Sheel potato lectin showed the strongest agglutination activity. After and before treatment of EAC cells with the lectins, different phases of cell cycle were studied by using FACS flow cytometry. The effects of different lectins on the different phases of the cell cycle were also different. Effects of the lectins

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Covalently crosslinked PEG hydrogels and self-assembled peptide gels for drug delivery and antibacterial applications

Hydrogels are covalently crosslinked polymer networks, with the ability to absorb water and swell1-3. Owing to their viscoelastic characteristics, hydrogels resemble living tissues and molecules are able to diffuse in and out of these networks. Consequently, hydrogels are used in sensing, drug delivery1-2, and tissue engineering applications3. Use of poly(ethylene glycol) / PEG polymers in biomaterial application has generated significant research interest because these polymers are chemically inert, nontoxic, non-immunogenic, and nondegradable4. PEGs are eliminated from the body intact and considered biocompatible. Our current research is focussed on the fabrication and evaluation of PEG-based hydrogels and self-assembled peptide gels for drug/microbicide delivery and wound healing applications. PEG-based biodegradable hydrogels were fabricated by intermolecular crosslinking of PEG polymers through degradable hydrazone linkages. Hydrogels formed rapidly, with gelation time <1 minute, degree of swellings up to 280%, and storage modulus of up to 1 kPa, depending on pH and concentrations used. These hydrogels exhibited pH-responsive release of a chemotherapy, doxorubicin, in vitro. Self-assembled peptide gels were fabricated from Boc-protected αγ-hybrid diphenylalanine derivatives in aqueous DMSO and their rheological properties, surface morphology, and swelling and degradation profiles were characterized. These gels exhibited broad spectrum antibacterial activities against *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Bacillus subtilis*.

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Breast Cancer: Factors Dominating, Causitives and Early Detection

India is experiencing an unprecedented rise in the number of breast cancer cases across all sections of society, as are also other countries. According to recent Indian surveys, breast cancer is the most common form of cancer in women in the most of cities, whereas it is second most common in rural areas. This is why it is such an important disease to understand. First there will be a brief discussion on the normal and altered physiology of the breast followed by the etiology and possible causative factors. Next there will be signs and symptoms. Finally it will end up with need of awareness.

The female breast is primarily made up of lobules, ducts, and stroma. Lobules are milk producing glands, ducts are the milk passages that connect the lobules to the nipple and stroma is fatty and connective tissue that surrounds the ducts, lobules, blood vessels and lymphatic vessels. Lymphatic vessels carry lymph, a clear fluid containing waste products and immune cells. The lymph nodes along the lymphatic vessels are bean-shaped collections of immune cells. During the change from a normal cell to a cancerous cell, however, the cells require many different gene alterations. Eventually these altered genes form a tumor which may be benign or malignant.

There are believed to be many risk factors of this disease, unfortunately, the reasons for the many of the risks are often unclear. Hereditary, dietary and lifestyle factors are also contributors to breast cancer risk. Cancers in the young tend to be more common in India some cancer are considered aggressive. Many of these cancers are HER2 positive and ER/PR negative, or HER2/ER/PR all three negative, and they have a worse prognosis than those who have ER/PR positive tumors. Women whose mothers had breast cancer are at twice the risk for developing this disease. Diets high in fat are also linked to this illness; because more fat cells produce more estrogen. Increased alcohol consumption also promotes increased estrogen levels. The significant symptom of breast cancer is enlarged lymph nodes.

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The prognosis of lung cancer(LC)

I**ntroduction:** The prognosis of lung cancer(LC) depends on various factors and stage at the time of diagnosis is an important prognostic factor. Cyfra-21 is a marker related with disease response and prognosis of cancer. Search of available literature on this biomarker revealed some studies in other countries. However data regarding studies on the role of this lung cancer biomarker in India is lacking. Hence the present study was planned to detect association of cifra-21 with LC, disease response and prognosis of disease.

Materials & Methods: An observational case-control study was done. 20 patients with proven lung cancer who were planned for chemotherapy, 20 patients of other respiratory diseases and 20 healthy individuals were randomly recruited for the study. Besides the history and examination, blood samples were collected twice and stored for carrying out cifra-21 and SAA by ELISA. Tumor response was evaluated as per modified RECIST criteria.

Results: Median levels of SAA(ng/mL) were found to be 66895 , 15952.5 and 1088.5 in lung cancer patients, case controls and healthy individuals. The levels of cifra-21 were found to be statistically significantly higher among LC patients in comparison to other two groups (p=0.001)
There was statistically significant decrease observed in the serum levels of cifra-21-1 in LC patients on C4 cycle of chemotherapy in comparison to C1 cycle indicating that it could be used as a prognostic marker.

Conclusion:SAA and cifra -21-1 could be valuable diagnostic biomarkers in lung cancer. However in addition cyfra-21-1 could also be used as a prognostic biomarker. Larger studies are required to establish the exact diagnostic and prognostic role.

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Oral Cancer: Primary Prevention to Tertiary care - Dental Professional Role

Oral carcinoma is a global health problem with increasing prevalence and mortality rates. It is the sixth most common cancer in the world. Worldwide, the annual incidence exceeds 3,000,000 new cases. Oral cancer accounts for 2% cancer death in males and 1% in females. Majority of oral cancers involve tongue, oropharynx and floor of the mouth. The lips, gingiva, dorsum of the tongue and palate are less common sites. Oral cancer is a disease of increasing age. Approximately 95% of cases occur in people older than 40 years. The age related incidence suggests that time dependent factors results in initiation and progression of genetic events that results in malignant change. The incidence of oral cancer is clearly age related which may reflect declining immune surveillance with age, time for accumulation of genetic changes and duration of exposure to initiators and promoters.

Tobacco and alcohol are acknowledged with factors for oral cancers. . The combined effect of alcohol and tobacco result in synergistic effect on the development of oral cancer .The mechanism may include dehydrating effects of alcohol on the mucosa, increasing mucosal permeability and the effect of carcinogens contained in alcohol/tobacco. In lip cancer, sun exposure and tendency to burn, pipe smoking and alcohol are identified risk factors. Primary prevention that aims at avoiding or reducing the risk factors, is achieved in community by various means such as motivation by various communication imparts such as personal communications, films, newspaper articles, radio programs, folk-art, posters. In dental practice Primary prevention includes use of routine questionnaire about the use of tobacco, complimenting those who do not use tobacco of any kind, encouraging the tobacco users to stop it, display of suitable educational materials in the waiting room and also distribution of such material to the patients.

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Modulating stemness promoters induce chemosensitivity of breast cancer stem cells

Although different treatment strategies have proved to be effective for various types of breast cancers, relapse of tumors still render this disease incurable in a large number of affected women all over the world. Previous studies examining breast cancer tissues have demonstrated the presence of breast cancer stem cells (brCSCs) within the tumors which are fiercely chemoresistant. Stem cells were isolated and enriched from normal breast and triple negative human breast tumors, and MDA-MB-231 breast cancer cells, using flow cytometry and the expression of self-renewal markers, like Wnt, Sox-2, Oct4 and Nanog, were analyzed. A paclitaxel inhibition test was also conducted in order to detect resistance of brCSCs. Finally, a microarray analysis was done to determine differential gene expression in normal stem cells versus cancer stem cells. The brCSCs revealed elevated $CD44^{+}/CD24^{-/low}$ subset, and high expression of chemoresistance and self-renewal markers, particularly Sox-2, which is essential for derivation of embryonic stem cells (ESCs) from the inner cell mass and for the maintenance of ESCs themselves. In addition, Sox-2 is a marker of stem and progenitor cells in diverse adult tissues, including epithelia of the breast and is closely associated with poor prognosis in patients with breast cancer. In light of these findings, Sox-2 may be linked with stemness of cells of diverse solid tumors. Sox-2 in turn is associated with other genes, which help them to maintain stemness properties of the brCSCs and eventually lead to cell migration and metastasis. Therefore, modulation of Sox-2 expression will reduce drug resistance and tumorigenecity in brCSCs, and prove to be a beneficial therapeutic strategy in future.

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Biochemical Studies on the Effect of Quercetin along with Adriamycin on DEN induced Experimental Hepatocellular Carcinoma

Introduction: Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. Cancer is caused by both external factors (tobacco, infectious organisms, chemicals, and radiation) and internal factors (inherited mutations, hormones, immune conditions, and mutations that occur from metabolism). These causal factors may act together or in sequence to initiate or promote carcinogenesis. Hepatocellular carcinoma, like any other cancer, develops when there is a mutation to the cellular machinery that causes the cell to replicate at a higher rate and/or results in the cell avoiding apoptosis. Hepatocellular carcinoma (HCC) is currently the sixth most common type of cancer with a high mortality rate and an increasing incidence worldwide. Its etiology is usually linked to environmental, dietary or lifestyle factors. Adriamycin is a widely used chemotherapeutic drug to treat many different forms of cancer, but causes side effects by damaging normal cells leading to cardiotoxicity and nephrotoxicity through the production of free radicals.

Material and Method: In the present study Quercetin, a bioflavonoid which is present in capers, apples, tea, onions, red grapes, citrus fruits, leafy green vegetables, cherries, and raspberries is used along with adriamycin to treat DEN induced hepatocellular cancer in experimental rats.

Result: Various biochemical parameters were tested along with the expression of apoptosis gene by RT-PCR and the protein expression by western blotting.

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Compliance of COTPA among Tobacco vendors, Educational Institutions and Public places in Bengaluru city

Background: Tobacco has been the arch criminal of most head & neck cancers in the world. Many laws have been implemented to control this menace but still this slow poison persists. Effectiveness of these laws have always been a matter of concern to the authorities. The present study was conducted to observe the compliance of COTPA among public places, educational institutions and among tobacco vendors in Bengaluru city.
Methods: A cross-sectional observational study was done to assess the violations at public places, educational institutions and tobacco vendors. Violations for Sections 4, 5, 6 &7 of COTPA was assessed from 25 each of these places in the 8 zones of Bengaluru city. The study areas were chosen by convenience sampling method and using a questionnaire the violations were recorded. Data was analyzed in Microsoft Excel to find out the percentage of violations.
Results: The COTPA sec 4 and 5 violation was 134(67%) and 94(47%) respectively. 124(62%) of the educational institutions had tobacco vendors within 100 yards and only 30(15%) had sign board for prohibition of tobacco use. Around 14 tobacco vendors had beedis without proper pictorial warning with them which violated Sec 7 of COTPA.
Conclusion: For proper implementation of COTPA laws we should create awareness about the laws, what amounts to violations and also the health hazards to tobacco use among general population. The law enforcing personnel should act on those who violate the law. There is a need for a sensitization workshop and advocacy for all the stakeholders.

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Use of Softwares in Drug Discovery

Computer-aided drug design plays an important role in drug discovery and development. It has become an indispensable tool in the pharmaceutical industry. Researchers can take advantage of various software and resources in the computer-aided drug design field for the purposes of discovering and optimizing biologically active compounds. Computer-aided drug design (CADD) provides valuable insights into experimental findings and mechanism of action, new suggestions for molecular structures to synthesize, and can help make cost-effective decisions before expensive synthesis is started. Numerous compounds that were discovered and/or optimized using CADD methods have reached the level of clinical studies. Many CADD techniques are used at various stages of a drug-discovery project, and one cannot designate a single 'best' computational drug-design technique in general. Hence, computational medicinal chemists should be aware of and willing to take advantage of all kinds of software and resources related to CADD during their routine work, although individually they may focus on, and subsequently become an expert in, the use of just one or a few specific techniques.

Various software like Chemdraw, SPSS, Graph Prism Pad are widely used for drug development. Chemists can use ChemDraw Professional to draw and submit chemical compound and reaction searches direct to SciFinder, with no more time-consuming cutting and pasting. Scientists can quickly, effectively and accurately communicate research and ideas using an extensive set of biological templates and drawing objects to create compelling illustrations of cells and pathways, including live chemical objects as needed. Scientists save time and increase data accuracy by using ChemDraw Professional to predict properties, generate spectra, construct correct IUPAC names, and calculate reaction stoichiometry. Graph prism Pad is a easy to use graphing and analysis software, originally designed for experimental biologists in medical schools and drug companies, especially those in pharmacology and physiology.

Statistical Package for the Social Science, SPSS Statistics is a software package used for logical batched and non-batched statistical analysis. It is used by social science researchers, market researchers, health researchers, survey companies, government, education researchers, marketing organizations, data miners. SPSS includes descriptive statics, bivariate statistics, Prediction for numerical outcomes and Prediction for identifying groups.

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Recent Advancements in Ayurvedic Pharmacy

The concept of Ayurvedic pharmacy (aka *Rasa Shastra evam Bhaishajya Kalpana*) was laid down thousands of years ago, as certain evidences of basic Ayurvedic dosage forms can be traced from ancient Vedic literature. *Panchavidha Kashaya Kalpana* (PKK) means five modes of processing of drugs or five types of extractions. These are the basic/elementary/prime preparations of Ayurvedic pharmacy, namely *Svarasa* (extracted juice), *Kalka* , *Kwatha*, *Hima* and *Phanta*. With the need of time (i.e. to enhance the potency, selectivity in the pharmacological actions, commercialisation etc) and to overcome certain limitations of PKK (such as non-availability of crude drugs all the time, very short shelf-life, inconvenient taste and dose etc), many more new dosage forms were developed by using these five basic PKK, such as *Churna* (herbal powder), *Vati* (tablets), *Lepa* (ointment), *Taila-Ghrita* (oil/ghee based formulations), *Asava-Arishta* (fermentative formulations), *Avaleha* (medicated confection), *Arka* (distilled formulations) etc. The development is still continue as per need of current era with advancement in technology and emergence of new Ayurvedic products viz tinctures, aerosols, lozenges, jams, jellies, tetra-packed health drinks, beverages, nutraceuticals, cosmetics, and new drug delivery systems (viz liposomes, Phytosomes, etc.). Present report encompasses: past trends in Ayurvedic pharmacy, need of advancement, areas of advancement, and future trends.

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Biofuels and enzyme production using Bioresources: Technology innovations and applications

The technology development for production of bioresources such as biofuels and enzymes is transforming at a rapid pace to make their production more efficient and cost effective. Biofuel production has evolved through various generations starting with production of oil from food crops, to bioethanol production from lignocellulosic biomass such as wheat straw, rice straw, bagasse, kans grass etc., to biodiesel derived from algae cultivated in raceway ponds and photo-bioreactors. The contentious issue with first generation biofuel is food vs fuel, as the majority of fuels have been produced directly from food crops. This has necessitated efficient utilization of carbon in agricultural waste such as sugarcane bagasse, switchgrass, corn stover, wheat straw, rice straw, industrial and municipal waste, lignin derived from wood and paper processing plants, waste paper etc. Biodiesel production from algae is another alternative to reduce dependency on food crops. Here the main aim is to produce more energy per acre than conventional crops and to meet this challenge, focus is on increasing algal productivity by emphasizing on technology development for increasing CO2 residence time in ponds/bioreactor, use of pH stat techniques to maintain high CO2 concentrations and to simulate the bio-process by utilizing flue gases from industries. Furthermore, design of raceway ponds and photobioreactors using techniques such as CFD is a key research area. In our laboratory, we have developed a patented technology called fractional hydrolysis for converting lignocellulosic biomass of kans grass into fractions of soluble sugars in single step. Substrate pretreatment and detoxification steps have been circumvented, as minimal amount of phenolic and other toxic compounds are produced. Sugar recovery of > 90% is achieved which is followed by co-fermentation to give high ethanol yield. Botrycoccus brunni has been cultivated in flat panel photo-bioreactor at high CO2 concentration using pH stat technology achieving high biomass productivity and lipid yield. Solid-state fermentation (SSF) is an attractive technology for enzyme production such as phytase, tannase, cellulase, pectinase etc., which in contrast to submerged fermentation involves utilization of cheap agricultural waste such as wheat bran, rice bran, oil cakes, orange peel, cassava, soybean, apple pomace etc as substrate, gives highly

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Estimation of genotype and phenotype frequencies of Minor Histocompatibility Antigens and its Implications in Hematopoietic Stem Cell Transplantation in Asian Indians

Background: **Minor Hisotocompatibility(H) antigens are polymorphic peptides having significant roles in alloimmune responses after human leukocyte antigen-matched solid organ and stem cell transplantation (SCT) and are instrumental in the process of transplant rejection, GVHD and in the curative graft-versus-tumor effect of SCT.**

Methods: **The study population consisted of 114 locally available, randomly selected healthy subjects and transplant donors. DNA was isolated using the local standard procedures used for HLA typing. Genotyping of ten autosomally encoded minor H antigens and of HY was performed using the PCR-SSP technique. All PCR-SSP samples were analysed on agarose gel. If the internal control PCRs failed for one of the two allele of a particular minor H antigen, the typing for that minor H antigen was marked as incomplete and data were excluded from the analyses.**

Results: **The statistical significance of differences in allele, genotype and phenotype frequencies of ten minor H antigens were determined by Chi-square analysis. P-values lower than 0.05 were considered statistically significant.**

Conclusion: **Here we report differences in minor H antigen genotype and phenotype frequencies and its probable role in stem cell transplantation**

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Identification of Serum-based MicroRNAs for Histological Differentiation of Non-Small Cell Lung Cancer Using Small RNA Sequencing

Introduction: Current therapeutic approaches for the management of non-small cell lung cancer (NSCLC), especially lung adenocarcinoma (ADC), include molecular targeted therapies based on the type of driver mutations in tissue biopsy. However, the derivation of tissue biopsy for the diagnosis of NSCLC is highly invasive and risky procedure and is not always feasible. Hence, biomarkers, which can be detected in body fluids such as blood collected using less-invasive methods, needs to be identified for histological differentiation of NSCLC and making appropriate therapy choices. Aberrant expression of miRNAs has been found in various human cancers and has not only been used as diagnostic, prognostic, and predictive biomarkers, but also as potential therapeutic target. In this study, we did global miRNA profiling using small RNA sequencing for finding serum miRNAs-based biomarkers for differentiation of various histological subtypes of NSCLC, mainly lung ADC & lung squamous cell carcinoma (SqCC).

Methods: For this prospective pilot study, a total of six subjects were recruited, two each of lung ADC, lung SqCC, & healthy controls from the outpatient Department of Pulmonary Medicine & Sleep Disorders, AIIMS, New Delhi. Approximately 5 ml. of blood was collected; serum was separated & RNA was isolated using miRNeasy serum/plasma kit (QIAGEN). Quality and quantity of purified RNA was checked using Bioanalyzer 2100 (Agilent) and Qubit 3.0 Fluorimeter (Thermo Fisher Scientific). Small RNAs were purified from total RNA; libraries of 18 to 50 nt small RNAs were prepared with the TruSeq RNA Library Prep Kit (Illumina), & mature miRNAs were profiled using illumina TruSeq Sequencing Chemistry on illumina HiSeq 2000 platform. Quality check was performed & high quality raw data was mapped on to miRBase database. The expression profile of miRNAs in each subject was analyzed using miRNAkey software & fold change was performed to identify differentially expressed miRNAs in different histological subtypes of NSCLC.

Results: We were able to detect 1074, 1013, & 907 known miRNAs in the serum of lung ADC, lung SqCC, & controls, respectively. A number of miRNAs (total = 116), such as miR-126-3p, miR-125-5p, miR-101-3p, miR-130a-3p, miR-42-3p, miR-146b-5p, miR-155-5p, miR-181b-5p, miR-186-5p, miR-192-5p, miR-195-5p, miR-200b-3p, miR-24-3p, miR-30b-5p, miR-32-5p, miR-34b-5p, miR-374a-5p, miR-378a-3p, & miR-4448 were found to be differentially expressed in lung ADC as compared to lung SqCC (>2 fold change; $p<0.05$). Further, few miRNAs, including miR-93-3p, miR-130b-5p, miR-196b-5p, miR-337-3p, miR-378f, miR-382-5p, miR-424-3p, & miR-1271-3p were found to be specifically expressed in NSCLC as compared to controls (>2 fold change; $p<0.05$).

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Trop-2 is up-regulated in invasive prostate cancer and displaces FAK from focal contacts

In this study, we show that the transmembrane glycoprotein Trop-2 is up-regulated in human prostate cancer (PCa) with extracapsular extension (stages pT3/pT4) as compared to organ-confined (stage pT2) PCa. Consistent with this evidence, Trop-2 expression is found to be increased in metastatic prostate tumors of Transgenic Adenocarcinoma of Mouse Prostate mice and to strongly correlate with α5β1 integrin levels. Using PCa cells, we show that Trop-2 specifically associates with the α5 integrin subunit, as binding to α3 is not observed, and that Trop-2 displaces focal adhesion kinase from focal contacts. In support of the role of Trop-2 as a promoter of PCa metastatic phenotype, we observe high expression of this molecule in exosomes purified from Trop-2-positive PCa cells. These vesicles are then found to promote migration of Trop-2-negative PCa cells on fibronectin, an α5β1 integrin/focal adhesion kinase substrate, thus suggesting that the biological function of Trop-2 may be propagated to recipient cells. In summary, our findings show that Trop-2 promotes an α5β1 integrin-dependent pro-metastatic signaling pathway in PCa cells and that the altered expression of Trop-2 may be utilized for early identification of capsule-invading PCa.

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Breast Cancer: Factors Dominating, Causitives and Early Detection

Objective: When cancer starts in liver cells, it is called primary liver cancer. Hepatocellular carcinoma (HC) one of the most frequent tumors commonly evolves from cirrhosis. Because the evolution from chronic hepatitis of various origins to, in most cases, cirrhosis and then liver cancer, the need often arises to differentiate liver cirrhosis from HC. Liver function tests (also called a liver panel) are a group of blood chemistry tests that are often ordered together. While they do not diagnose liver cancer, they can tell the doctor that there may be a problem with the liver. After a long term study association of biochemical analytes selected via multivariate discriminate analysis could best to differentiate between cirrhosis and HC. To avoid recourse to liver biopsy which is considered to 'gold standard' for differentiating between these two conditions, multivariate discriminate analyte selection is very useful to discriminate HC from cirrhosis.

Materials and Methods: The patients belonged to the age group of 30-86 years were selected for the study. Serum from each patient was collected and processed within 2 hours for the analysis of aspartate transaminses (AST), alanine transaminases (ALT), bilirubins (T-Bil & D-Bil), total alkaline phosphatases (ALKP), gamma glutamyltransferases (GGT), lactate dehydrogenases (LDH), total protein (TP). Albumins (ALB) were estimated using Beckman coulter kits on fully automated Beckman coulter AU2700 chemistry analyzer. In addition other biochemical panel total cholesterol (CHOL), high & low density lipoprotein (HDL & LDL), triglycerides (TG), glucose, urea, iron, total iron binding capacity (TIBC) were also evaluated using Beckman coulter kits on fully automated Beckman coulter AU2700 analyzer. Serum AFP and Ferritin assays were carried out on fully automated immunoassay analyzer Architect i2000sr system. Other hematochemical indices were evaluated with a fully automated analyzer with reagents from reputed and traceable company.

Results: None of the biochemical variable evaluated discriminates between HC and cirrhosis satisfactorily because of the large overlap of values between the two populations. Therefore the panel of analytes included in the discriminate function appears so far to be the best indicator to discriminate between liver cirrhosis and HC.

Conclusion: The combination of unrelated biochemical tests selected by the multivariate discriminate analytes is an efficient tool for the differential diagnosis of cirrhosis and HC and perhaps for the monitoring of high risk group who may be evolving to HC that means for the early identification of neoplasia. Again monitoring of the post treatment and effectiveness of the therapy also well judged by these biochemical panel.

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BANGLADESH

Studies on Anti-oxidant Activities of White water Lily (Nymphaea nouchali) Tuber

The white water lily (*Nymphaeanouchali*) tuber has been taken as indigenous food item in Bangladesh. The objective of the present work was to the studies on nutritional composition and anti-oxidant properties of white water lily tuber. From this study it was observed that the white water lily (*Nymphaeanouchali*) tuber is a very good source of carbohydrate 78.21% and protein (10.79±0.062)%. It hasalso (5.35±0.27)% moisture, (2.75±0.015)% ash, (0.43±0.025)%fat, (2.47±.101)% crude fiber and (27.57±0.12) mg vitamin C/100gm in tuber dry powder.It is also a good source of phenolics (353.66±2.985) mg/gm tannic acid equivalent in 1 gm of methanol extract. The total flavonoid contents is about (102.86 ±14.136)mg catechin equivalent in 1gm of methanolic extract. The totalproanthocyanidins contents is about (4.42± 2.669) mg catechin equivalent in 1gm of methanolic extract. The totaltannin contents is about (378.14 ± 21.286) mg tannic acid equivalent in 1gm of methanolic extract. The total antioxidant capacity is about (159.78±23.116) mg ascorbic acid equivalent in 1gm of methanolic extract.The reducing power of methanolic extract of Nymphaeanouchali tuber was found to be correlated with increasing absorbance (at 700 nm) as compared with ascorbic acid. The EC_{50} of ascorbic acid and extract is 44.42µg/ml and 164.5 µg/ml respectively. The free radical scavenging activity of Nymphaeanouchali tuber extract was measured by using 2, 2-diphenyl-1-picryl-hydrazyl (DPPH) .The IC50 valuefor the free radical scavenging activity of standard ascorbic acid and extract is 13.77µg/ml and 26.44µg/ml respectively.

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Effect of Biogenic Silver Nanoparticles from Zizyphus mauritiana Extract on Human U87 Primary Glioblastoma Cell Line and Ehrlich Ascites Carcinoma Cells

Introduction: Now a day, silver has attracted due to its disinfecting nature and tremendous medicinal value to culinary items as well as showing enormous effectiveness as an anticancer agents. The green synthesis of silver nanoparticles (AgNPs) gained a lot of interest due to the usage of natural resources, rapidness, eco-friendliness and benignancy. Moreover plant mediated synthesis of AgNPs do not produce any toxic byproducts. In the plant various biomolecules such as enzymes, proteins, flavonoids, terpenoids, and cofactors are present that act as reducing and capping agents of silver. Till now, the biosynthesis of AgNPs from *Z. mauritiana* fruits extract and its anticancer activity is not reported. Therefore, the aim of this study was to synthesize AgNPs and investigate anticancer activity on human primary glioblastoma cell line (U87) and Ehrlich ascites carcinoma (EAC) cells.

METHODS: Silver nanoparticles (AgNPs) were biosynthesized by using *Zizyphus mauritiana* fruits extract and it was characterized by color, UV-visible spectroscopy, Fourier-transform infrared spectroscopy (FTIR), Transmission Electron Microscope (TEM) and energy dispersive X-ray (EDX) spectrophotometer. The antiproliferative activity against U87 cell line and EAC cells was checked with different concentrations of AgNPs using MTT assay.

RESULTS: Biogenic AgNPs were confirmed primarily by colour changed and peak was found at 430 nm. The average particle size was obtained 15.6 nm and it was calculated by 'Image J' software. The presence of silver was confirmed by EDX spectrophotometer. Various functional groups of AgNPs were obtained. Antiproliferative study revealed that the AgNPs inhibited human U87 primary glioblastoma cells and EAC cells growth significantly and in a dose dependent manner.

CONCLUSIONS: Biogenic AgNPs showed marked antiproliferative activity against Human U87 cells and EAC cells. Therefore, it has a potential to be used for the formulation of anticancer drugs in pharmaceutical and biomedical industries.

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Liposome encapsulated tumor-associated antigens elicited humoral and cellular immune response in mice bearing tumor

Chemically induced tumors in mice provide a system to investigate tumor-associated antigens (TAAs). The cell surface glycoproteins on such tumor cells have been identified as suitable targets for immune attack. The induction of immune response against tumor associated antigens (TAA) in N-nitrosodiethylamine (DEN) exposed mice has been examined. In order to present antigens to the immune system, the liposome was used as vehicle to deliver the TAA. Liposomal-TAA formulation, elicited both humoral and the cellular immune responses, when administered intramuscularly in DEN-exposed mice. Presences of circulating antibodies against TAA and the induction of cellular responses in immunized mice were monitored using ELISA and *in vitro* cell proliferation assay of lymphocytes respectively. Specificity of antibody against TAA in immune sera was analyzed using immunoblotting technique. Based on these results, it is proposed that the liposome encapsulated TAA may successfully be used to induced humoral and cellular immune response against tumor.

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Oral Malignancies in Young Cohorts: A Paradigm Shift in Cancer Predators

Oral cancer has increased amongst young cohorts a new emerging head and neck cancer patient population. Historically Oral cancer has been a disease of elderly habituated to tobacco and alcohol. There has been a gradual change in demographics of oral malignancies as most of its predators seem to be young teetotalers. Absence of a tobacco habit or alcohol consumption might contribute to delay, as cancer is not suspected immediately, hence it is prudent not to stereotype who may or may not get cancer. Human papilloma virus a new entity would be soon replacing tobacco as the primary cause for Oral cancer.

Young adults with oral malignancies are distinct from the older adult cancer population with respect to their spectrum of disease due to the tumor biology, their turbulent developmental status of life, psychosocial needs, and long term complications of cancer in terms of recurrence, distant metastasis and treatment side effects.A prior knowledge of oral cancer by our patients was not instrumental in accepting their diagnosis nor did it prompt them to visit a health care professional for the inbuilt belief they had that Oral cancers are for those who are habituated to established risk factors .The amount of time in recognizing the innocuous symptoms, prompt visit to a dentist can vary depending on the “preventive care” approach of the patient, also there can be a further delay in seeking the concerned specialist, histopathological examination and mandatory investigations. The culmination of patient delay, hierarchical specialists delay, awareness of dentists in recognizing early malignant ulcers that camouflage as traumatic ulcers in cryptic locations of the oral cavity can all have a detrimental impact on the prognosis.

A series of cases of oral malignancies in young adults, aged under 35 years are presented and the literature reviewed with respect to its clinical presentation and treatment considerations in these ambiguous predators. Delay in diagnosis, fear of death, physical and psychological burden amongst the young cohorts who are yet to blossom in their life, inability to make patients comprehend as to how they got succumbed to oral cancer due to lack of evidence are some of the concerns that would always echo the clinicians in the years to come.

Dr. Md. Masudul Hasan Khan
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Exploration of Therapeutic Potentiality of Stephania japonica Leaf Extract in the Treatment of Cancer

Currently, cancer is one of the leading causes of human death all over the world. Cancer is a broad term for a class of diseases characterized by abnormal proliferation of cells due to abnormality of genetic materials of an organism and invades healthy cells in an organism. Different approaches have been employed and are still in use, individually or in combination, in the treatment of cancer. Medicinal plant extracts have been potential source for the treatment of cancer. *Stephania japonica* (Thumb.) Miers is one of them which known for its anti-hyperglycemic and anti-cancer properties. It is a slender twining shrub with greenish yellow flowers and large tubers. To extract functional compounds from plant leafs, a variety of solvents have been selected according to multiple phyto-constituents and their properties. In this study, acetone, chloroform, ethyl acetate, methanol and ethanol were used to extracts bioactive compounds from the leaves of *S. japonica*. Antioxidant activities of these leaf extract were determined by DPPH and ABTS assay. It was found that leaf extracts of *S. japonica* obtained by acetone, methanol and ethanol showed high antioxidant activities. These there extracts with high antioxidants were used to determine the anticancer activity both *in vivo* and *in vitro* experiments. The results showed that morphological shape of Ehrlich ascites carcinoma (EAC) cells in *in vivo* assay were changed after treatment of crude extract in relevant dose at 100 mg/kg and 200 mg/kg body weight of

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Development and Production of Non-Conventional Drug/ Antibiotics (Daptomycin) in a Packed Bed Bioreactor using Streptomyces roseosporus by novel immobilization technique

Drug resistance is a global threat to human health in today's era. Several conventional and non-conventional antibiotics have become inefficient to tackle this problem. Daptomycin is a novel cyclic lipopeptide antibiotic produced by *Streptomyces roseosporus* through fermentation process. It has progressed as a significant anti-MRSA (methicillin-resistant Staphylococcus aureus) antibiotic. But, the applicability of this highly valued antibiotic is deterred by its low production and stringent processing methodology. The production of this life-saving drug needs to be ameliorated to reduce the cost of its industrial production. Though several researchers are engaged in the direction of its biosynthesis and strain improvement by genetical manipulations, there are still lacunae in its bioprocess design and development. The involvement of free cells for antibiotic fermentation often faces difficulties such as product inhibition and substrate inhibition which deter the overall productivity. Whole cell immobilization has many operational and economical benefits such as improved metabolic activities, cell reusability and prevention of cell washout at higher fermentation dilution rates. The present study was aimed to improve the production of Daptomycin using Streptomyces roseosporus immobilized in calcium alginate beads, silk sachets, and loofah sponge in a packed bed bioreactor; run in a continuous mode. The structural analysis of the porous matrices was done using Scanning Electron Microscopy (SEM). 1.5 grams of cells per grams of carrier was found to be suitable for whole cell immobilization studies in an indigenously designed and developed packed bed bioreactor. Continuous production of Daptomycin was done in the bioreactor at fixed substrate concentration and at different dilution rates. The dilution rate was varied from 0.01 h-1 to 0.040 h-1substrate.The substrate consumption increased while the product formation depleted with increasing dilution rate. The highest productivity was accounted for the loofah sponge at dilution rate of 0.02 h-1. With varying dilution rates, applicability of the whole cell immobilization improved substrate utilization and minimized the amount of substrate lost in the product stream. The residence time was increased due to cell immobilization which led to enhanced productivity and better substrate utilization.

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Poly(lactide)-based polymeric micelles-mediated delivery of chlorin e6: An effective photodynamic therapy in cancer

Although significant advancement has been made in the area of photodynamic therapy (PDT) till date, however, effective PDT is still not achieved. Main drawbacks of PDT could be sub-optimal delivery of photosensitizers to the cancer cells, and poor penetration of light in the deeper tumor tissues, which limits its effective clinical translation. In our study, A second generation photosensitizer, Chlorin e6 (Ce6) has been incorporated in methoxy-polyethylene glycol-poly(lactic acid) (mPEG-PLA) diblock co-polymeric micelles. Following preparation by dialysis method, the Ce6 nano-formulations (Ce6-mPEG-PLA-micelles) were physico-chemically characterized for particle size, surface charge, and evaluated to determine their ability to generate reactive oxygen species upon illumination of near infrared light (633 nm). Therapeutic efficacy of the Ce6-mPEG-PLA micelles following laser treatment was evaluated in vitro in two- and three-dimensional cell culture systems by using Human lung carcinoma cells (A549) and Human cervical cancer cells (HeLa). mPEG-PLA entrapped Ce6 generated singlet oxygen in much higher amount compared to free Ce6. Micellar form were taken up by the cancer cells more efficiently compared to free Ce6 in both the tested cell lines, and in both the cell culture model systems. The physico-chemical characterization, cellular uptake, ROS generating potential, and therapeutic efficacy in the in vitro and in vivo assay systems will be presented.

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Current perspectives in Patenting and Commercialisation in cancer Immuno-therapeutics

Objective: The current study attempts to analyse patenting trends in the area of nano biotechnology based medicinal preparations containing antigen antibodies paying attention to cancer treatment and diagnostics with a special focus on cancer immunotherapy as a target application area.

Method: Medicinal preparations containing antigen antibodies and preparations thereof were identified based on the search using Classification systems (IPC/CPC) as well as keywords conducted on Questel Orbit-2016 (a web-based patent and portfolio analysis platform). Growth of filing/grants, geographical distribution, inventors activities and their major assignments, collaborations globally and broad areas of distribution was analysed. Claim analysis of the selected patents was done to identify challenges in prosecution of applications.

Result: As per the analysis US and Europe are the top patent filing countries in nano immuno-therapeutics area. Technology distribution mapping analysis indicates the majority of the filings were in pharmaceuticals sector. There is an increase in patenting activity in this area from the year 2002 and that continued until the year 2013, with a special rise show in the time period of the years 2010-2011.Majority of the patent applications filed were from the Institutes as an applicant's which indicates the major R&D work. As per the assignment and commercialization activity is concerned, Immunomedics, a USA based company has the highest no. of patents in its portfolio, followed by Univ.of California. The detailed claim analysis of the 256 patents shows majority of the applications were product by process claims and further followed by Markush structures.

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Molecular mechanisms of anti-angiogenic potential of the novel biomolecule T11 target structure (T11TS) in malignant glioma abrogation: a preclinical study.

The crucial role of angiogenesis in malignant glioma progression makes it a potential target of therapeutic intervention in glioma.T11 target structure (T11TS), a novel bioactive molecule has been documented by us as an anti-neoplastic agent in glioma induced rats and also in human glioma in vitro. The present preclinical study deciphers the anti-angiogenic potential of T11TS and the underlying molecular mechanisms in malignant glioma.

Glioma associated brain endothelial cells (GABEC) were isolated and characterised with phenotypic markers of endothelial cells (CD31 and CD34), whose level diminished with T11TS administration, inhibiting the cell grip.

T11TS administration significantly downregulates the expression of integrin αv and Matrix metalloproteinases (MMP-2 and −9) which enzymatically remodel the ECM and upregulate the inhibitors TIMP-1 and TIMP-2.

In GABEC T11TS administration disrupt initiation of glioma angiogenesis by significantly downregulating VEGF/VEGFR-2 expression and pro-survival PI3K/Akt/eNOS proteins alongwith eNOS phosphorylation and NO production, but significantly upregulates PTEN expression. T11TS therapy remarkably inhibits endothelial angiopoietin-1/Tie-2 signaling associated with vessel maturation and stabilization. It simultaneously antagonizes EGFR activation and components of Raf/MEK/ERK pathway, which are essential for angiogenesis induction and proliferation.

T11TS dampens pro-inflammatory cytokines which are indispensable for tumour growth and metastatic propagation but upregulates anti–inflammatory cytokines resulting complete abrogation of glioma inflammation and angiogenesis.

T11TS triggers apoptosis in GABEC via activation of intrinsic pathway as well extrinsic pathway.

Taken together our findings suggest that T11TS can be introduced as an effective angiogenesis inhibitor in human glioma as T11TS targets multiple levels of angiogenic signalling cascade impeding glioma neovascularisation.

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Hematopoietic stem/progenitor compartment and microenvironmental analysis by signaling molecules in experimental leukaemia

One of the most devastating haematological catastrophe is LEUKAEMIA. Every year millions of people worldwide are diagnosed with this particular neoplasm and epidemiological data suggests leukemia to be the 11th most common cause of cancer related deaths. Although unparallel scientific efforts have been made globally to understand the underlying mechanism behind emergence of the disease and its subsequent prevention some lacunae still persists which opens avenues for further studies. In our laboratory we have made a generous attempt to resolve the mystery of the immortal nature of leukemic cells and the involvement of the supportive hematopoietic niche behind the progression of the disorder. The clinical manifestations of this dreadful disorder includes: bone marrow failure, accumulation of undifferentiated blasts in the marrow cavity and leukocytosis. Primarily, the study was focused on characterization of N-N'Ethylnitrosourea (ENU) induced mouse model of leukemia by peripheral blood hemogram, bone marrow cytology, histology, short-term bone marrow culture, cytochemical staining , scanning electron microscopic study and above all flowcytometric analysis. We have also channelized our study in various directions throwing some light into single cell proteomic analysis of the primitive leukemic bone marrow compartment, alteration of some crucial signaling molecules, certain leukemic cell specific receptor expression, cell cycle regulation in leukemic bone marrow and lastly the alteration in conventional and hematopoiesis specific p53 pathways and its associated molecules which further defined the root cause of disease initiation and progression to detrimental state. A part of our study also unravelled bone marrow microenvironmental dysregulation contributing to leukaemic progression which covered the long-term stromal culture, receptor expression pattern by stromal cells etc. Altogether, we have put some effort to flowcytometrically analyze the multiple facets of “leukemic stem cells” and the involvement of “leukemic microenvironment” that eventually led to leukemogenesis.

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Protein structure prediction and protein designing using pattern value of short sequences

As protein structure defines its function so it is very important to find out its three dimensional structure. There are several methods to find out its structures and functions but they are not satisfying to study about proteins three dimensional structures and to get function. Major algorithms use multiple sequence alignment to find out homology in structure. But still the question lies that how could we find out the three dimensional structure more accurately in order to get its function in accurate way with the existing knowledge of structure and function? We know that homology modeling plays a vital role to find out the protein structures. Still it is inadequate to determine structure accurately. Here is an algorithm which takes as input a sequence and split it with short sequences (tokens) with its unique value and its three dimensional structure which have unique pattern value. If we say Si is the token sequence value and Pi is the pattern value then. Every Si has the several Pis. In Si next Pi is being set by decision mathematics.

The reverse will be very interesting that, when drug target will fix, by designing its corresponding protein structure and get the pattern value which lead to its sequence value. By this we can get probable sequence and search for original in the database. It is the easiest way to drug target discovery. This method introduces a new way of structure prediction and in drug designing.

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Formulation and Evaluation of Ophthalmic Inserts containing Aceclofenac

Aceclofenac circular ophthalmic inserts were prepared by solvent casting methods, using gelatin as a polymer at two different concentration (10% w/v and 15% w/v) and glycerin as plasticizers in two different concentration (70% v/v and 50% v/v) on dry weight of gelatin. An in vitro method was designed and utilised for the study. Inserts release the drug as a function of square root of time. In vivo release of the inserts was determined in albino rabbits eye. In vitro methods simulate in vivo conditions, which was confirmed by strong positive correlation between the two results indicate that inserts can control drug release and might improve ocular bioavailability and reduce toxicity of Aceclofenac.

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Epstein Barr Virus Latent Membrane Protein 2A induces downregulation HLA Class Ia in Gastric Cancer cells

Cancer is a disease of abnormal cell proliferation and differentiation. Viruses, especially Epstein Barr Virus (EBV) have been documented in carcinogenesis. Amongst others, tumor cells manifest immune evasion to facilitate their growth and invasion. One of the immune escape strategies is the downregulation of the Human Leukocyte Antigen HLA Class I (HLA- A, -B, -C) which are otherwise associated with presentation of endogenous peptides including viral and tumor antigens to cytotoxic T lymphocytes for immune mediated destruction. Interestingly, EBV Latent Membrane Protein 2A (LMP2A) has been found to be responsible for this HLA downregulation in gastric cancer cells as observed by flow cytometry analysis, quantitative real time PCR as well as siRNA studies. Furthermore, the Sonic Hedgehog pathway was established to be involved in LMP2A mediated HLA downregulation as confirmed by immunoblotting and real time PCR experiments. Thus it was observed that Epstein Barr Virus Latent Membrane Protein 2A mediated activation of Sonic Hedgehog pathway was responsible for HLA Class Ia downregulation in Gastric Cancer cells.

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Eucalyptus methanolic extract-induced apoptosis in in vivo culture of Ehrlich Ascites Carcinoma (EAC) cells through the inactivation of NF-B

Eucalyptus species have been exploited commercially for medicinal and pharmaceutical purposes, as well as for food additives. Methanolic extract of Eucalyptus bark (MEEB) induced apoptotic cell death has been reported against Ehrlich Ascites Carcinoma (EAC) cells in Swiss Albino mice. The underling mechanism of apoptotic cell death of eucalyptus extract in EAC cells has not yet been studied. The growth inhibitory effect of MEEB was investigated in EAC cells in Swiss Albino mice. MEEB treatment effectively induced a cytotoxic effect in 5 days in dose- dependant manner as compared control treatment. The apoptotic parameters were measured on characteristic morphological changes by Hoecst staining and DNA fragmentation assay and caspase-3 expression confirmed apoptosis. MEEB inhibited nuclear factor- B(NF- B) activity and no significant change was observed in intracellular reactive oxygen species (ROS) generation. These results suggest that the anticancer effect of MEEB is associated with expression through inactivation of NF- B in EAC cells.

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Knowledge, Attitude and Practices Related to Antibiotic Use and Resistance among Doctors in BPKIHS

Introduction: Inappropriate and excess use of antibiotics is one of the major reason of antibiotic resistance. Assessment of knowledge, attitudes, and practices (KAP) of doctors may help in developing interventions to improve antibiotics use and prevent resistance both at local and national level. Our aim was to evaluate the current KAP regarding antibiotic use and its resistance among doctors in BPKIHS.

Methods: A cross sectional, questionnaire based study was conducted among the interns, Junior Residents, Senior Residents and faculties of a BPKIHS from January to March, 2016 and their KAP regarding antibiotic use and resistance was assessed by using a five point Likert scale, whose responses ranged from 'strongly agree' to 'strongly disagree,' 'always' to 'never and 'very useful' to 'not useful at all'. The data was analyzed by using simple descriptive statistics percentage and frequency.

Results: The response rate was 68.2%. One hundred and forty four (45.4%) respondents were residents, 25.6% interns and 24.3% faculty. 50.2% reported prescribing of antibiotics more than once daily. 49.5% respondents used to take help from their seniors on their antimicrobial selections. 65.3% respondents stated that they had received antibiotic education at a formal lecture on ward rounds, 49.5% during CME and 30.3% at a pharmaceutical company– sponsored lectures. 87.4% respondents agreed that antimicrobials are overused in general and 177 (55.8%) agreed that they are also overused at BPKIHS. One hundred thirty four respondents (42.3%) agreed that patient demands for antibiotics contribute to antibiotic overuse for patients. Majority (88.6%) agreed that better use of antibiotics will reduce problems with antibiotic resistant organisms. 70.7% believed that locally developed guidelines for antimicrobial use would be more useful than national ones. Most of the respondents (89.9%) wanted more ongoing education on antibiotic use and its resistance.

Conclusion: Our study reveals that antibiotics were frequently prescribed in most of the departments and it also provides an important insight regarding the knowledge, attitudes and practices of antibiotic prescription and its resistance among the doctors, which can be utilized to plan an effective guidelines and targeted interventions. More CME on antibiotic use and its resistance should be conducted to enhance the awareness among prescribing doctors.

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Exploration of Therapeutic Potentiality of Stephania japonica Leaf Extract in the Treatment of Cancer

Currently, cancer is one of the leading causes of human death all over the world. Cancer is a broad term for a class of diseases characterized by abnormal proliferation of cells due to abnormality of genetic materials of an organism and invades healthy cells in an organism. Different approaches have been employed and are still in use, individually or in combination, in the treatment of cancer. Medicinal plant extracts have been potential source for the treatment of cancer. *Stephania japonica* (Thumb.) Miers is one of them which known for its anti-hyperglycemic and anti-cancer properties. It is a slender twining shrub with greenish yellow flowers and large tubers. To extract functional compounds from plant leafs, a variety of solvents have been selected according to multiple phyto-constituents and their properties. In this study, acetone, chloroform, ethyl acetate, methanol and ethanol were used to extracts bioactive compounds from the leaves of *S. japonica*. Antioxidant activities of these leaf extract were determined by DPPH and ABTS assay. It was found that leaf extracts of *S. japonica* obtained by acetone, methanol and ethanol showed high antioxidant activities. These there extracts with high antioxidants were used to determine the anticancer activity both *in vivo* and *in vitro* experiments. The results showed that morphological shape of Ehrlich ascites carcinoma (EAC) cells in *in vivo* assay were changed after treatment of crude extract in relevant dose at 100 mg/kg and 200 mg/kg body weight of Swiss albino mice at 7 days. In MTT assay, it was found that the percent of inhibition was increased with the increasing concentration of leaf extracts.

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Antimicrobial activity of flavonoid enriched fractions from Terminalia bellerica against Multi Drug Resistant Staphylococcus aureus.

Present work is an attempt to search an herbal remedy in order to inhibit multi drug resistant (MDR) *Staphylococcus aureus* which primarily constitutes enrichment of flavonoids from ethanolic extract of *Terminalia bellerica* using Partition technique. *S aureus* which was found to be resistant to five different antibiotics was tested for antimicrobial activity of ethanolic extract of *T bellerica* outer coat, fruit and seed followed by determination of MIC_{90}. Ethanolic extract of *T bellerica* outer coat having lowest MIC_{90} was further fractionated to eight fractions F1 (water), F2 (50% Ethanol and water), F3 (Ethanol), F4 (Acetone) F5 (Ethyl acetate) F6 (Butanol) F7 (Chloroform) and F8 (Hexane) and were tested for antimicrobial activity against isolated MDR. *T bellerica* crude extract of outer coat obtained by maceration gave highest zone of inhibition 3.14± 0.03 cm in comparison to standard antibiotic Cefixime. *S aureus* showed highest degree of resistance against Cefixime having MIC_{90} 23.66 ± 0.33 µg/ml. Phytochemical tests for all the fractions were done where only F5 and F6 were found to contain flavonoids. Fraction F6 gave significant zone of inhibition 2.56±0.05cm with MIC_{90} 50± 0.33 µg/ml. The extractive value and yield of fraction F6 is 150mg and 0.030%. Thus it was concluded that Flavonoids of *T bellerica* have a potential antibacterial activity against MDR *S aureus* and could be used as a potential drug or a resistance modifier in near future.

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Strain Improvement of Penicillium sp. To Increase The Production Of Penicillin

Improvement of the biosynthetic capabilities of industrially relevant microbes to produce desired metabolite in higher quantities is one of the important advancements of modern Biotechnology. Present study constitutes intense classical strain improvement of Penicilliumsp by UV induced mutagenesis for high yield production of Penicillin. The work involves a comparative study of net yield of Penicillin from a non-mutated and an UV- mutated Penicillium sp. The results depicted 15.58± 0.2 % increase in Penicillin production from mutated strain with MIC_{90} value 150± 0.1 µg/ml against coagulase positive S aureus which is significantly lower than MIC_{90} value 180± 0.1 µg/ml for non-mutated strain. Thus it was concluded that UV-mutation has both enhanced the quality and quantity of Penicillin produced from Penicillium sp.

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Phytochemical, antioxidant and anthelmintic potentialities of Pouzolzia zeylanica (L.) Benn Root extract

For thousands of years mankind is using plant sources to alleviate or cure illness. Traditionally, Pouzolzia zeylanica is used for the treatment of different diseases. The current study investigated presence of various phytoconstituents, antioxidant and anthelmintic activities of methanolic extract of Pouzolzia zeylanica (L) Benn which was tested by using different methods. Preliminary physiochemical screenings with the crude extract demonstrated the presence of various phytoconstituents. The plant extract showed very good antioxidant and anthelmintic activity in dose dependent manner.

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Formulation and Evaluation of Dexamethasone Floating tablets using Basella alba fruit mucilage

The improvement of bioavailability of drug is a major concern now a days. Prolonging the gastric retention time is one of the approaches to enhance bioavailability. The floating tablets have less bulk density than the gastric fluids and thus remain buoyant in the stomach for a prolonged period of time resulting in significant increase in gastric retention time. The aim of the study is to develop a floating drug delivery system which will prolong the gastric retention time of drug after oral administration and control the release of drug for achieving sustained effect of the drug. The model drug used in the study is Dexamethasone having biological half life of 3hours. This corticosteroid prevent the release of substances in the body that cause inflammation. The formulations were designed using Hydroxypropyl methyl cellulose (polymer responsible for increasing the buoyancy of tablet due to its low density), *Basella alba* fruit mucilage, Polyvinyl pyrrolidone(binder), talc and magnesium stearate. Direct compression method was used to prepare the tablets. The prepared formulations were evaluated for bulk density, compressibility index, hausner ratio, angle of repose, weight variation, hardness, friability, floating test, swelling study and in-vitro dissolution study. The tablets showed acceptable physicochemical properties as per IP. Swelling studies indicated significant water uptake.

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Preparation & Evaluation of Prednisolone Acetate Loaded Chitosan Alginate Coated Emulsion

For the treatment of ulcerative colitis, localized delivery of drug at the site of inflammation, is a promising way. This requires prevention of drug release while passing through the gastrointestinal tract especially at the acidic condition of stomach. The project aimed to prepare stable castor oil in water emulsion (O/W) coated with chitosan and alginate for the delivery of prednisolone acetate for the treatment of ulcerative colitis. The design of stability study for different compositions of emulsion was performed by the help of "DESIGN EXPERT® "software. 22 formulations were prepared of different compositions.pH, conductivity and viscosity were taken as the stability parameters and the stability study was performed for seven days. Stable formulation was then optimized by studying the parameters which were not too much varied during the study period. The finally selected formulation (having viscosity2.54 cP at the day 1 and 2.55 centipoises at the day 7 of stability study, pH 7.2 at day 1 & 7.0 at day 7, conductivity 0.06mS & 0.05mS at day 1 & day 7) was coated with alginate & chitosan & rigidization of coating was done by calcium chloride to prevent the leakage of drug in the stomach (acidic pH). The zeta potential of coated emulsion was -3.59 mV whereas that of uncoated emulsion was -14.1 mV. This increase in zeta potential confirms the coating. Coating also changed the z-average diameter of emulsion droplet (276nm and 215nm for coated and uncoated droplets respectively). The effect of coating on leaching of drug at acidic pH was studied by equilibrium method. It was found that not more than 5% of loaded drug was leached during 3hr at pH 1.2.

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Formulation and Characterization of sustained release microbeads of Norfloxacin by Ionotropic Gelation Technique

Norfloxacin is a synthetic antibacterial fluoroquinolone and active against a broad spectrum of gram-positive and gram-negative aerobic bacteria, its shorter biological half life (3 hrs.) necessitates that it to be administered in frequent doses of 400mg. The main objective of this study was to develop suitable micro particulate system of Norfloxacin for controlled release delivery system by varying the alginate concentrations, calcium chloride concentrations and curing time. In the present work, Norfloxacin microbeads were prepared by ionotropic gelation technique. Prepared microbeads were evaluated for granulometric studies, micrometric, scanning electron microscopy, drug entrapment efficiency, swelling studies and in-vitro dissolution studies. The prepared beads were free flowing and white in color. The drug loaded beads showed 37.26% to 91.73% drug entrapment, which was found to increase with increase in alginate concentration. In vitro drug release study of these microbeads indicated controlled release for Norfloxacin 96.19 – 97.83% release after 12 hours. Hence the observations of all results of the different batches, A3 showed controlled release action and improved drug availability.

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Comparitive Study of the Physical properties of natural mucoadhesive from the fruit pulp of ziziphus mauritiana with methyl cellulose and sodium alginate

Plant-derived natural excipients have established their worth in the development of pharmaceutical formulations. Gums and mucoadhesive agents are extensively used natural materials for conventional and novel dosage form.
The present work aims at determination of physical properties of Mucoadhesive material from fruit pulp of Ziziphus *mauritiana*(MMZM), such as mucoadhesive strength(Shear stress determination), swelling index, pH,viscosity,angle of repose,carrs index,density d and its comparative study with synthetic polymers Methyl cellulose and Sodium Alginate.
The most important properties such as mucoadhesive strength of MMZM (3% w/v)was found to be more than sodium alginate(3% w/v) but less than Methyl cellulose (3% w/v) whereas the swelling index of MMZM at pH 6.5 and pH 7.4 was found to be better than both Methyl cellulose and Sodium alginate at the same pH.
From the study it can be concluded that MMZM has potential to be better mucoadhesive than Methyl cellulose and sodium alginate in respect of mucoadhesive strength.

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Pharmacognostical Evaluation of Leaucanea leucocephala leaves

Leucaena leucocephala,commonly known as Sababul,belongs to the Leguminosae family and is one of the fastest growing tree. Leucaena foliage is used as animal feed and the leaves and seeds are used as human food,and as a potential source of commercial gum. The plant was reported to have antifungal,antidiabetic and as anticancer activities.

Different pharmacognostic parameter like organoleptic characters,macroscopic study,microscopic study of the leaf was carried out. Dry powder test and fluorescence analysis was performed with dry powder.
Physicochemical study of percentage weight loss in dry leaf is found to be less than of green leaf. Total ash value was determined for powder drug. Comparative extractive value for both dry and young leaf was shown that methanol extractive value is high in dry leaf powder where as n-hexane, chloroform and methanol extractive value in young leaf is respectively 15.01$\pm$ 0.02, 12.25$\pm$ 0.08 and 17.90$\pm$ 0.05.

The crude powder drug extracted in different solvents was tested for presence of alkaloids, flavonoids, tanins, phenols, cardiac glycosides , triterpenes and saponins.

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Cytochrome P450 Mediated Inhibition Potential of Some Medicinal Plants used in Diabetes: A Review

Cytochrome P450 (CYP450) enzymes are major drug metabolizing enzymes, that catalyze the oxidation of enormous number of endogenous and exogenous chemicals including drugs. Inhibition of CYP450 may increase plasma levels of simultaneously administered drugs, thereby increasing the incident of drug-induced toxicity. Diabetes mellitus, the chronic metabolic disorder, is a worldwide concern today. Parallel to synthetic medicines, often people opt for herbal antidiabetics as well. But phytomedicines may severely affect the disposition of coadministered conventional drugs by inhibiting cytochromes. However, common people are unaware of this fact. Therefore present review aims to explore the cytochrome inhibition potential of some commonly consumed and easily available medicinal plants, used in diabetes. Such plants, selected for this study are: *Trigonella foenum graceum, Swertia chirata, Aegle marmelos, Morus alba, Murraya koenigii, Zingiber officinale.* For understanding of CYP 450 inhibition potential, usually CYP450 CO complex assay and CYP450 enzyme inhibition study by fluorogenic assay are carried out, taking ketoconazole and Quinidine as positive control for CYP3A4 and CYP2D6 respectively. Among all CYP isozymes, CYP3A4 and CYP2D6 are involved in the metabolism of more than 80% of the drugs. The review shows that almost all the abovementioned plants and their bioactive molecules have quite less inhibitory effect than the standard drugs. Hence they are safe as

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