CANCER-COMPREHENSIVE APPROACHES IN DRUG DISCOVERY AND DEVELOPMENT

(C-CADD 2012)

Proceedings of the Conference
# INDEX

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Content</th>
<th>Page No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Acknowledgement</td>
<td>1 - 2</td>
</tr>
<tr>
<td>2.</td>
<td>Messages&lt;br&gt;1. From the Organizer’s Desk&lt;br&gt;2. From Eminent Personalities</td>
<td>3 - 8</td>
</tr>
<tr>
<td>3.</td>
<td>Introduction to the Theme of the Conference</td>
<td>9 - 11</td>
</tr>
<tr>
<td>4.</td>
<td>Profile of the Speakers and their Abstracts</td>
<td>12 - 21</td>
</tr>
<tr>
<td>5.</td>
<td>Abstracts of Posters Selected</td>
<td>22 - 84</td>
</tr>
<tr>
<td>6.</td>
<td>Feedback from Participants</td>
<td>85 - 87</td>
</tr>
<tr>
<td>7.</td>
<td>Photographs</td>
<td>88 - 98</td>
</tr>
<tr>
<td>8.</td>
<td>Glossary</td>
<td>99 - 100</td>
</tr>
</tbody>
</table>
ACKNOWLEDGEMENT

I take this privilege and pleasure to acknowledge the contributions of many individuals who have been inspirational and supportive throughout the planning and execution of all the activities in DST Sponsored two days National Conference on Cancer, entitled, “C-CADD-2011”. The success of this conference bears the imprint of all those people I am grateful to.

With great pleasure and profound sense of gratitude, I express my most cordial and humble thanks to our beloved Principal, Dr. Supriya Shidhaye, for her valuable guidance and encouragement. Her time-to-time appreciation of work was the impetus to do hard work for better outcomes.

I am also grateful to our Management and trustees for their overall support to this conference.

Also I extend my thanks to all the teaching and non-teaching staff of my college for their meticulous work, hard efforts and involvement in the task assigned to them.

I express sincere thanks to all my colleagues in Department of Pharmaceutical Chemistry who have worked day-in and out. I thank them for their great involvement, full support, best cooperation and active participation in planning, coordinating and executing all the events of this conference.

I am also thankful to Department of Science and Technology (DST), Govt. of India, New Delhi for their financial assistance to this conference.

I would be failing in my duties if I do not thank all our Speakers, esteemed scientists from national laboratories and academic institutes who consented to participate in this activity and shared their piece of knowledge with the audience. Thanks are also due to the delegates across the state and few from outside, who participated with full zeal and enthusiasm, to make this event a grand success.
The support of **Homi Bhabha National Centre of Science Education, Mumbai** in terms of poster boards is also deeply appreciated.

From deepest depth of my heart to express my thanks to all the **volunteers** students who contributed and supported all teaching staff with their great passion, discipline and humble behavior.

The special thanks are extended to **Swasti Pandey, Ruchi Singh and Ashok Ramakrishnan** of **Third Year B. Pharm.** for their initiative and involvement in all activities. They immensely contributed to a greater extent for this conference.

Last but not the least I wish to thank one and all for each and everything.

**Dr. Rakesh R. Somani**
Coordinator, C-CADD
MESSAGES
MESSAGE FROM THE ORGANIZER’S DESK

DR. SUPRIYA SHIDHAYE, Principal, VESCOP

Two days DST sponsored seminar on Cancer-Comprehensive Approaches in Drug Discovery and Development 2011 (C-CADD 2011) held on 16th and 17th September, 2011 was a great success. I extend my heartfelt compliments to the Coordinator, Dr. Rakesh Somani and the other members of the Organizing Committee for strong initiatives and efficient execution of activities planned. The resource persons were eminent speakers of international repute. Cancer is a dreadful disease posing challenges to the researchers in prevention or cure. The speakers have dealt with various areas such as Cancer Stem calls, use of COX-1 Inhibitor, Nano-technology, herbal antioxidants, anti-metastatic drugs, protein interactions and drug development. It is glad to know that all the delegates were satisfied with the deliberation and overall management of the seminar successfully. We are looking forward to hold many such informative seminars in future to provide the scientific platform for interaction among the researchers, academicians, industry professional and students.
It is my immense pleasure to write forewords for DST sponsored two-day conference entitled, “Cancer-Comprehensive Approaches on Drug Discovery and Development” held on 16th and 17th of September, 2011 at VES College of Pharmacy, Chembur, Mumbai.

It was a unique opportunity for the researchers from different walks of life to provide the information on cutting edge research taking place in various fields on cancer, on one platform. The seminar brought in a confluence of experts including the pharmacologist, the formulation scientist, the medicinal chemist, the herbal scientist and the cell scientists, having their own angle of solving problems related to cancer.

The aim was to elucidate the study of cancer from its causal root to its approachable treatments and drug developments. The programme was designed in such a way to elicit all possible information from various sources to meet the needs of students and researchers who wish to venture into the area of development of new anticancer drug molecules.

Modern drug development has moved from empiricism to rational design. C-CADD conference served as a medium in connecting scientists and researchers with teachers and students to meet and discuss the advancements of research in cancer science, making it an intellectual interaction amongst all. It reviewed and highlighted the emerging strategies and technologies to help gain a better understanding of biology of the disease, which could improve drug development strategies and a scope for newer techniques.

Organizing a ‘Poster Competition’ for the students provided a platform to display their knowledge on various topics related to cancer. It is proud, indeed, to see the zealous participation from various colleges across Maharashtra and few from beyond the state border.

The appreciations we received for our hospitality and organization have encouraged us to conduct the forthcoming seminars in the best of their way without any compromise.

I would like to thank the delegates, teachers, students and the organizing team of C-CADD 2011 for making this conference ‘a grand success’.

DR. RAKESH R. SOMANI, Coordinator, C-CADD & Associate Professor
MESSAGES FROM EMINENT PERSONALITIES

CHIEF MINISTER
MAHARASHTRA

14th September, 2011

Message

I am pleased to know that Vivekanand Education Society’s College of Pharmacy has organized two days National Conference on C-CADD 2011.

The conference would no doubt prove beneficial to exchange views for the scientists and researchers of cancer. The conference would enlighten the participants in the emerging strategies and technologies of this disease.

I convey my best wishes for the event.

(Prithviraj Chavan)

Dr. Supriya Shidhaye, Principal,
Vivekanand Education Society’s
College of Pharmacy,
2nd Floor, Conference Hall,
Hashu Advani Memorial Complex,
Chembur (East), Mumbai- 400 074.

MANTRALAYA, MUMBAI 400 032, Telephone: 22025151, 22025222, Fax: 22029214
It gives me immense pleasure to know that Vivekanand Education Society’s College of Pharmacy has organized two days National Conference on Cancer Comprehensive Approach in Drug Discovery and Development.

Cancer is indeed a dreadful disease. Common people get afraid only by it’s name. There are many misunderstandings in people’s mind about the disease. Due to modern technology and research many new medicines are available. But people are not aware of it. I expect that the conference will give through information about the disease and new medicines. The conference will be useful not only for students but also the common people.

I wish all success to the conference.

( Rajesh Tope )

---

Mantralaya, Mumbai 400 032, Telephone : 022 2202 5247 / 2202 4850

www.maharashtra.gov.in
The VES College of Pharmacy is organizing a two day symposium on “Cancer-Comprehensive Approaches in Drug Discovery & Development, 2011”. This is indeed an important event which has brought together several leading scientists of India working in areas of drug discovery and cancer research to share their expertise and experiences. I wish to congratulate the Principal of the College, Dr. Shidhaye and coordinator Dr. Somani for organizing this meeting at a time when Industry Academia interactions are receiving a lot of attention. A meeting of this nature will further strengthen these ties and help in fostering collaborative research in various disciplines.

The program is very well organized and the audience would get an exposure to cutting edge research in various disciplines such as drug discovery, cancer stem cell, nanotechnology, cancer chemoprevention, anti-metastatic drugs and protein interactions and drug development etc. The meeting would be an intellectual feast to all attending.

Due to prior commitments I am unable to attend this meeting but I take this opportunity to wish this meeting to be grand success. I once again congratulate the organizers of this meeting for their efforts in putting up a wonderful scientific program.
INTRODUCTION TO THE THEME OF THE CONFERENCE
INTRODUCTION TO THE THEME OF THE CONFERENCE

Cancer is undoubtedly one of the deadliest diseases of this century. According to reports by W.H.O., one out of three women and one out of four men are prone to cancer in the world. Now with such alarming figures the task of physicians and researchers has become very challenging. Today the use of modern technology has brought the cure rate of cancer to almost 70-80%. The pace of anticancer drug discovery and development has accelerated over recent years based upon a better understanding of tumors biology at the molecular level. Modern drug development has moved from empiricism to rational design and this is theme of our conference.

The Cancer-Comprehensive Approaches in Drug Discovery and Development (C-CADD) conference will serve as a catalyst in connecting scientists & researchers with teachers to meet and discuss the advancements of research in cancer science. Thus it will review and highlight emerging strategies and technologies to help gain a better understanding of disease biology, which will improve drug development strategies and new techniques.

The agenda of the conference includes:

1. Focusing on new advances in the treatment of cancer as well as to provide updates of conventional therapies for a number of the most common tumor types.

2. Introducing the audience to the latest information on targeted therapies and emerging treatments in the pharmaceutical development pipeline.

This conference will serve as a catalyst in connecting scientists & researchers with teachers to meet and discuss the advancements of research in Cancer Science. Thus it will highlight emerging strategies and technologies to help you gain a better understanding of disease biology, which will improve your drug development strategies and new techniques, whether you are trying to develop small molecule drugs, protein therapeutics or other biologics.

Objectives and importance of the Event

Thus, the conference agenda will focus on new translational advances in the treatment of cancer as well as provide updates of conventional therapies for a number of the most common tumor types. The Conference program is designed to meet the educational needs of scientists, physicians, Pharmacists, researchers, and other health care personnel practicing oncology in all disciplines as well as fellows in training interested in the development of new anticancer agents.
Thus the main objectives of this event are as follows:

1. To discuss various strategies presently available to combat the cancer.
2. To discuss various newer strategies being practiced for the treatment of cancer.
3. To introduce the audience to the latest information on targeted therapies and emerging treatments in the pharmaceutical development pipeline.

The importance of the event:

Each topic will be covered by an expert and renowned scientists in their fields of interest. This conference highlights emerging strategies and technologies to help a researcher gain a better understanding of cancer biology, which will improve their drug development efforts from target discovery and lead finding, to nominating compounds and making better patient care decisions.

Topics to be discussed:

Following topics would be covered in the various deliberations.

1. Prodrugs approach for treatment of colon cancer
2. Molecular biology of cancer
3. Anti-cancer drug development
4. Nanotechnology and cancer
5. Food habits to avoid cancer
6. Chemotherapeutics
7. Biotechnology and cancer

Poster presentation:

Young scientists will have an opportunity to present a concise overview of the scientific achievements and conclusions drawn from their research. The posters will provide a platform to share information and discuss topics of interest, thus form a forum to exchange ideas and collaborate within different areas of drug development and discovery.

This is a very unique and tailor made conference which would cover versatile aspects related to cancer drug discovery, making the participant more knowledgeable and broadens their thinking horizon in the field of cancer.

Future outcome:

This conference will serve as a catalyst in connecting scientists & researchers to meet and discuss the advancements of research in Cancer Science hence accelerating applications that benefit ongoing Cancer research also highlights emerging strategies and technologies to help you gain a better understanding of disease biology, which will improve your drug development strategies and new techniques, whether you are trying to develop small molecule drugs, protein therapeutics or other biologics, the importance of incorporating clinical data with biological and chemical information as part of a discovery and development effort continues to be validated. This exciting event revolutionizes the way of drug discovery and diagnostic developments are being performed and explore solutions to some of the continuing challenges of drug discovery and development today.
PROFILE OF THE SPEAKERS AND THEIR ABSTRACTS
Achievements:

- Post-doctoral Associate, Medical School, Iowa City, USA
- Ph.D. Cancer Research Institute, Tata Memorial Centre, Mumbai
- With the excellence in areas of new drug discovery in the therapeutic areas of Rheumatology, Oncology, and Respiratory Disorders.
- She has given a commendable bench to bed side contribution in the discovery of seven INDs i.e. investigational new drugs.
- Her dynamism and initiative in the above areas has gained her awards like Women of the Year-2007”, by Rotary Club.
- She is the Recipient of the prestigious Doordarshan’s “HIRKANI PURASKAR” for 2009-2010
- Recipient of the first prestigious “Maharashtrian of the Year 2010” award in the field of science and technology (felicitated by Chief Minister of Maharashtra.
- To her credit she has 30, Publications and 45, Abstracts.

Abstract: “SEARCHING FOR THE “ACHILLES’ HEEL” OF CANCER”

The presentation will talk about new drug discoveries at PLSL and our contribution from bench to bedside in the field of oncology. Having nearly twenty years of experience in new drug discovery in the area of inflammation and cancer and heading the Oncology Drug Discovery Programme for last 11 years, the presentation will deal with the various drug discoveries to combat cancer.
DR. SHARMILA BAPAT
Senior Scientist, NCCS, Pune

Achievements:

- She has received her Ph. D. in the field of biochemistry from Pune University
- Member of Board of Studies in Stem Cells & Regenerative Medicine, D. Y. Patil University, Kolhapur
- National Woman Bio scientist Award 2008
- She has 21 publications to her credit
- Edited a book - “Cancer Stem Cells”
- She is the author for various books on the topics ranging from Drug Discovery Strategies: Advances in Biochemistry and Biotechnology; Stem Cells in Human Epithelial Ovarian Cancer, etc.

Abstract: “CANCER STEM CELLS”

The primary characteristics of adult stem cells are maintaining prolonged quiescence, ability to self-renew and plasticity to differentiate into multiple cell types. Tumors contain a minor population of tumor-initiating cells, called “cancer stem cells” that maintain some similarities in self-renewal and differentiation recognized as features of normal adult stem cells. Therefore, various methods developed originally for the analysis and characterization of adult stem cells are being extended to evaluate cancer stem cells. Over the last decade, a combination of fluorescence-activated cell sorting with In-vitro colony forming units in colony initiating assays, and competitive repopulating assays in animal models towards evaluation of functionality has enabled the prospective purification and enrichment of cancer stem cells (CSCs) in leukemia and certain solid tumors. Some of the recent concepts defining cancer stem cell biology, and their involvement in disease progression and implications in cancer therapy will be highlighted briefly.
DR. GIRISH MARU
Senior Scientist, ACTREC, Navi Mumbai

Achievements:


- Visiting Scientist, International Agency for Research on Cancer (IARC), Lyon, France (1987-1989), invited expert member in “WHO Study Group Meeting” on Smokeless Tobacco'. Geneva, June 1-6, (1987), Nearly 30 years of research experience in the area of “Carcinogenesis & Chemoprevention”

Abstract: “CANCER PREVENTION BY HERBAL ANTIOXIDANTS: CURRENT STATUS AND FUTURE PERSPECTIVES”

Majority of human cancers are attributed to environmental factors including pollutants in the air and water, infections, workplace exposure, radiation and personal habits such as smoking/chewing (of tobacco) and dietary patterns. Identification of specific causative factors and evaluation of their relative importance have proved to be difficult since majority of cancers result from complex interactions between environmental and host factors. Efforts to eliminate known human carcinogens from the environment and current cancer treatment approaches have met with limited success. A number of plant-derived antioxidants have shown cancer preventive activities against diverse carcinogens in experimental systems. Carcinogenesis being a complex multi-step, multi-factorial process, a number of chemo preventive interventions can be employed. These strategies are generally directed against two broad events of carcinogenesis i.e. initiation and promotion / progression. A brief summary of environmental chemo preventive agents and mechanisms of their chemo preventive action will be covered.
**DR. MANGAL NAGARSENKAR**

*Head, Department of Pharmaceutics, Bombay College of Pharmacy, Mumbai*

---

**Achievements:**

- She has guided 34 M. Pharm. and 18 Ph. D. students
- She has 63 publications (*International: 39 & National: 24*) in the field of novel drug delivery, nanotechnology and pharmaceutical.
- She has 2 Indian patents in controlled drug delivery to her credit and has filed 3 Indian patents in the field of Nanotechnology.
- She has won G.P. Nair IDMA Gold Medal for top rank in University of Mumbai, for B. Pharm. Sc. Course
- Her research interests are 1) polymeric and lipid based systems and Nano carriers for improved drug delivery, 2) Drug Nano crystals for improved oral and topical delivery, 3) pulmonary drug delivery and 4) synthesis of novel ligands for targeted drug delivery.

**Abstract: “NANO-SYSTEMS IN CANCER THERAPY”**

Cancer has been cause of increasing number of deaths in recent years. Drugs used in treatment of cancer are facing number of challenges like insolubility, instability, lack of specificity etc. Nano sized Drug Delivery Systems can present drugs more effectively by overcoming their limitations. This presentation will cover briefly some approaches which successfully impart target specificity to drug delivery in cancer.
Achievements:

- He has worked with G.S medical college and with KEM hospital as research assistant. He then collaborated with Cancer Research Institute, where he is still working even more than 2 decades. He is a well acclaimed teacher of the University of Mumbai and Homo Bhabha National Institute; under his guidance 5 students, have been awarded a Ph.D. degree and 3 students are persuading the same.

- He is part of editorial committee of international “Chinese Journal of Clinicians” and a reviewer of various other journals in the field of Biochemistry, Molecular Medicine and Pharmacology. He was awarded for 3 best poster presentations and has total 33 publications to his credit. An array of projects with the Council of Scientific and Industrial Research, Intramural research Funds from Tata Memorial Centre, Indian Council of Medical Research, and Department of Science & Technology are in the pipeline.

Abstract:  “MECHANISM OF ACTION OF METHYLXANTHINE DERIVATIVE IN METASTASIS AND ANGIOGENESIS USING B16F10 MELANOMA MODEL”

Drugs that can intervene the processes of rapid tumor growth and metastasis are of clinical importance in treatment of malignant melanoma. Pentoxifylline (PTX), a methyl xanthine derivative has been shown to inhibit B16F10 melanoma tumor growth and metastasis. We hypothesized that combining Suramin combined with PTX in simultaneous or sequential fashion potentiates its cytotoxic effects on B16F10 cells using B16F10 mouse melanoma model, thus enhancing its antineoplastic effects. PTX arrested cells in G0-G1 phase and suramin augmented the effects. PTX and suramin inhibited F10 adhesion to laminin, matrigel and collagen type IV and showed enhanced inhibition when combined. The combination also demonstrated significantly higher inhibition in cell motility (p=0.002) and invasion through matrigel (p=0.005) as compared to the single agents. DBA2/J mice intradermally implanted with B16F10 tumor were used as a model to study tumor growth and angiogenesis. Animals were intratumorally treated with 50mg/Kg of PTX, 10mg/Kg of suramin and their combinations. Simultaneous administration of the drugs inhibited tumor growth by 5-6 folds. In conclusion, the novel combination of PTX and suramin has synergistic anti-tumor and antimetastatic activity in B16F10 melanoma, hence may be a promising approach in treatment of patients suffering from malignant melanoma.
Achievements:

- He is a doctorate from Jiwaji University, Gwalior and is focused in field of X-Ray crystallographic studies of biomolecules.

- His research experience includes projects in collaboration with All India Institute of Medical Sciences, Harvard Medical School Boston, USA and Boston Biomedical Research Institute, Boston, USA.

- His Research graft ranges from the field of molecular biology to structural biology, including proteomics & structural bioinformatics. He has published 14 research papers over the widespread journals.

Abstract: “PROTEIN-PROTEIN INTERACTIONS AND DRUG DEVELOPMENT”

The main goal of protein structure determination is to unravel the complexities of each disease at atomic level. Accurately determined three dimensional structure of protein helps in elaborating the location of an active site and provides information about the position of the ligand at the protein-protein interface. Currently, it is a challenge for structural/computational biologists to find small molecule drug-leads looking at the experimentally determined structures. However, finding a suitable target for drug development using structure-based activity relationships is not a biased approach. Combination of in silico and in-vitro approach at the interface of protein-protein interactions where functional aspects are regulated by only few amino acids is a hot point. After analyzing the interactions at the protein-ligand interface, need to envisage the surrounding regions, i.e. the hot regions. Weak intermolecular interaction at the protein-protein interface play important role in drug development. My Lab is very much focused on BRCA1 its associated binding partners. From the crystal structures of functional domains of BRCA1, complexes with substrate-analogue and synthetic ligands, the important interactions would be recognized. After analyzing the interactions between BRCA1 and potential binding partners, considering BRCA1 as a target, new interactions at recognition sites are introduced. This kind of cycle may produce functional important molecules with desired potencies for medicinal therapy. The BRCA1/2 protein can thus be used as a target for rational structure-based drug design against breast cancer.
Achievements:

- In her tenure of 29 years, she has guided more than 60 M. Pharm. and Ph. D. students and has more than 35 papers published in International Journals.

- She has also published a book on the ‘Instrumental Methods of Analysis’ and is a Fellow member of Research Journal of Chemistry and Environment.

- She is an active member of the Association of Pharmacy Teachers of India (APTI) and Indian Pharmaceutical Association (IPA) and also a member of Editorial Board of Indian Drugs.

Abstract:  “COX-2 INHIBITORS AS ANTICANCER AGENTS”

Cyclooxygenase (COX) is a prostaglandin synthetase enzyme. Its two isoforms, cyclooxygenase-1 and -2, catalyze the initial step in the formation of prostaglandins in a variety of pathophysiological processes. More recently, their role in carcinogenesis has become more evident. They seem to influence apoptosis, angiogenesis, and invasion, and play a role in the production of carcinogens. A large volume of research data has shown that COX-2 is often up-regulated in many malignant tumors, rendering it an attractive candidate target for cancer therapeutics. Several COX-2-selective inhibitors are currently under evaluation in preclinical and clinical studies, either as single agents or in combination with conventional chemotherapy, radiotherapy and other new molecularly-targeted compounds, with promising results. Pharmacophore mapping with the help of Computer Aided Drug Designing (CADD) has shown that Celecoxib and Rofecoxib bind with their polar sulfonamide side chain to a hydrophilic side pocket region close to the active COX-2 binding site. This has provided a hope for new pharmacological opportunities.
DR. RAMADASAN KUTTAN
Director Of Amala Cancer Research Center, Assistant Research Professor In University Of Arizona, University Of Rode Island, Pharmacology

Achievements:

- He has also worked persistently as an assistant research professor in field of developmental therapeutics at M. D. Anderson hospital.

- He is successfully guided 27 Ph. D students & is also an executive member of Indian Association of Cancer research.

- His dedicated persona has been acknowledged by being a gold medalist recipient of the Raman Research prize and by being awarded young investigator award by the National Cancer Institute, USA.

- He has published 275 research papers.

Abstract: “USE OF HERBAL DRUGS IN THE PREVENTION AND TREATMENT OF CANCER"

Cancer is one of the major diseases of the world which affect nearly 25% of the population in the developing countries. Although there are several treatment approaches for cancer, major drawback of these systems is the toxicity which may even lead to death. Development of Non-toxic drugs which can be useful in cancer treatment is the most important need of the hour. Herbal drugs have been used in the treatment and prevention of various diseases including cancer. Active ingredients from plants such as Vincristine, Toxol and Camptothecin are being used in the cancer treatment presently. Herbal drugs have significant role not only in the treatment of cancer but also in the prevention of cancer as immunomodulatory agent, protection from the side effects of radiation and chemotherapy. However these properties have not been fully exploited. Present study is an evaluation of some of the plants as well as plant products which have significant potential in cancer treatment strategies. These plants include turmeric as well as its active ingredient curcumin, Viscum abulum preparation Iscador, Phyllanthus amarus, plant carotenoids as well as herbal formulation Rasayanas. Salient results using these plants will be presented.
Achievements:

- He has procured many best poster awards and has 14 research publications on his record.
- His affiliations comprise of being a member of Association of Radiation Oncologists of India, American Society of Radiation Oncology and European Society of Radiation Oncology.

Abstract: “MOLECULAR IMPACT ON TREATMENT OF CANCER”

Science has evolved enormously over the past decade and there has been an immense stride in our quest to know the unknown. More specifically, the growth at each and every level of understanding about the human body and the disease affecting it has made possible to define and find the cure for a lot of disorders.

There was always a doubt, whether we will be able to translate the benefit from the ‘lab’ to the ‘clinic’. But now we have the answer from so many properly conducted clinical studies. As of today for most of the prevalent common cancers, there is a definite role of genetic or molecular studies for diagnostic, therapeutic and prognostic decision making. Future holds even more promise as we look to explore ‘targeted’ treatment of this dreaded disease.
ABSTRACTS OF POSTERS SELECTED
ABSTRACT: Cancer is suspected based on the symptoms a person might present followed by the results of a physical examination and sometimes the results of screening tests. To confirm that cancer is present, more detailed tests (termed diagnostic tests) are required. Conventional cancer diagnosis depends on cellular pathology (cytopathology) such as tissue biopsy, endoscopy, and imaging, all of them investigating the microscopic cellular appearance. The most precise is biopsy which involves the removal of a sample of the tissue on the abnormal area or sometimes of the whole tumor, followed by cytopathological examination of the sample. Other methods used for cancer diagnosis are endoscopy, X-ray, CT (computed tomography), ultrasonography or MRI (magnetic resonance imaging). The traditional cancer treatment relies on various techniques such as surgery, radiation, hormone therapy and more recently chemotherapy, immunotherapy or their combination.

Bio-imaging is an important technique to visualize phenomena and migration of substances in biological systems by using. Fluorescence bio-imaging in the NIR range of 0.8 to 2.0 mm attracts a great deal of attention for the visualization of deeper lying images in living body without damage, because the use of the NIR light can reduce light scattering which is a major cause of the loss of both excitation and fluorescence lights in a living body in vivo. Semiconductor Nano crystals, or so called quantum dots (QDs), possess unique optical properties that make them potential candidates as luminescent Nano probes for biological applications, ranging from immunoassays to live cell and tissue imaging. These QDs have recently attracted much attention as new generation probes for optical bio imaging.

Gold nanoparticles-polymeric conjugates can serve to intracellular detection and are able to assist with cancer therapy by Plasmon heating. In photo thermal therapy the irradiated tissue temperature can often rise to 46°C, leading to the inactivation of the normal cellular processes (apoptosis), whereas above 46°C, extensive necrosis occurs? Several methods are employed for inducing therapeutically hyperthermia in the presence of proper agents by applying an alternating magnetic or radiofrequency field, or by laser irradiation, usually with near-infrared light. Light-induced heating of nanoparticles in resonance with their Plasmon band seems to be the most efficient since, in contrast to nanoparticle heating in a alternating magnetic field, lower quantities of nanoparticles are required in the later case. Moreover, the Plasmon band of these nanoparticles can be adjusted from visible to the near-infrared (NIR) range (820 nm) where optical transmission through tissue is optimal, so deep tissue treatment (~1 cm) is feasible. Few recent examples of such therapeutically approach use metal Nano shells, gold Nano rods and Nano cages or other anisotropic noble metal nanoparticles, usually embedded in a biocompatible polymeric shell.

REFERENCES:
OBJECTIVES: The systematic review of randomized clinical trials (RCTs) was carried to assess the benefits and harms of the novel Gonadotropin Releasing Hormone (GnRH) antagonist for patients with advanced, hormone sensitive prostate cancer.

INTRODUCTION: Prostate cancer is one of the most common cancers in men and the second most common cause of cancer death. Degarelix is a gonadotropin-releasing hormone (GnRH) receptor antagonist that produces rapid androgen deprivation by immediate inhibition of GnRH receptors in the anterior pituitary gland. Degarelix treatment results in suppression of gonadotropins, testosterone, and prostate-specific antigen (PSA) in prostate cancer, without apparent testosterone surges.

METHODS: Literature Search: The PubMed database was searched from the date of its inception to the end of 20 August 2011 using Medical Subject Headings (MeSH) search terms “Degarelix,” alone. All English articles reporting use of Degarelix in advanced prostate cancer recruiting adult patients were included in this review. The following information was extracted from each study: first author, year of publication, study type, study population characteristics, number of patients, and key outcomes. Finally, a conclusion was formulated based on the validity of the studies identified, taking into consideration the source and the strength of the RCTs.

RESULTS AND DISCUSSION: Of the 68 titles and abstracts screened, 7 studies were identified by full-text review to be RCTs and to have follow-up data of six months or more. The overall study quality was average. A total of 2982 patients were assessed and the highest number of trials available for any one comparison was four: degarelix compared with leuprolide alone (n=2440)3, 5, 6, 7. None of the studies were blinded & only five studies have stated the intention to treat1, 2, 3, 4, 6. Three trials had no loss to follow up and all the studies have defined the outcome assessment1, 5, 6. Randomized control trials with subcutaneous degarelix of 200 mg followed by subcutaneous monthly injection of 60 or 80 mg for a year in patients with histologically confirmed prostate cancer and a baseline of PSA ≥ 2 mg/ml resulted in a reduction of testosterone level (≤ 0.5 mg/ml) one month after the initial injection in about 88% patients. Patients receiving maintenance dose of 60 mg and 80 mg showed testosterone level ≥ 0.5 mg/ml in 93% and 98% of patients respectively at monthly and one year level. In another open label study 187 patients with histologically confirmed adenocarcinoma received subcutaneous dose of 200mg or 240 mg, followed by monthly subcutaneous dose of 80 mg, 120 mg or 160 mg2, 3, 4, 5. The testosterone level (≥ 0.5 mg/ml)
up to 1 year in all patients receiving maintenance dose of 160 mg. PSA levels decreased by 97-98% in groups receiving 200 mg initially followed by monthly 80 mg maintenance dose. There was no evidence of testosterone surges in either study and degarelix was well tolerated according to investigators. The randomized open label comparison studies done with leuprolide showed the suppression of testosterone level between day 28 and day 364 in more than 95% patients who confirmed non-inferiority criteria by degarelix treatment as well as PSA levels also decreased by 64% & 65% in degarelix therapy group versus 18% in leuprolide therapy group after the start of treatment. After 28th day PSA levels decreased by 85% & 83% among degarelix patients compared with those who were given leuprolide (P < 0.001). Rates of treatment emergent adverse events were similar in the treatment groups and most of the events were mild & moderate. Chills were significantly common with degarelix whereas arthralgia & urinary tract infection were significant with leuprolide. Rate of discontinuation were seen more with leuprolide group because of non-fatal adverse events.

In men with prostate cancer, degarelix and leuprolide have similar cardiovascular safety profiles because of hypogonadism rather than direct drug effect.

CONCLUSION: Medial castration with agents that target the hypothalamic-pituitary is the primary androgen deprivation therapy of choice. Though the side effect profile appears similar and efficacy after one month appears to be identical but still GnRH antagonists are better accepted because of its negligible flare of symptoms because of unsuppressed testosterone levels. Long term data of this new drug is not available but considered to be well tolerated with reasonable dosing schedule.

REFERENCES:


3. SYNTHESIS AND EVALUATION OF SOME NEW SUBSTITUTED BENZIMIDAZOLE DERIVATIVES AND THEIR ANTICANCER ACTIVITY

Santosh G.Jadhav & Shashikant R.Pattan*, 1Department of Pharmaceutical Chemistry, Indira Institute of Pharmacy, Sadavali (Devrukh) 415804, India, 2Department of Pharmaceutical Chemistry, Pravara Rural College of Pharmacy, Pravaranagar, Loni 413713, India, Department of Pharmaceutical Chemistry, Indira Institute of Pharmacy, Sadavali, (Devrukh), Tal: Sangmeshwar, Dist: Ratnagiri-415804, India, E-mail ID: santosh JadHAV75@yahoo.co.in

KEYWORDS: Benzimidazole, Anticancer Activity against MCF-7 Cell line.

OBJECTIVES: A new series of substituted Benz imidazole derivatives has synthesized,
characterized and all the compounds have been screened for anticancer activities against MCF-7 Cell line.

**INTRODUCTION:** The incorporation of Benz imidazole nuclei is an important synthetic strategy in drug discovery. Benzimidazole derivatives are of wide interest because of their diverse biological activity.

**EXPERIMENTAL METHODS:** All the compounds synthesized from the synthetic method and these compounds confirmed by spectral data such as IR, $^1$H NMR and Mass.

**Final Synthesized compounds:**

<chemistry>
\[ \text{Synthesized Compounds } D_1-D_{10} \]
\[ \text{Anticancer Activity: } \text{Potential anticancer activity against MCF-7 (breast cancer cell line). Compounds } D_1-D_{10} \text{ was tested by in vitro using SRB (Sulforhodamine) assay protocols. Each drug is tested at 4 dose levels (1x10^{-7} m, 1x10^{-6} m, 1x10^{-5} m, 1x10^{-4} m OR 10,20,40,80 \mu g/ml. Results are given in terms of G150, TGI & LC50 valve.} \]
\[ \begin{align*}
G150 & = \text{Concentration of the drug that produces 50\% inhibition of the cells.} \\
TGI & = \text{Concentration of the drug that produces total inhibition of the cells.} \\
LC50 & = \text{Concentration of the drug that kill 50\% of the cells.}
\end{align*} \]

**RESULTS AND DISCUSSION:** The title compounds were synthesized as per the scheme. The structures of the compounds were confirmed by IR, NMR and Mass. All these compounds were screened for anticancer activity against MCF-7 by SRB assay Protocols. Most of the compounds have promising anti-cancer activity.

**CONCLUSION:** Compounds $D_2$, $D_6$, $D_7$, $D_8$, $D_9$, and $D_{10}$ have shown maximum anticancer activity. Compounds $D_1$, $D_3$, and $D_5$ have also shown the average anticancer activity against MCF-7 cell line. When compared to the standard anticancer drug Adriamycin (ADR).

**REFERENCES:**

4. NATURAL PRODUCT AS PROMISING ANTICANCER AGENT
Aniket Jadhav*, Nilesh Masal, Patrakar Ramling, Shree Santkrupa College of Pharmacy, Ghogaon, Tq-Karad Dist-Satara (MH)

**ABSTRACT:** Human beings have relied on natural products as a resource of drugs for thousands of years. Plant-based drugs have formed the basis of traditional medicine systems that have been used for centuries in many countries. Cancer is a major public health burden in both developed and developing countries. It was estimated that there were 10.9 million new cases, 6.7 million deaths. Of the 92 anticancer drugs commercially available prior to 1983 in the US and among worldwide approved anticancer drugs between 1983 and 1994, 60% are of natural origin. Improved cytotoxic agents continue to be an important line in the discovery of modern anticancer drugs. The huge structural diversity of natural compounds and their bioactivity potential have meant that several products isolated from plants, marine flora and microorganisms can serve as “lead” compounds for improvement of their therapeutic potential by molecular modification. In this topic we described discovery and development of various anticancer agents obtained from herbs which are under preclinical and clinical phase. The present article helps researchers for further investigation of anticancer agents.

**KEY WORDS:** Natural products, Anticancer, Clinical uses, Dietary sources.

5. ROLE OF NUTRIENTS IN CHEMOPREVENTION AND CANCER
Priyanka Gandhi*, Akanksha Mahajan, Zelia D'Silva & Dr. Aruna Jadhav
Bharati Vidyapeeth’s College of Pharmacy, Sector-8, C.B.D., Belapur, Navi Mumbai - 400 614.

**KEYWORDS:** Nutrients, cancer

**OBJECTIVE:** The objective of this review is to emphasize the importance of the chemopreventive role of nutrients in cancer.

**INTRODUCTION:** The declaration of the "war on cancer," research on carcinogenesis has led to the realization that cancer is not a single disease. Cancer is, in fact, a bio medically complex group of diseases resulting partly from changes in genes that control cell growth and behavior and partly from interactions between these genetic changes and the cellular stresses from specific environmental and behavioral factors, including lifestyle choices such as diet. Cancer is a growing health problem around the world particularly with the steady rise in life expectancy, increasing urbanization and the subsequent changes in environmental conditions, including lifestyle. According to a recent report by the World Health Organization (WHO), there are now more than 10 million cases of cancer per year worldwide. Although there is no ‘magic bullet' that can completely conquer cancer, many types of the disease might be avoidable. Cancer risk can be reduced by eliminating the identified carcinogens — or at least minimizing exposure to them. Reduction of cancer risk by either preventing carcinogenesis or stopping carcinogenesis in its early stages is a logical approach for reducing the cancer burden, both for high-risk individuals and for the general population. Prevention is the ultimate approach to controlling cancer. Cancer chemoprevention is the prevention of induction and inhibition of the development of preinvasive and invasive cancer.
and its progression or treatment of identifiable precancers. The areas of dietary modification and chemoprevention show considerable promise as effective approaches for cancer prevention and are a focus of research efforts.

**Diet and cancer:** The bright green world of the nutrients is the heart and soul of a cancer prevention program. The source of these precious jewels is located in our local grocery store. So rather than waiting for cancer cure to be found in some high tech lab, why not turn to nature’s chemicals for high dose of prevention? Diet and cancer studies show that, generally, vegetables and fruits, dietary fiber, and certain nutrients seem to be protective against cancer, whereas fat, excessive calories and alcohol seem to increase cancer risk. Chemoprevention research is closely linked to diet and cancer research and represents a logical research progression. A study in India used Vitamin A and beta-carotene: researchers observed complete remission of the leukoplakia at a rate ten times greater than the placebo group. Other epidemiological studies have shown that dietary deficiencies in vitamin A, vitamin E, beta-carotene, and vitamin C increase the risk of cervical cancer. Beta-carotene supplementation actually has been shown to prevent cervical cancer. In recent years, attention has focused on the role of nutrients as chemo preventive agents. The concept of using micronutrients for the chemoprevention of cancer is based on the evidence from human epidemiology, the results of a few clinical trials, and studies of animal carcinogenesis models for cancer-inhibiting potential of these substances. Basic research has identified nutrients as agents that inhibit mutagenesis and hyper proliferation, as well as those that induce apoptosis or differentiation as critical characteristics for chemoprevention.

**CONCLUSION:** Having gone outside our bodies and nature in search of high-tech medicines to cure our gravest ills, we have now made a big loop and come circling back home. Mother Nature has answers for many things. We should reflect back on the fact that we are not machines awaiting the touch of magic medical button but whole people whose existence and ultimate fate is clearly related to the steady, day-by-day conditions of our entire lives. What we do to our bodies determines pretty much what our bodies will do to us.

Nutritional science offers us the greatest hope in our fight against cancer and several other degenerative diseases. They not only help prevent cancer but may actually enhance the traditional chemo- and radiation therapy. The future of cancer prevention, then, seems to be very bright indeed.

**REFERENCES:**

2. Ray D. Strand. What Your Doctor Doesn’t Know About Nutritional Medicine May Be Killing You. 70 - 84.
6. TRIPLE NEGATIVE BREAST CANCER: AN OVERVIEW
Parpiani Jaya, Mevekari Anjum, Parpiani Gunjan, Chewle Surahit, Institute of Chemical Technology, Matunga, Mumbai - 400019. jparpiani@gmail.com

Review outlines the understanding and management of triple negative breast cancer.

INTRODUCTION: Breast cancer is the most common type of female cancer. Breast cancer can be divided into different types based on several criteria including the marker proteins they express. Over a million cases of breast cancer occur worldwide out of which more than approximately 15% are of triple negative breast cancer. The associated problems make research in this area important. The term “triple negative breast cancer” that is TNBC is an immunophenotype of breast cancer, in which offending tumor is immunologically estrogen receptor-negative, progesterone receptor-negative and HER2-negative. TNBC is biologically more aggressive and one of the most challenging groups of breast cancers. Three prominent hallmarks of TNBC which is associated with poor relapse-free and overall survival are over expression of epidermal growth factor receptor (EGFR), hyper activation of MEK/ERK transduction pathway and high sensitivity to DNA damaging agents. Histologically, such cancers are poorly differentiated, and mostly fall into the basal subgroup of breast cancers & have many similarities to BRCA1-associated breast cancers.

Targeted Agents That Are Currently Being Investigated Include: TNBC is sensitive to chemotherapy BUT early relapse is more likely in patients with TNBC than with other subtypes, and visceral metastasis, including brain metastasis, is commonly seen. A challenge for clinicians since they lack a specific treatment target that, when inhibited, ameliorates the prognosis of the patients. This makes targeted therapy an intensive subject of research for TNBC.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Target</th>
<th>Ongoing studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytotoxic with agents that cause interstrand breaks (e.g., platinum-based drugs) &amp; double-stranded breaks but not with agents that target mitotic-spindle apparatus (e.g., vinca alkaloids &amp; taxanes)</td>
<td>DNA</td>
<td>Study planned to assess activity of platinum-based drugs compared with taxanes (BRCA1 triple -ve cancers &amp; sporadic triple -ve cancers)</td>
</tr>
<tr>
<td>PARP inhibition (AZD2281)</td>
<td>PARP</td>
<td>Phase-II studies</td>
</tr>
<tr>
<td>Antibody treatment (e.g., cetuximab) Small molecule inhibitors of receptor tyrosine kinase activity (e.g., gefitinib)</td>
<td>EGFR</td>
<td>Phase-II studies</td>
</tr>
<tr>
<td>c-KIT tyrosine kinase inhibitor (e.g., imatinib)</td>
<td>c-KIT</td>
<td>Phase-II studies</td>
</tr>
<tr>
<td>Multikinase inhibitors (e.g., lapatinib &amp; pertuzumab)</td>
<td>EGFR / ERBB2</td>
<td>Phase-II studies</td>
</tr>
<tr>
<td>Second-messenger inhibition (e.g., Rasfarnesylation, Raf, MEK, MTOR, Src, HSP90)</td>
<td>Rasfarnesylation, Raf, MEK, MTOR, Src, HSP90</td>
<td>Phase-I &amp; II</td>
</tr>
</tbody>
</table>
Future Perspective: There is an effort to develop more effective therapies for the triple negative group. The preclinical and clinical evidence suggest that androgens and androgen signaling pathway play a critical role in breast carcinogenesis, and may provide a novel treatment approach in ER-negative/AR-positive tumors. Antiangiogenic approach can also be effective. The large research interest now devoted to this entity is likely to better understanding of what is positive about triple negative breast cancer.

KEYWORDS: triple negative breast cancer, targeted agents.

7. PRODUCTION OF TUMOR INHIBITORY ENZYME, L-ASPARAGINASE, THROUGH SOLID STATE FERMENTATION USING FUSARIUM OXYSPORIUM

R. SAIPRASANTH, VISHAL ROKADE, SNEHA PATIL, VES COLLEGE OF PHARMACY, CHEMBUR (EAST), MUMBAI-400 074, EMAIL ID:biharijiwidsai@gmail.com

KEYWORDS: L-Asparagenase, Fusarium oxysporium, Process parameters, Solid state fermentation, Optimization.

OBJECTIVE: L-asparaginase plays a vital role in treating different forms of cancer. The main objective of the present study is to optimize the production of L-asparaginase. The maximum yield of L-asparaginase (8.14 IU) was achieved.

INTRODUCTION:

The enzyme, L-asparaginase (L-asparagine amido hydrolase, E.C. 3.5.1.1) is amides that catalyze the hydrolysis of L-asparagine to L-aspartic acid and ammonia1. It had received a great attention in recent years because of its tumor inhibitory property especially in treating acute lymphoblastic leukemia (ALL). Cancer Cells differentiate themselves from normal cells in diminished expression of L-asparagine. Hence, they are not capable of producing L-asparagine, and mainly they depend on external L-asparagine from the circulating Blood plasma and thus they die due to unavailability of asparagine. The above two figures illustrate
this difference in a normal and cancerous or tumor cells respectively. Thus it becomes important to produce and preserve this enzyme for the treatment of cancer.

**CONCLUSION:** In the present study, the maximum value of Lasparaginase activity obtained after the optimization of all the fermentation parameters was 8.14 IU; which clearly demonstrated the scope for exploring filamentous fungi for the production of therapeutic enzymes like L-Asparaginase using SSF (Solid State Fermentation).

**EFFECT OF FERMENTATION:**
Effect of fermentation time on the production of L-asparaginase. After 5 days enzyme production started decreasing as the growth of organism couldn’t balance with available nutrients.

**EFFECT OF INITIAL MOISTURE CONTENT**
Maximum enzyme activity was observed at 60% v/w.

**EFFECT OF INOCULUM VOLUME**
The maximum L-asparaginase yield was observed when a volume of 1.5ml was added to 7 days old F. Oxysporum. A low volume may produce insufficient biomass whereas a higher may produce too much biomass.

**EFFECT OF pH:** the fermentation medium pH was adjusted according with help of 1N HCl/ NaOH from 4-9. Fermentation was carried for 5 days. The maximum L-asparaginase was produced at a Ph of 7.0 as shown in the graph below.

**EFFECT OF INCUBATION TEMPERATURE:** Fermentation was carried at temperatures ranging from 24-36degC for 5 days where maximum activity was found at 30degC.
**EFFECT OF CARBON SOURCE:** glucose enhances the production of L-asparaginase enzyme. This may attribute to the positive influence of additional carbon source on enhanced biosynthesis.

**EFFECT OF NITROGEN SOURCE:** nitrogen source is the limiting factor of any fermentation process so the nitrogen source like malt extract is the best source for maximal L-asparaginase production.

**REFERENCE:**

3. Diagrams from www.d.umn.edu/~jftzake/Lectures/DMED/Antineoplastic/ProteinFunctionInhibitors/L-Asparaginase.html

---

8. **THALIDOMIDE IN MULTIPLE MYELOMA**

**AUTHORS:** KARNIK R.N, BADE N.D, CHAVAN U.A, NALAWDE V.V.

rajaskarnik28@gmail.com

VES COLLEGE OF PHARMACY, COLLECTOR COLONY, CHEMBUR, MUMBAI

**ABSTRACT:** Thalidomide, used in the late 1950s and early 1960s as a sedative and anti-nausea medication, became the ultimate symbol of pharmacopeia gone awry. In 1956, thalidomide was introduced by Chemie Grunenthal, a West German pharmaceutical company, as a sedative and was marketed under the name of Contergan. The drug was thought to have sedative effects superior to those of comparator drugs and was thought to be virtually nontoxic. When taken by pregnant women for morning sickness, it resulted in congenital defects as well as organ damage and death in thousands of fetuses.[1] Thalidomide is the worst teratogen known in the history of medicine. Due to its side effects like teratogenicity and peripheral neuropathy, thalidomide was withdrawn from the worldwide market long back in 1961. Yet recently, on May 26, 2006, the U.S. Food and Drug Administration granted accelerated approval for thalidomide in combination with dexamethasone for the treatment of newly diagnosed multiple myeloma.[2] In multiple myeloma, a group of plasma cells (myeloma cells) becomes cancerous and multiplies, raising the number of plasma cells to a higher than normal level. Since these cells normally make antibodies, the level of abnormal proteins in blood also may go up. Health problems caused by multiple myeloma can affect bones, immune system, kidneys and red blood cell count. Thalidomide may interfere with the formation of new blood vessels (angiogenesis),
which tumors use to get nourishment to help them grow and spread. If thalidomide prevents the formation of blood vessels to tumors, it could stop the growth and spread of some cancers. Preliminary clinical studies have found that thalidomide, when combined with other drugs, may show some promise in treating several types of cancers. Its antiangiogenic properties were recognized in the early 1990s during a period where the importance of angiogenesis became increasingly apparent as a critical step in the proliferation and spread of malignant neoplasms. This led to the evaluation of thalidomide as an antiangiogenic agent in the treatment of several cancers. Although multiple myeloma remains incurable with conventional treatments, management of the disease has recently been transformed with the introduction of three novel agents, bortezomib, thalidomide, and lenalidomide. Thalidomide plus dexamethasone is approved as frontline treatment of multiple myeloma. Other combination regimens including thalidomide have demonstrated substantial activity in both relapsed and frontline settings. Recently, the thalidomide analogue lenalidomide has been approved, in combination with dexamethasone, for the treatment of patients who have received one prior therapy; this regimen has shown promising results in the frontline setting. These agents represent a new generation of treatments for multiple myeloma that affect both specific intracellular signaling pathways and the tumor microenvironment. Thalidomide has been extensively studied alone and in combination in patients with relapsed myeloma, demonstrating substantial efficacy, and is therefore widely used in this setting. The toxicity profile is dose and duration-linked, with lower doses appearing to be better tolerated. Lenalidomide plus dexamethasone has been shown to have significantly greater activity than dexamethasone alone in the relapsed setting, with impressive duration of disease control. Some aspects of the toxicity profile appear significantly reduced relative to thalidomide, although myelosuppression is increased. Thus, thalidomide, once discarded as the worst teratogen, is again regaining status as a drug in the treatment of diseases like cancers and related complications.

**KEY WORDS:** Thalidomide, Teratogenicity, immunomodulatory, peripheral neuropathy, dexamethasone, teratogen, angiogenesis, myeloma cells.

**REFERENCES:**

2. Perri III A J, and Hsu S MD, Dermatology Online Journal 9 (3)
3. Richardson P G, MD; Dana-Farber Cancer Institute, Harvard Medical School.

9. **SIGNALING PATHWAYS: GROUND BREAKING TARGET FOR ANTI-CANCER STEM CELLS THERAPIES**

Sandbhor P. S., Thanekar Dr., Dhodi J. B., Juvekar A. R., Institute of Chemical Technology, Nathalal Parekh Marg, Matunga, Mumbai - 400019, India,

Address for Correspondence: p_sandbhor@rediffmail.com

**KEYWORDS:** Cancer Stem Cells, Signaling pathways, Cell Surface Markers, Microenvironment, Targeted Therapy, Chemo resistance, Cancer Recurrence.

**INTRODUCTION:** There is increasing evidence that malignant tumor such as leukemia, breast cancer and brain cancer contains cells that maintain the characteristics of tissue
specific stem cells and are malignant. Such cells are called as cancer stem cells (CSCs), tumor initiating cells or progenitor cells. CSC was initially defined by their extensive self renewal capacity, tumorigenicity and multipotentiality. In a variety of tumors, CSCs seem to be particularly resistant to conventional chemo and radiation therapies as compared to other tumor cells. Furthermore CSCs are found to be particularly adept in stimulating angiogenesis to promote tumor growth and increase overall tumor aggressiveness both before and after therapy. Several studies point out that radio resistance, chemotherapy resistance and angiogenesis in these CSCs in humans could particularly explain tumor recurrences in advance or aggressive tumors treated with radiation. Hence it is necessary to develop anti-CSC therapies that have minimal or no effect on normal stem cells for complete cancer cure. The aim of anti-CSC therapies will be to kill, differentiate or prevent the metastasis of cancer stem cells. There are three broad targets present for anti-CSCs therapy, viz. cell surface markers, signaling pathways and microenvironment of CSCs. Limited efficacy has been seen with the use of cell surface markers in clinical trials. The neoplastic proliferation of cancer stem cells is likely to be driven by mutations that inappropriately activate pathways like WNT/β-catenin, BMI1-dependent pathways, hedgehog(SHH), epidermal growth factor receptor(EGFR), Notch, Stromal cell- derived factor(SDF-1), CXC chemokine receptor 4 (CXCR4) and/or polycomb group (PcG) protein signaling pathways. Receptor ligand interaction, cytosolic signaling components and nuclear signaling component are major targets for any signaling pathway. Various studies have shown that it is possible to target cancer stem cells without affecting normal stem cells. We would like to suggest novel targeted drug delivery system for the same.

10. STARVING THE TUMOR---USING ANGIOGENESIS INHIBITORS

Sridhar V, Vivekanand Education Society’s College of Pharmacy, Hashu Advani Memorial Complex, Behind Collector Colony, Chembur, Mumbai - 400 074
Email: blackvin30@yahoo.co.in

KEYWORDS: “angiogenesis, tumor growth”,

OBJECTIVES: A review on the use of angiogenesis inhibitors in conjunction with the in-use chemotherapeutic agents to optimize anti-cancer treatment and possibly reduce the severe side-effects associated with the treatment procedures.

INTRODUCTION: Like all cells, cancer cells require a constant supply of nutrients and oxygen in order to grow and divide. Without an adequate blood supply tumors will not grow. Tumors produce factors that stimulate the formation of blood vessels to provide them with the food and oxygen they need. The process of blood vessel formation is termed angiogenesis. Scientists have found a number of different pathways that cancer cells can use to cause blood vessel growth. Each step in these pathways is a possible target for cancer treatment.

DISCUSSION: It is estimated that about 85% cases of death among cancer patients involve metastasis of the tumor. Along with treatments that destroy the tumors due attention is to be given to drugs that prevent metastasis and tumor growth. These include:

- Matrix metalloproteinase inhibitors
Endothelial cell inhibitors

Angiogenesis inhibitors

**Focusing on Angiogenesis Inhibitors**

Anti-angiogenesis drugs may have any or both of the following mechanisms:

- Block sending of growth signals from tumor cells
- Stop nearby blood vessel cells from receiving these signals

These agents, maybe:

1) Monoclonal antibodies directed against specific proangiogenic growth factors or
2) Kinase inhibitors of multiple proangiogenic growth factor receptors

**Monoclonal antibodies**: Chemicals called growth factors attach to receptors on the surface of normal cells and cancer cells, signaling the cells to grow. Certain cancer cells make extra copies of the growth factor receptor. This makes them grow faster than the normal cells. Monoclonal antibodies can block these receptors and prevent the growth signal from getting through. One of the most important proteins, vascular endothelial growth factor (VEGF) is not made in large amounts by normal cells, but some cancer cells make it and release it into the area around them. VEGF then attaches to a VEGF receptor (or VEGFR) on the surface of nearby endothelial cells. This signals the cells' control centers, to start growing and forming new blood vessels. Bevacizumab (Avastin®) is a monoclonal antibody - a man-made version of an immune system protein - that binds to VEGF and keeps it from reaching the VEGF receptor.

**Kinase inhibitors in cancer cells**: Abnormal kinase activity is typically the cause of many diseases such as cancer. If the activity of an abnormal kinase within a cancer cell is disrupted, the cancer cell may stop growing and dividing, could even lead to cancer cell death, also called apoptosis. In cancer cells, cell proliferation consisting of growth and division along with other cellular pathways are constantly activated because the protein kinases that would normally control such unrestrained growth and division no longer work. Drugs like sunitinib (Sutent®) and sorafenib (Nexavar®) are small molecules that attach to the VEGF receptor itself (mentioned above), keeping it from being turned on and making new blood vessels.

**Side effects**: For the most part, anti-angiogenesis drugs tend to have milder side effects than chemotherapy drugs. Unlike chemotherapy drugs, anti-angiogenesis drugs do not harm the normal cells. They act where new blood vessels are forming, so they usually do not cause the typical kinds of side effects. However, because of the way anti-angiogenesis drugs work, they are only useful in treating cancers that form tumors. They won't work against blood cancers like leukemia's.

**CONCLUSION**: A suitable combination therapy could be proposed using normal chemotherapeutic agents along with anti-angiogenesis drugs and thus the frequency of chemotherapy doses could be reduced also providing maximum efficiency to the treatment of cancer. Angiogenesis inhibitors could help prevent tumor recurrences and has been clinically proven to increase the life of patients who normally received only a traditional chemotherapy treatment.
REFERENCES:

- Angio.org
- Cancerquest.org
- Mesotheliomaweb.org

11. VALIDATION OF BIOMARKERS IN PANCREATIC CANCER:
Radhakrishnan R, Ramakrishnan. A, Vivekanand Education Society’s College Of Pharmacy, Hashu Advani Memorial Complex, Chembur (E), Mumbai, India 400074
Email: rashmi_r812003@yahoo.co.in

ABSTRACT: Pancreatic cancer is the fourth leading cause of cancer-related death in the world. Hence, there is a need to understand the molecular mechanisms underlying this disease for effective therapy. Biomarkers are patient diagnostic tools that have recently risen as an important element of healthcare research because newer technologies, such as proteomics, transcriptomics and genetic tests which help to rapidly demonstrate pharmacological effect and efficacy more quickly, in smaller trials. For successful biomarker validations, there is a great need for establishment of good specimen collections. A perfect biomarker for cancer prediction among asymptomatic populations would be able to yield a test (classification rule) that is either positive or negative with 100% sensitivity and specificity. Different approaches for validation of biomarkers in pancreatic cancer include:

1. MicroRNA: Abnormal expression levels of microRNA’s (miRs), the 17- to 25- nucleotide long non-coding RNA’s, regulate expression of approximately 30% of the protein-coding genes at the post transcriptional level and have emerged as critical components of the complex functional pathway networks. They have been implicated to play important roles in the oncogenic processes, functioning both as oncogenes and as tumor suppressor genes. Elucidation of the genetic networks regulated by the abnormally expressing miRs in cancer cells is proving to be extremely significant in understanding the role of these miRs in the induction of malignant-transformation-associated phenotypic changes. Hence, miRs involved in the oncogenic transformation process are being investigated as novel biomarkers of disease detection and prognosis as well as potential therapeutic targets for human cancers. MiRs play roles in cancer initiation, invasion and progression processes and, therefore, may prove to be informative biomarkers of detection, diagnosis and prognosis besides being potential targets of therapy. Recently demonstrated that differentially expressing miRs in pancreatic ductal adenocarcinoma (PDAC) can also be profiled in blood as a minimally invasive biomarker assay for pancreatic cancer. Also, up regulation of miR-155, miR-203, miR-210 and miR-222 was also found to be significantly associated with poorer survival of patients with pancreatic carcinomas

2. The PLAT protein is known to be over expressed in pancreatic cancer tissues. Several studies have reported elevated LCN2 mRNA levels in pancreatic cancer and LCN2 protein in human pancreatic juice in patients with pancreatic cancer while the presence of LCN2 protein in pancreatic adenocarcinoma is less well characterized. Reports validating this over expression are very scarce. The expression of KRT& protein is suggested as a marker of normal pancreatic duct epithelial cells playing a role in cell
differentiation. These help to explain why there was no observation of significant
difference in expression levels between both sample types.

3. Src: Increase in Src (a protein) activity promotes an invasive tumor phenotype
characterized by breakdown of cell-cell adhesion, increased cell-matrix adhesion, and
formation of focal adhesions. Accordingly, inhibition of Src activity in preclinical models
restores cell-cell adhesion, inhibits cell migration and invasion, and reverses the Src-
modulated invasive phenotype. Src is an important mediator of many downstream effects
of receptor tyrosine kinases including the epidermal growth factor receptor family.
These studies have used a proteomic approach of 2D gel electrophoresis and mass
spectroscopy (MS) to identify differentially expressed proteins.

CONCLUSION: There is an increasing need for clinical management in pancreatic cancer as
there are very less treatment available for pancreatic cancer. Use of biomarkers in early
detection and effective diagnosis of cancer seems promising and fruitful.

REFERENCES:

biology to biomarkers of disease, J. Biosci. 36(3), August 2011, 481-491, Indian
Academy of Sciences.
2. Antonio Jimeno and Manuel Hidalgo, Molecular biomarkers: their increasing role in the
diagnosis, characterization, and therapy guidance in pancreatic cancer; Molecular
3. N.V. Rajesh Kumar, Aik Choon Tan, Elizabeth De Oliveria, Antitumor Effects and
biomarkers of Activity of AZD0530, a Src inhibitor, in Pancreatic Cancer; aacrjournals,
August 24, 2011.

12. PHOTODYNAMIC THERAPY IN CANCER TREATMENT
Authors: Toraskar Natasha, Mehta Mitisha, Affiliations: Vivekanand Education Society’s
College of Pharmacy, Email: sweetangelpie29@hotmail.com

KEY WORDS: Lasers, LEDs, Photosensitizing agents, intravenously, topically, Oxygen
Singlet [O], outpatient procedure, Poryphorins, Nanotechnology and Radiation Therapy.

OBJECTIVE: PDT ultimately provides a Long and Improved Quality of Life to the patients
with no Long Term problems. But yet it is not widely used today.

INTRODUCTION: Photodynamic therapy (PDT) is also commonly termed as Photo radiation
therapy, Phototherapy or Photo chemotherapy. It was first used over a hundred years
ago(1). It involves the use of Drugs called Photosensitizing agents, along with light and,
tissue oxygen to kill Cancer Cells. Each photosensitizing agent is activated by a light of a
specific wavelength of light and this wavelength determines how far a light can penetrate
through the body (2). Depending upon the part of the body to be treated, the
photosensitizing agent is either administered intravenously or applied topically as a cream
(3). The Drug gets absorbed in both the normal tissue cells as well as the Cancerous Cell.
After about 24-72 hours (depending on the drug used) the drug leaves the normal tissue cell
but continues to reside and accumulate within the Cancer Cells (3). Hence if the light is now applied to the area to be treated, it activates the photosensitizing agents to undergo a toxic chemical reaction between the light source, the agent, and tissue oxygen to produce a very reactive species of oxygen-The Oxygen Singlet \([O] (3,4,5)\). This Oxygen Singlet destroys the Cancerous cells i.e. apoptosis occurs. These activated photosensitizing agents also cause the tumors to shrink: by causing destruction of the blood vessels that feed these cancerous cells (thus depriving them of nutrients) and, by triggering an immune system to attack these cells (3,4, 5, 6). Laser light can be directed through fiber optic cables (thin fibers that transmit light) to deliver light to areas inside the body (4). For example, a fiber optic cable can be inserted through an endoscope (a thin, lighted tube used to look at tissues inside the body) into the lungs or esophagus to treat cancer in these organs. Other light sources include light-emitting diodes (LEDs), which may be used for surface tumors, such as skin cancer (7). In addition, PDT has a few advantages over the conventional treatment therapies like, it has no side effects when used properly and the time required for treatment is short and mostly it is performed as an outpatient procedure(8,9)(without being admitted in the hospital). The tumors at specific locations can be treated and it is usually performed just once but, can be repeated at the same sites many times if needed (9). This non-operative procedure leave no scars after healing and, only causes some swelling, little pain and irritation which can be easily overcome by a prescribed pain killer and an anti-pruritic drug respectively (9). But yet, PDT has its own setbacks and it cannot be used to treat tumors that have undergone metastasis (spread to many places) and after treatment the patient continues to remain sensitive to light for a while depending the drug reaction intensity and its concentration (9). Hence patients are advised to remain unexposed to light. PDT cannot be used in people who have certain blood diseases like acute intermittent porphyria or people who are allergic to porphorins (9). Also, PDT is limited to treat tumors only in areas where light can reach and hence it can treat cancer infested areas under the skin, or in the lining of the internal organs.

**Future research aspects:** Researchers continue to study ways to improve the effectiveness of PDT and expand it to other cancers. Clinical trials (research studies) are under way to evaluate the use of PDT for cancers of the brain, skin, prostate, cervix, and peritoneal cavity (the space in the abdomen that contains the intestines, stomach, and liver). Other research is focused in combining PDT with Nanotechnology and Radiation therapy to develop photosensitizers that are more powerful, more specifically target cancer cells(3,5,7)and are activated by light that can penetrate tissue and treat deep or large tumors (as by using it in combination with x-rays) (4). Researchers are also investigating ways to improve equipment (3) and the delivery of the activating light (7).

**REFERENCES:**

13. NANOTUBES: EVOLUTIONARY WEAPON AGAINST CANCER

Gurav P., Kasar H., Mali S., Shri. D. D. Vispute College of Pharmacy & Research Center, Devad - Vichumbe, Tal. Panvel, Dist. Raigad, Email id: pranvg320@gmail.com

OBJECTIVE: To focus on use of nanotubes to destroy cancer tumors

KEY WORDS: Nanotubes, Chromophores, Folate, Protein denaturation

INTRODUCTION: Cancer is a disease characterized by uncontrolled multiplication and spread of abnormal forms of the body own cells. Nano technology is a multidisciplinary field, which recently has been entered in the field of cancer treatment. Nano technology plays a role in diagnosis, treatment and prevention of cancer disease. The major aim of developing carbon nanotubes as a drug delivery system is to enhance the therapeutic effect or reduce toxicity of therapeutically active materials. Carbon nanotubes recently have gained importance in the field of cancer treatment. Carbon nanotubes exhibit physical properties that render them ideal candidates for application as a noninvasive therapy in cancer treatment.

EXPERIMENTAL METHOD: Carbon Nanotubes are synthetic rods that are only half the width of a DNA molecule. A property of carbon nanotubes is that they absorb near-infrared light waves and pass harmlessly through cells. However, when a beam of near-infrared light (NIR) falls on a carbon nanotube, results in the excitation of electron in the nanotube thus increasing the excess energy in the form of heat which leads to thermal destruction of cancer cells in vivo & in vitro. Biological systems largely lack chromospheres that absorb in the NIR region; lesions can be treated without the need for direct access to the tumour site. The surface of a cancer cell contains numerous receptors for a vitamin known as folate, the nanotubes coated with folate molecules would only be attracted to diseased cells with folate receptors. This treatment induces coagulative necrosis, a form of cell death that involves protein denaturation and membrane lysis. Use of Multi-Walled Carbon Nanotubes (MWCNT) enables ablation of tumours with low laser powers (3 W/cm²) and very short treatment times (a single 30-sec treatment) with minimal local toxicity and no evident systemic toxicity.

RESULTS:

1) 

Fig. 1. MWCNTs produces a greater temperature increase than SWCNTs in response to NIR illumination.
CONCLUSION:
1) CNTs are promising needle-like carriers of both small drug molecules as well as macromolecules such as genes and proteins.
2) CNTs have exclusive properties that would make them appropriate in the medical field such as their ability to adsorb pathogenic microorganisms and conduct heat.

REFERENCE:

14. GENTAL ELECTROTHERAPY TARGETTING RIBONUCLEOTIDE REDUCTASE - A LOW COST AND EFFECTIVE CANCER TREATMENT
Shendge S., Ghogare J., Bharati S., Shri. D. D. Vispute College of Pharmacy & Research Center, Devad-Vichumbe, Tal. Panvel, Dist. Raigad, Email id: shendgesandhya@gmail.com

INTRODUCTION: Cancer is a large, heterogeneous class of disease in which group of cell display uncontrolled growth and destroy adjacent tissue. DNA replication is important process of a cell division. The key enzyme Rib nucleotide reeducates (RR) converts building blocks of RNA into those of DNA in a critical step of DNA synthesis due to this pivotal role, the activity of Rib nucleotide reeducates is tightly linked, much more than any other enzyme to cancerous growth. Electrotherapy uses low level electric current to treat the cancer by neutralization of free radical which is essential for activity of RR.

OBJECTIVE: A novel way of arresting the activity pivotal enzyme i.e. Rib nucleotide reeducates in cell growth by fact that the active site of RR contains a free radical which is essential for activity.
METHOD: GEIPE-RR (Gentle electrotherapy to inhibit a pivotal enzyme-Rib nucleotide reductases) selectively target the malignant cells where concentration of enzyme RR is exponentially higher. Treatment can be offered in two modalities:
1. Noninvasive GEIPE therapy: low level of current pass from GEIPE device after placing surface of electrode near the tumor.
2. Semi-invasive GEIPE therapy: Here similar low level of current passes from GEIPE device after placing surface of electrode away from the tumor.

RESULT: This is a non-toxic, low-cost and highly effective cancer therapy called as “the most scientific” and this therapy blocks the most critical enzyme for cell growth i.e. RR to have an effect on proliferating cancer cells.

DISCUSSION: Recently, Angiogenesis-based tumor therapy was hailed as a major advance. Initial Electrotherapy can be considered as a promising approach; however it needs to be studied extensively.

CONCLUSION: As a recent human trial has shown promising results, further exploration of such an inexpensive and effective therapy is highly recommended.

KEY WORDS: “Rib nucleotide reductase (RR), Free radical, Angiogenesis-based tumor therapy.”

REFERENCE:

15. PHOTODYNAMIC THERAPY—AN NOVEL APPROACH TO COMBAT CANCER
HAK D., RASKAR A., KOLAMBKAR D., Shri. D. D. Vispute College of Pharmacy & Research Center, Devad-Vichumbe, Tal. Panvel, Dist. Raigad, Email id: dollyhake@gmail.com

OBJECTIVE: Combination of a drug (photosensitizer or photosensitizing agent) with a specific type of light to kill cancer cells.

INTRODUCTION: Cancer is a disease characterized by abnormal and uncontrolled division of cells that then invade and destroy the surrounding tissues. PDT is a non-thermal light chemical reaction and need oxygen, photosensitive substance (photo-sensitizer) and laser simultaneously. Photo-sensitizer is absorbed by neoplasm tissue and accumulates in the cells for a long
time. Photo-sensitizer is activated with the appropriate wavelength of light and reacts with oxygen to generate reactive single state oxygen and photochemical substance that are toxic to cells leads to apoptosis and necrosis of cancer. PDT is of interest for organs, including the brain, bronchial system, and intestine that must retain microscopic tissue structure to maintain functionality. The photoactive substance is more enriched in the tumor than in the surrounding tissue because of the higher metabolic activity, more permeable vessels, and lower lymphatic drain of the tumor. The common malignant childhood tumor retinoblastoma (RB) is treated by photocoagulation.

PDT METHODOLOGY: Photosensitizer (Photofrin, porfimer sodium), 2mg/kg, is administrated intravenously. 48 hours after photosensitizer administration, 630-nm red laser light is delivered through optic cables (thin fibers that transmit light) to deliver light to areas inside the body. The light used for PDT can come from a laser or other sources of light. The total light dose administered ranges from 20 to 30 J/sq.cm. The light irritation is often repeated 72 hours after photosensitizer administration. The delivery of laser fiber may be through endoscopes, such as gastrointestinal endoscope (for esophageal or gastric cancer) or bronchendoscope (for lung cancer).

CONCLUSION:

PDT is relatively selective and specific for tumorous cells and does not cause immunosuppression. Additionally, when combined with other therapies (chemo/radiotherapies); they have a complementary effect. Also, it has short treatment time and efficacy occurs within 48-72 hours.

KEY WORDS: “Photo-sensitizer, apoptosis, necrosis”.

REFERENCE:


16. MICROWAVE ASSISTED SYNTHESIS OF SOME BENZIMIDAZOLE ERIVATIVES AND BIOLOGICAL EVALUATION FOR ANTICANCER ACTIVITY

Kankate R.S¹, Gide P.S², Belsare D.⁴, Addresses: ¹For correspondence Lecturer, ²MET’s Institute of Pharmacy, Bhujbal Knowledge City, Adgaon, Nasik - 422 003 Contact No. 95030 58875, Kankate_rani@yahoo.co.in, ³Principal, MET’s Institute of Pharmacy, Bhujbal Knowledge City, Adgaon, Nasik - 422 003, Contact No. 95030 58875, ⁴Asst.professor, Department of Pharmaceutical Chemistry, NDMVP’S College of Pharmacy, Gangapur Road, Nashik - 422 002.Contact No.9423174015
**ABSTRACT:** The emerging area of green chemistry envisages minimum hazard as the performance criteria while designing new chemical processes, one of the thrust areas for achieving the target is to explore alternative reaction condition and the media to accomplish the desired chemical transformation with minimized by products or waste as well as eliminates the use of conventional organic solvents. If possible among the important tools the use of microwaves (MW) as an energy source is becoming an attractive alternative. Although benzimidazole compounds have proven active against various cancers, there are recent reports on their combinatorial use with platinum’s to treat cancer. Platinum’s are chemotherapeutic drugs consisting of platinum (II) complexed with various donor ligands. Cisplatin (cis-diamminedichloroplatinum(II)) is one of the platinum’s that has gained worldwide popularity since 1970s. Cisplatin (cis-diamminedichloroplatinum(II)) is a widely used chemotherapeutic agent for the treatment of testicular cancer and it is used in combination regimens for a variety of other tumors, including ovarian, cervical, bladder, lung and those of the head and neck. Despite the success of cisplatin, problems regarding intrinsic or acquired resistance and side effects have encouraged the development of new platinum drugs. Therefore we turned to synthesize various substituted 2-α-hydroxybenzylbenzimidazol derivatives and decided to screen them for anticancer activity.

DL-mandelic acid 2.28 g (15 mmol.) and 1,2- phenylenediamine (4-substituted derivative) 1.08 g (10 mmol) were dissolved in 10 ml 4 N hydrochloric acid and kept in microwave oven for 15 min. The reaction mixture was then allowed to cool to room temperature and placed in a refrigerator (5 °C) for 1 h. A white precipitate, formed, was filtered off and then dissolved in 25 ml water. The clear solution was neutralized with a solution of 20% aqueous solution of K2CO3 and a white precipitate which formed was filtered off. To a stirred solution of substituted 2-α-hydroxybenzylbenzimidazol (0.45 g, 2 mmol) in 0.5 N HCl (10 ml) was added a solution of K2PtCl4 (0.415 g, 1 mmol) in 0.5 N HCl (10 ml) drop wise over 2 h at room temperature. The complexes were characterized by elemental analysis, mass, infrared (IR) and 1HNMR spectra.

**17. MICROWAVE ASSISTED SYNTHESIS OF PLATINATE II COMPLEX OF SUBSTITUTED 2-PYRIDYL BENZIMIDAZOL AND BIOLOGICAL EVALUATION FOR ANTICANCER ACTIVITY**

Chaudhari B.N1, Kankate R.S2, Gide P.S3, Belsare D.P4, Addresses: *For correspondence, M. Pharm. Student, 1MET’s Institute of Pharmacy, Bhujbal Knowledge City, Adgaon, Nasik - 422 003, Contact No. 95797 24272, bhavinnchudhari@gmail.com

Lecturer, 2MET’s Institute of Pharmacy, Bhujbal Knowledge City, Adgaon, Nasik - 422 003, Contact No. 95030 58875, kankate_rani@yahoo.co.in

3Principal, MET’s Institute of Pharmacy, Bhujbal Knowledge City, Adgaon, Nasik - 422 003, Contact No. 95030 58875

4Asst.professor, Department of Pharmaceutical Chemistry, NDMVP’S College of Pharmacy, Gangapur road, Nashik - 422 002, Contact No.94231 74015

**OBJECTIVE:** The object of the research was to synthesize various 2(2-pyridyl) benzimidazole derivatives and their complexation with platinum II metal and evaluation of the resulting compound for anticancer activity.
ABSTRACT: Medicinal chemistry is dealing with synthesis of new compound. Synthesis of organic compound is critical one. So the main task for the researcher in this field always remained for the development of the chemical entities which are better than the existing one and to synthesis them by developing economical and less time consuming procedure. For this problem we have to overcome by using microwave assisted synthesis. The area of green chemistry is one of the thrust area in developing the ecofriendly synthetic routes for various chemical entities which aims to perform the chemical transformation with minimum usage of toxic solvents and with minimum generation of hazardous wastes. The ability of benzimidazole and its derivatives to form complexes with transition metals has been widely reported in literature. Studies performed on the complexes of this nature have confirmed a wide variety of biological properties associated with them. These include, cytotoxicity, antiviral, antiamoebic, antimicrobial and DNA cleaving properties. In the present study we condensed the o-phenylenediamine derivative with the pyridine-2-carboxylic acid in presence of HCl gave the 2-(2-pyridyl)-1H-benzimidazole derivative series which were found to possess anti-cancer activity. In an attempt to further enhance the anticancer activity the complexation of the said derivative was done with platinum-II metal. Of utmost importance is the steric hindered environment provided by these ligands, which reduces the ease of replacement by sulfur containing molecules in the cell. The complexes were characterized by elemental analysis, mass, infrared (IR) and 1HNMR spectra.

18. MicroRNA- A PROGNOSTIC AND THERAPEUTIC TOOL IN CANCER
Ramakrishnan, A., Radhakrishnan. R., Vivekanand Education Society’s College Of Pharmacy, Hashu Advani Memorial Complex, Chembur (E), Mumbai - 400 074,
Email ID: ashokpicasso91@yahoo.com

ABSTRACT:

OBJECTIVE: Use of MicroRNA as potential biomarker and its therapeutic application in cancer.

INTRODUCTION: MicroRNAs are a family of endogenous, small (approximately 22 nucleotides in length), noncoding functional RNAs [1]. They regulate gene expression post-transcriptionally. MicroRNAs play a key role in diverse biological processes, including development, cell proliferation, differentiation, and apoptosis. Up to 30% of human protein coding genes may be regulated by miRNAs. This makes miRNAs one of the most abundant classes of regulatory genes in humans [3]. MicroRNAs play a potential role in human cancer. They serve as important biomarkers in diseased states. Recently, they have been explored as a target for therapy.

EXPERIMENTAL METHODS: MicroRNAs as Biomarkers: MicroRNAs (miR) have been used as biomarkers for detection of cancers of breast, hepatocellular, colo-rectum, lungs, and pancreas, prostate and chronic lymphocytic leukemia. Their production or expression of MicroRNA gene might be up- or down-regulated in a tumor [1][2].For example, in breast cancer, up-regulation of miR-373 and miR-520c promotes metastasis by inhibiting CD44 expression. Increased expression of the CD44 isoform 'CD44s' is associated with overall survival in breast cancer patients. On the other hand, a MicroRNA miR-91, has been found to be down-regulated in breast cancer [1][6].
**MicroRNAs as Target Sites and Therapeutic Agents:** Regulatory RNAs may also have therapeutic applications by which disease-causing miRNAs could be antagonized or functional miRNAs restored. The most intuitive choice of molecules to correct altered miRNA–messenger RNA interactions is RNA oligonucleotides. For example: Modified cholesterol-conjugated antisense RNAs designated “antagomirs” could effectively inhibit miRNA function in vivo in the adult mouse [2]. In other studies, synthetic miRNAs were prepared to target overexpressed tumor proteins, such as HER-2 protein in ovarian cancer cells which were effective[2]. Therapeutic delivery of miR-26a suppressed tumor genesis in mice [5].

**RESULTS & DISCUSSION:** MicroRNAs are present in bodily fluids and represent useful clinical biomarkers. Reliable methods have been developed for extracting microRNAs from bodily fluids and for evaluating their abundance. They can also act as sites for targeting using modified antisense RNA oligonucleotides. One limitation of antisense RNA therapies is the restricted number of cells that can be targeted.

**CONCLUSION:** miRNAs promise to have an impact on laboratory medicine as new diagnostic and prognostic markers, as indicators of therapeutic response, and as targets of novel therapies. The applications of microarray, microfluidics, Nano fluidics, qRT-PCR and bioinformatics have enabled the discoveries of a number of circulating miRNAs as potential biomarkers for cancer prognosis and therapy [4].

**KEY WORDS:** Post-transcriptionally, apoptosis, biomarkers, antisense RNA oligonucleotides, microarray, microfluidics, Nano fluidics, bioinformatics.

**REFERENCES:**


**19. ENZYME-PRODRUG DIRECTED THERAPY FOR COLON CANCER**

Dr. Somani R.R., Pandey S., Ramakrishnan. A., Vivekanand Education Society’s College Of Pharmacy, Hashu Advani Memorial Complex, Chembur (E), Mumbai-400074, Email ID: pandeyswasti@yahoo.com

**ABSTRACT:**

**OBJECTIVES:** Use of Enzyme-Prodrugs directed therapeutic approaches for colon or colorectal cancer.

**INTRODUCTION:** Colorectal cancer is one of the leading causes of cancer-related deaths worldwide. Surgical resection is the only curative option in this situation, but fewer than 10% of patients are candidates for surgery because of multi facility and/or the extent of the disease. The results of other treatments, in particular radiotherapy, immunotherapy and
systemic chemotherapy have failed to provide curative potential. Thus, novel therapeutic strategies such as Enzyme-Prodrugs Directed Therapies are in the process of development.

**EXPERIMENTAL METHODS:** 5-Fluorouracil [5-FU] is one of the most active chemotherapeutic agents known for the treatment of colorectal cancer. However, the efficacy of systemic treatment with 5-FU is limited by gastrointestinal and hematological toxicity [1]. To circumvent this systemic toxicity and to increase tumor selectivity, the development of enzyme-pro drug therapies are useful. The various strategies under it are as follows:

*Antibody-Directed Enzyme Prodrug Therapy (ADEPT)*
An antibody directed against a tumor-associated antigen is linked to an enzyme and given i. v., resulting in selective accumulation of the enzyme in the tumor. When the discrimination between tumor and normal tissue enzyme levels is sufficient, a pro drug is given i. v., which is converted to an active cytotoxic drug by the enzyme within the tumor. Selectivity is achieved by the tumor specificity of the antibody and by delaying pro drug administration until there is a large differential between tumor and normal tissue enzyme levels [2] [3] [4]. The gpA33 antigen is a promising target for ADEPT in colon cancer, as it is expressed by >95% of human colon cancers, but is absent in all non-gastrointestinal tissues. Designing of a recombinant fusion construct of a phage display-generated anti-gpA33 single chain fragment with cytosine deaminase (CD) from yeast, which converts 5-fluorocytosine (5-FC) into 5-fluorouracil (5-FU) has proven to show toxicity in mice bearing colon cancer [5].

*Gene-Directed Enzyme Prodrug Therapy (GDEPT) or Suicide Gene Therapy*
This includes delivery of a gene that encodes for the enzyme which activates a specific pro drug to create toxic products [1][4][6][7]. In colorectal cancer the CD gene that encodes for cytosine deaminase enzyme, can be introduced either by Physical methods: Development and use of nanoparticles like calcium phosphate nanoparticles (CPNP) for safe and efficient gene delivery [8]. Viral vectors method [4]: Using viral vectors such as Vaccine virus [9], lent virus [7] and adenovirus [6].

**RESULTS & DISCUSSION:**

*GDEPT:* The most important characteristic of suicide gene therapy is its bystander effect. Although the viral or non-viral gene delivery systems currently available have poor efficacy for in vivo gene transfer, complete eradication of tumors has been seen in some experimental animal models, which is thought to depend on the bystander killing effect. The limiting factors for successful suicide GDEPT is transfection efficiency [6][7].

*ADEPT:* This therapy has demonstrated anti-cancer effect characterized by selective localization [2][3].

**CONCLUSION:** ADEPT and GDEPT have proved to be effective in animal models. However further more studies conducted in in vivo animal models are necessary to demonstrate the anti-cancer potentiality of such strategy characterized by selective delivery of inert pro drug into potent anti-tumor agent [3][5].

**KEYWORDS:** Colorectal cancer, radiotherapy, immunotherapy, chemotherapy, antibody, pro drug, nanoparticles.
REFERENCES:

20. NEW ANTICANCER AGENTS AND THERAPEUTIC STRATEGIES IN DEVELOPMENT OF SOLID CANCER: CLINICAL PERSPECTIVE

[1] Vivekanand Education Society's College of Pharmacy, Mumbai, India, [2] Bombay College of Pharmacy, Mumbai, India, Email: singh.ruchi69@gmail.com

KEYWORDS: Novel cytotoxic agents, epothilone compounds, farnesyl transferase case in addition to well-known chemotherapeutic agents used in the treatment of solid cancer, promising novel cytotoxic agents are being investigated. Advances in cancer biology over the last decade and a half have uncovered numerous genetic and epigenetic alterations that induce and/or promote oncogenes and cancer progression by activating oncogenes and/or inactivating tumor suppressor. The completion human genome sequence project and the enormous progress made on the human cancer genome anatomy project have laid solid foundations for the applications of tools from the burgeoning fields of genomics (i.e., DNA microarrays, siRNA), proteomics, and bioinformatics for the rapid identification and validation of novel cancer molecular targets. It is now possible to go from gene to target in a short span of time, as shown recently by the use of bioinformatics tools in mining the expressed sequence tags (ESTs) in the human cancer genome anatomy database to identify and validate a novel potential solid. Among them are analogs of existing cytotoxic agents, aimed at improving the therapeutic index, and new families such as epothilone compounds. Agents that target the tyrosine kinase dependent pathways, farnesyl transferase modulators, Raf kinase inhibitors, antisense molecules to Bcl-2 and proteasome modulators, agents that bind to key proteins involved in critical phases of cell cycle, as well as anti angiogenesis strategies, are all promising approaches in the treatment of solid cancer. The combination of cytotoxic, hormonal agents and radiotherapy with new molecular targeted therapies represents one of the main strategies to improve survival in solid cancers. A clinical perspective of these agents as monotherapy or chemotherapy will be presented in this poster.

CONCLUSION: In the near future, the major challenges will be their integration into existing treatment modalities of metastatic solid tumors, and ultimately their move to the adjuvant setting. The scope of potential opportunities to improve patient care is rapidly advancing. As an example gene and protein arrays, automated immunostaining and other molecular biological techniques and finding will permit more efficient individualization of tumor in near future, which will hopefully lead to discovery of critical targets in cancer cells and consequently the development of inhibitors with better therapeutic index. The main aim of
these combinations is to obtain a synergistic or additive effect and to prevent or delay the appearance of resistant cancer cells. The key issues in the clinical development of these novel agents (cytotoxic and molecular targeted therapies) are the documentation of the optimal dose, schedule and sequence, as well as any pharmacokinetic interaction.

**REFERENCE:**
1) Novel anticancer agents in clinical development: Adjei A. A., Rowinsky E.K.
2) New Anticancer Agents and Therapeutic Strategies in Development of Solid Cancer: Clinical Perspective: Ahmad Awada, Alain Helendliz and, Artin Piccard

**21. ERYTHROCYTE-MEMBRANE CAMOFLAGGED POLYMERIC NANOPARTICLES AS A BIOMIMETIC DELIVERY PLATFORM**

Authors: Anaita L., Jessica D., Tanaya B., Affiliations: Vivekananda Education Society’s College of Pharmacy, Email: anaita_92@rediffmail.com

**KEYWORDS:** “Biomimetic nanoparticle, long circulation, PLGA nanoparticle”

**ABSTRACT:** Efforts to extend nanoparticle residence time in vivo have inspired many strategies in particle surface modifications to bypass macrophage uptake and systemic clearance. Here we report a top-down biomimetic approach in particle functionalization by coating biodegradable polymeric nanoparticles with natural erythrocyte membranes, including both membrane lipids and associated membrane proteins for long-circulating cargo delivery. Nanoparticles can be modeled after RBCs, which are nature’s long circulating delivery vehicles. We herein develop an RBC-membrane-camouflaged polymeric nanoparticle. By extruding polylactic-co-glycolic acid (PLGA) particles with preformed RBC membrane-derived vesicles, we coat the sub-100-nm polymeric particles with the bilayered RBC membranes including both lipids and the corresponding surface proteins. This approach aims to camouflage the nanoparticle surface with the erythrocyte exterior for long circulation while retaining the applicability of the polymeric core. The preparation process of the RBC-membrane-coated nanoparticles is divided into two parts: membrane vesicle derivation from RBCs and vesicle-particle fusion. Briefly, RBCs were first purified from the fresh blood of male Imprinting Control Region (ICR) mice (6-8 week) by centrifugation and PBS wash. The resulting PLGA nanoparticles were subsequently fused with the RBC-membrane-derived vesicles through mechanical extrusion. The bilayer structure of the RBC membranes is retained throughout the entire preparation process to minimize the loss of and damages to the membrane protein. The RBC-membrane-coated nanoparticles have longer elimination half-life, which suggests that the RBC-membrane coating is superior in retarding in vivo clearance compared to the conventional PEG stealth coating.

**CONCLUSION:** The adopted technique aims to fabricate cell-mimicking nanoparticles that bypass the labor-intensive processes of protein identifications, purifications, and conjugations. The proposed method also provides a bilayered medium for trans-membrane protein anchorage and avoids chemical modifications that could compromise the integrity and functionalities of target proteins. The lipid layer is derived directly from the natural RBCs collected from the host blood; they are expected to stimulate negligible immune response after they are Trans located to the surface of polymeric nanoparticles. The translocation of natural cellular membranes and their associated functionalities to the particle surface represents a unique and robust top-down approach in nanoparticle functionalization.
REFERENCES:
1) Liang fang Zhang, et al., Erythrocyte membrane-camouflaged polymeric nanoparticles as a biomimetic delivery platform, *PNAS*, June 20, 2011

22. ONCOLYTIC VIRUS THERAPY (GENETICS)
Anjana Viswanathan, Bhagyashree Utekar, Shruti Surendran Shri. D. D. Vispute College of Pharmacy and Research Centre; New Panvel - 401 206
Email id: aj_v@in.com; bhagyashreeutekar12@gmail.com; shrutisu1@gmail.com

ABSTRACT: The objective of this paper was to review a new category of gene therapy using oncolytic viruses for the treatment of cancer. The eligibility and feasibility of oncolytic virus therapy as a novel therapeutic agent against cancer are discussed as well as basic research for clinical trials, including a historical perspective and the current status of these novel agents. Even combination therapy, such as surgery with radiation and chemotherapy, has not significantly improved the survival rate of cancer. Radiation damages skin, mouth, throat and bowel cells, and can lead to fatigue, nausea, and permanent hair loss. On the other hand chemotherapy can produce hearing loss and damage to a number of organs, including the heart and kidneys. Oncolytic virus therapy is not a new concept, but recent technical advances in the genetic modification of Oncolytic viruses have improved their tumor specificity, leading to the development of new weapons for the war against cancer. Oncolytic viruses have been genetically engineered to target specific molecules or signal transduction pathways in cancer cells in order to achieve efficient and selective replication. The nature of viral delivery, infection, and replication makes Oncolytic virus therapy useful for treating cancer patients, especially those with inoperable tumors. Oncolytic virus therapy targets cancer cells to achieve a strong catalytic effect. Oncolytic virus infections are believed to induce tumor cell death in three main ways. In the first instance (i), viruses infect and replicate in malignant cells, (ii) may induce apoptotic induction, followed by (iii) cell lyses and the expulsion of numerous progeny viral particles. This can subsequently infect additional surrounding malignant cells, thereby enabling further lytic destruction within the tumor micro-environment.

Mechanism of antitumoral efficacy of Oncolytic viruses:

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Direct cell lysis due to viral replication</td>
<td>Adenoviruses Herpes simplex viruses</td>
</tr>
<tr>
<td>2. Direct cytotoxicity of viral protein</td>
<td>Adenovirus E4ORF4</td>
</tr>
<tr>
<td>4. Sensitization to chemotherapy and radiation therapy</td>
<td>Adenovirus (E1A)</td>
</tr>
<tr>
<td></td>
<td>Adenovirus (AdTK-RC)</td>
</tr>
<tr>
<td>5. Transgene expression</td>
<td>Herpes simplex virus (rRp450)</td>
</tr>
<tr>
<td></td>
<td>Vaccinia virus (GM-CSF)</td>
</tr>
</tbody>
</table>
Under the right circumstances, viruses are capable of targeting and destroying cancer cells in human cancer patients. Cancer gene therapy is a rapidly maturing field which will be a part of future cancer therapies. Many of past obstacles and barriers are being actively overcome now. With the advent of genetic engineering and biotechnology, a wide range of viruses are being manipulated and evaluated in various types of cancers. Significant active research is being done to improve the accessibility, safety and efficacy of Oncolytic virus therapy. Recent advances in molecular biology, and other large-scale genome modification tools, have made it possible that newer Oncolytic virus will be heavily engineered non-viral intracellular parasites, unrecognizable synthetic hybrid vectors, or still yet unforeseen large-scale gene delivery systems.

**KEYWORDS:** “Apoptotic induction, Oncolytic virus, Adenovirus, Herpes simplex virus”

**REFERENCES:**

**23. NANOSHELLS - A GIFT IN GOLD WRAPPER FOR TRATMENT OF CANCER**
Harkal Kailas M., Kandharkar Kaustubh V., Biradar Jalappa D. Nanded pharmacy College, Nanded, **E mails:** kmharkal@gmail.com, kaustubh.kandharkar@gmail.com, jalapabiradar@gmail.com
OBJECTIVE: The objective of present study is use of Nano shells to create high-resolution images of tumors as well as a precise treatment procedure that cause cell death in tumors. Gold is the material of choice because it is dense and opaque to X-rays.

INTRODUCTION: Nano shells particles constitute a special class of Nano composite materials. They consist of concentric particles in which particles of one material are coated with a thin layer of another material. Nano shells can be engineered to target cancerous cells and at the same time designed to interact with specific wavelengths of light, Nano shells can either scatter or absorb light, creating applications as both a cancer imaging agent and therapeutic one.

Gold Nano shell design: Nano shells can come in many shapes and sizes. All are composed of a core and a shell. In case of gold Nano shell the core is a ball of silica and the shell is a thin layer of gold.

Gold Nano shell immune targeting: Billions of gold Nano shells are injected into the blood stream and begin to travel through the body’s blood stream. Nano shells are coated with polyethylene glycol for short which allows them to circulate in the blood stream without being targeted for removal. This allows the Nano shells to travel in the blood stream longer increasing the chance they come across cancer cells.

Applications:
- Used in photo thermal therapy
- Used in imaging study
- Biosensing
CONCLUSION: These particles are used in imaging cancer cells and other therapeutic applications. Gold Nano shells are fast becoming the forerunner of other Nano medicine technologies. The environmental friendly biocompatible aspect of Nano shells enables a broad range of applications.

REFERENCES:
Current science, vol.91, no.8, October 2006. Page no. 126
http://www.nanotech.net
http://www.nanoed.org/aunanoshells

24. A REVIEW ON AN IMMORTAL CANCER CELL LINE- HELA
Sridhar, V., Anand, R., Vivekanand Education Society’s College of Pharmacy, Hashu Advani Memorial Complex, Behind Collector Colony, Chembur, Mumbai - 400 074
E-mail: ramalakshianand@gmail.com

KEY WORDS: “Human Cancer cell lines, HeLa, Research applications”

INTRODUCTION: For decades, human immortal cancer cell lines have constituted an accessible, easily usable set of biological models to investigate cancer biology and to explore the potential efficacy of anticancer drugs. HeLa, a epithelial cell line derived from the cervix of a patient, Henrietta Lacks in 1951, was the first human cell line to prove successful in vitro, which was a scientific achievement. This cell line has been used not only in research studies on cancer but also in a variety of other studies. We present some interesting facts about this cell line and also a few interesting studies which have been carried out using this cell line.

DISCUSSION: HeLa cells are epithelial cells derived from cervical cancer cells were successfully grown in the laboratory by a scientist George Otto Gay at a time when the technique of growing cells in vitro was in its developing stage. These were the very first cell lines to survive and grow outside the human body. These cells were found to be immortal, i.e. they were capable of dividing continuously, if provided with proper conditions. HeLa cells have an active version of telomerase which prevents shortening of telomeres and hence aging and death. After over 20 years of using HeLa cells, there was mounting evidence to suggest that HeLa cells overgrew and contaminated other cell lines. HeLa cell line has been used in a variety of studies. Some of the interesting ones include:

1. Synergistic Enhancement of Cancer Therapy using a Combination of Carbon Nanotubes and Anti-tumor Drug
2. Detection of DNA Damage induced by Space Radiation in Mir and Space Shuttle
3. Studies involving poliomyelitis virus and HeLa cell cultures.
4. Study on shigella toxin binding glycolipid from HeLa cells

The above are just a few examples from innumerable studies which have been carried out using HeLa cell line.
**CONCLUSION:** HeLa cell culturing was a path breaking achievement because they were the first human cells to be cultured outside the body. These cells have been useful in carrying out many studies, some of which may have been difficult to carry out without in-vitro cell cultures.

**REFERENCES:**

---

**25. DNA AS AN EVOLVING TARGET FOR CANCER THERAPY**
Aniketh R., Ruchi S., Vivekanand Education Society’s College of Pharmacy, Mumbai, India
EMAIL: singh.ruchi69@gmail.com

**KEY WORDS:** DNA targeted chemotherapeutic agents, DNA is the molecular target for many of the drugs that are used in cancer therapeutics, and is viewed as a non-specific target of cytotoxic agents. Although this is true for traditional chemotherapy, other agents that were discovered more recently have shown enhanced efficacy. Furthermore, new generation of agents that target DNA-associated processes are anticipated to be far more specific and effective. Anticancer agents that target DNA are some of the most effective agents in clinical use and have produced significant increases in the survival of cancer patients when used in combination with drugs that have different mechanisms of action. But, unfortunately, they are extremely toxic Consequently, much effort has been put into finding agents that are more selective, and there is considerable excitement that the identification of cancer-specific molecular targets will yield a new generation of less toxic therapeutics; indeed, STI-571 (Gleevec), which targets the ABL (Abelson leukemia viral oncogene) kinase in patients with chronic myelogenous leukemia, is the forerunner of this new generation of compounds.

Table 1 shows DNA targeted drugs that are used or are in trial for treatment of cancer.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Clinical use</th>
<th>Mechanism of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Neuroblastoma; non-Hodgkin's lymphoma; retinoblastoma; breast cancer; small-cell lung cancer</td>
<td>Interstrand DNA cross linker</td>
</tr>
<tr>
<td>Melphalan</td>
<td>Multiple myeloma</td>
<td>Interstrand DNA cross linker</td>
</tr>
<tr>
<td>Mitomycin C</td>
<td>Stomach and gastrointestinal tract cancer</td>
<td>Interstrand DNA cross linker</td>
</tr>
<tr>
<td>Bizelesin</td>
<td>Phase I clinical trials</td>
<td>Interstrand DNA cross linker</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Testicular cancer; ovarian cancer; head and neck cancer</td>
<td>Interstrand DNA cross linker</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Rhabdomyosarcoma; breast cancer; adult acute leukaemia; complex endometrial cancer; stomach cancer; cervical cancer; non-Hodgkin’s lymphoma</td>
<td>Stabilizes topoisomerase-II–DNA cleavable complex</td>
</tr>
<tr>
<td>Etoposide</td>
<td>Testicular cancer; small-cell lung cancer</td>
<td>Stabilizes topoisomerase-II–DNA cleavable complex</td>
</tr>
</tbody>
</table>
CONCLUSION: The observation that some of the earliest cancer chemotherapeutic agents were DNA-targeted agents and the reality that these compounds are still in use should be considered as a positive attribute, not as a negative connotation. It is true that these agents have associated toxicities, but now with more sophisticated approaches to gene targeting - we do not need to wreck the train to derail a troublesome carriage; instead, we can employ an engineer to uncouple and sideline this carriage without damaging the rest of the train. For many of the newer targeted therapeutics that are in development for the treatment of cancer, it is expected that they will be used in combination with the more traditional agents, such as cisplatin, doxorubicin or SN-38. This is particularly true with chemotherapy of later-stage tumors, in which there are many genetic abnormalities and hitting a single target might not be sufficient to cause a response when used alone. In combination with a DNA-interactive drug, however, the chemotherapeutic agent might have considerably enhanced clinical efficacy. The future challenge will be to pair these agents appropriately in a pre-determined way on the basis of firm scientific principles. It is not yet clear how this rational pairing will be achieved. The complexities of interacting cell signaling pathways make this a daunting proposition. Conceivably, the newer tools from genomics and proteomics will provide the solution. Most importantly, DNA should no longer be considered as just a nucleophilic sink for reactive alkylating agents, but as a true molecular receptor that has cognitive (molecular recognition) features and response elements like many signaling molecules which transmit signals through protein interactions. We can already design and synthesize molecules that read DNA sequence information, and we are starting to appreciate the molecular consequences of specific binding interactions. We have certainly not seen the last of DNA as a molecular target for cancer therapeutics, but we are only just beginning to appreciate its real identity as a true Cinderella.

REFERENCES:
1) DNA and its associated processes as targets for cancer therapy: Laurence h. Hurley

26. HEPATIC ARTERIAL CHEMOEMBOLIZATION
Mittal Swati, Degweker .M.D., Naik .A.M., Pandey S.B., Vivekanand Education Society’s College of Pharmacy, Mumbai, India, VES College of Pharmacy, Chembur, Mumbai
Email: pandeyswasti@yahoo.com

ABSTRACT: Intra-arterial chemotherapy is used in liver cancer due to its unique blood supply. The liver has dual blood supply, from portal vein and hepatic artery. The normal liver receives 75% of blood flow supply from the portal vein and 25% of blood flow from hepatic artery. Hepatic tumors receive 90% of blood supply from hepatic artery. Thus the delivery of chemotherapeutic agents directly into the hepatic arterial system reaches the tumor sparing normal liver parenchyma. Drug delivery via hepatic artery allows higher doses of chemotherapeutic agents delivered to liver cancer, while minimizing systemic side.

Hepatic Trans arterial Embolization (TAE) : It involves radiographic placement of a percutaneous catheter into the hepatic artery, followed by an injection of embolizing substance that occludes the arterial blood flow at the tumor capillary level, thus producing
tumor ischemia. Various embolizing agents that have been administered include ethibloc, gelfoam cubes, ivalon particles etc. Embolization may be temporary or permanent. Steel coils and ivalon particles cause permanent occlusion and gelatin sponge particles, degradable starch result in temporary occlusion. A temporary occlusion can allow subsequent intra-arterial treatment after the vessel opens. Embolization is preferred over hepatic artery ligation since it is non-surgical procedure and associated with fewer collateral arteries. Different localized treatment approaches will continue to be applied in the management of this disease. Organ or site-specific drug delivery has several distinct advantages over other means of delivering drugs. Targeting organs or tissues in-vivo can greatly reduce the risk of toxic side effects and significantly increase the efficacy of a variety of drugs. Thus the significance of intra-arterial chemotherapy could be further improved by combining it with embolization. Hepatic artery chemoembolization represents an alternative treatment for patients whose neoplastic lesions are not amenable or have become refractory to other treatment modalities. Chemoembolization works in three ways

i. Chemotherapy is delivered directly to tumor and doesn't spread throughout the body hence higher doses of chemotherapeutic agents can be administered compared to doses used for systemic chemotherapy.

ii. Tiny particles embolize or block the artery and decrease the flow of blood to the tumor causing it to shrink.

iii. By blocking the artery, the particles help in keeping chemotherapeutic agent indirect contact of the tumor for a prolonged period of time.

Chemotherapeutic Agents and Embolizing Agents: In clinical studies mitomycin, doxorubicin and cisplatin are regarded as suitable cytostatics in the chemoembolization of liver tumors. Current embolization materials in clinical use include steel coils, polyvinyl alcohol particles (ivalon), degradable starch microspheres (DSM) and gelfoam particles. After temporary embolization using gelfoam or DSM the blood vessel may recanalize thus reestablishing the normal blood supply.

REFERENCES:
- Breedis C. and Young G.; “The blood supply of neoplasms in the liver”; Am. J. Pathol; 1954; 30; 969-985.
27. NANOTECHNOLOGY IN CANCER

Rasam Siddhi, Gupte Somesh, Gugnani Kuljeet Singh., Vivekanand Education Society's College of Pharmacy, Mumbai - 400 074,

Email id of the presenting author: someshgupte@yahoo.com

KEY WORDS: “Nanotechnology, Nano cantilevers, Nano shells, Nano SIMS, TNF, Auro shell, liposomes, NBTXR3”.

ABSTRACT: Nanotechnology is the development and engineering of devices so small that they are measured on a molecular scale. The use of Nanotechnology in cancer treatment offers some exciting possibilities, including the possibility of destroying cancer tumors with minimal damage to healthy tissue and organs, as well as the detection and elimination of cancer cells before they form tumors. Most efforts to improve cancer treatment through Nanotechnology are at the research or development stage. However, the effort to make these treatments a reality is highly focused. Nanotechnology offers the unprecedented and paradigm-changing opportunity to study and interact with normal and cancer cells in real time, at the molecular and cellular scales, and during the earliest stages of the cancer process. Through the concerted development of Nano scale devices or devices with Nano scale materials and components will facilitate integration within the existing cancer research infrastructure. The necessary tools for detection and elimination of such cancerous tumors. Use of Nano Cantilevers which are microscopic, flexible beams resembling a row of diving boards - are built using semiconductor lithographic techniques which are only used to provide rapid and sensitive detection of cancer-related molecules. Another application of Nano technology to detect cancer is use of Nano SIMS which employs a multi-collection detection system to allow for detection of seven different masses simultaneously. Another method to detect cancer by nanotechnology in clinical research is using Nano shells. A Nano shells is a type of spherical Nanoparticle consisting of a dielectric core which is covered by a thin metallic shell. Because of their size, Nano shells will preferentially concentrate in cancer lesion sites. Iron oxide Nanoparticles can be used to improve MRI images of cancer tumors which thus prove another method for detection of cancer. The first Nanotechnology-based cancer drugs have passed regulatory scrutiny and are already on the market including Doxil and Abraxane. The treatment of cancer using Nanotechnology has widened to scope of Nanotechnology to unextendable limits. Various clinical and preclinical trials have been conducted and proved showing positive results with minimal damage to other healthy body tissues. One of these includes tumor Necrosis factor Alpha (TNF). Attached to a gold Nanoparticle along with Thiol-Derivatized Polyethylene Glycol (PEG-THIOL). Hide the Nanoparticles from the immune system. Another heat therapy to destroy cancer tumors using Nanoparticles is called Auro shell an intriguing targeted chemotherapy method uses on Nanoparticle to deliver the chemotherapy drug and a separate Nanoparticle to deliver the chemotherapy drug and a separate Nanoparticle to guide the drug carrier to the tumor this Nanoparticle is usually a liposome. Using polymer Nanoparticles to deliver a molecule called JSI-124 to cancer tumors. This molecule degrades the ability of the cancer cells to suppress the immune system, possibly slowing the growth of cancer tumors, Nanoparticles-based therapeutics have been successfully delivered into tumors by exploiting the enhanced permeability and retention effect. A property that permits Nano Scale structure to be taken up passively into tumors without the assistance on antibodies. X-Ray therapy may be able to destroy cancer tumors using a Nano particle called Nbtxr3. Targeted heat therapy is being
developed to destroy breast cancer tumors. In this method antibodies that are strongly attracted to proteins produce in one type of breast cancer cell are attached to nanotubes, causing the nanotubes to accumulate at the tumor and incinerate the tumor.

**CONCLUSION:** Current cancer therapy primarily involves surgery, radiation therapy and chemotherapy. These methods of treatment are usually painful and kill normal cells in addition to producing adverse side effects. After decades of work in animal models, there is now evidence that the approach of Nanotechnology works in humans. These Nanoparticles can successfully home to proteins associated with cancer progression. Deliver medication and turn of those proteins. The idea of targeted Nanotechnology in cancer treatment and diagnosis will pioneer in the coming future generations and will lead to a cancer-free ambiencce.

**REFERENCES:**
http://www.nano.cancer.gov/

---

**28. TARGETTING ANGIOGENESIS FOR TREATMENT OF NON-SMALL CELL LUNG CANCER**

Hingane N., Iyer A.,
VES COLLEGE OF PHARMACY, CHEMBUR, MUMBAI - 400 071, (nikhilhingane@gmail.com)

**ABSTRACT:** Angiogenesis and its role in the growth and development of metastases has become a topic of increasing importance. In non-small cell lung cancer (NSCLC), vascular endothelial growth factor (VEGF) plays an important role in angiogenesis, growth of the primary tumor, and development of metastases. In addition, elevated expression in tissue samples is a negative prognostic feature. For these reasons, VEGF is a worthy target for novel therapies. Recent clinical trials have shown that the anti-VEGF monoclonal antibody bevacizumab adds to the effect of chemotherapy in the metastatic setting. Hypertension and protein urea are, as expected, commonly seen in this patient population, but the unexpected toxicity of life-threatening hemoptysis has also been observed. This makes careful patient selection especially important for this class of drugs. Our understanding of the VEGF pathway is increasing, as are the number of available targeted agents. In addition to the monoclonal antibody, bevacizumab, VEGF receptor tyrosine kinase inhibitors, multi targeted kinase inhibitors, and combination VEGF and epidermal growth factor receptor (EGFR) inhibition, are all being evaluated in NSCLC. Small phase I and II trials have suggested modest benefit when used alone; however, we now know that the anti-angiogenic therapies work best in combination with chemotherapy. The results of ongoing trials using these agents in combination with standard therapy will provide more insight into their potential benefit. As it is known that small tumors require angiogenesis to grow and metastasize, the use of anti-angiogenic therapies in the adjuvant setting may provide even greater benefit, and increase the potential cure rate in this population of patients. The results of well-designed phase III trials will be required to truly understand how to best use this class of targeted therapies in metastatic NSCLC.
29. VIRUSES NOW TO SAVE LIVES - ONCOLYTIC VIRUSES
Shetty A., Sridhar V., Bhavnani B, Vivekanand Education Society's College of Pharmacy, Hashu Advani Memorial Complex, Behind Collector Colony, Chembur, Mumbai - 400 074, Email: amullya215@gmail.com

KEYWORDS: “oncolytic viruses, reo virus, adenovirus, viro therapeutics”.

OBJECTIVES: A review on the use of viruses to selectively target cancer cells and cause tumor cell analysis with minimum or no damage to healthy cells. Development of these highly selective viruses to recognize and attack only tumor cells may provide a new look towards anti-cancer therapy in future.

INTRODUCTION: Oncolytic virotherapeutics- Here, viruses are harnessed to infect, multiply within, and subsequently lyse cancer cells -- all without affecting normal tissue. Depending on the type of virus, replication and viral gene expression can take place entirely in the cell cytoplasm (such as for vesicular stomatitis virus), or in the nucleus and cytoplasm (such as for adenovirus). In either case, the virus is largely dependent on cellular machinery for viral gene expression and synthesis of viral proteins.

DISCUSSION: Viral gene expression and replication within tumor cells leads to the activation of cellular antiviral defenses, such as apoptosis, that are operational in normal cells but are often inactivated in tumor cells. Expression of viral proteins will eventually lead to immune-mediated lysis of infected cells by CD8+ T cells, which recognize viral peptide epitopes that are presented by major histocompatibility complex (MHC) class I molecules on the surface of the infected cell. Alternatively, cells might be lysed owing to an overwhelming amount of budding and release of progeny visions from the cell surface.

Why viruses? Viruses can be rapidly modified by recombinant DNA technology, allowing for the rational creation of ‘designer viruses’. Owing to their ability to self-replicate within the cancer cell, oncolytic viruses have unique pharmacokinetic properties that are distinct from conventional therapeutics. In a sense, oncolytic viruses can be thought of as miniature biological machines that we can program to specifically target, replicate in and ultimately kill tumor cells.

Reovirus (Respiratory Enteric Orphan virus) model: It is a virus with no known associated disease. It replicates in the cytoplasm and therefore does not integrate into the cell's DNA. Reovirus is found everywhere in nature and has been isolated from untreated sewage, river, and stagnant waters. Reovirus normally infects cells of the gastrointestinal tract, where proteases can convert the non-infectious reovirus into an infectious form called the intermediate sub-viral particle (ISVP). When given intravenously, reovirus is not efficiently processed to the infectious form. However, it is possible to select for variants that have been converted into ISVP by the action of proteases that are overexpressed in the tumor microenvironment.

How does reovirus recognize the tumor cells? Viruses, naturally, prefer cells that can’t fight them off. Tumors bearing an activated R as pathway cannot activate the anti-viral response mediated by the host cellular protein, double-stranded RNA protein kinase (PKR). When the R as pathway is turned on, it turns off the virus defense mechanism in the cell so the virus can go in and replicate itself. It keeps replicating until its host the cancer cell is
overwhelmed and dies, which happens within three days. But when normal cells are infected with reovirus, the immune system can neutralize the virus. In metastatic cancers, which spread beyond the primary tumor, between 95% to 100% of tumor cells have the R as pathway.

**Side effects of oncolytic therapy:** The only observed side effects were flu-like symptoms, such as fever, chills, fatigue, headache, nausea and vomiting, which lasted up to 24 hours and could be treated with over-the-counter drugs.

**CONCLUSION:** So, a picture that is emerging is that oncolytic viruses not only mediate direct tumor oncolysis, but could, in combination with their inherent adjuvant properties, induce or reactivate cancer immuno surveillance programmes. In conjunction with present chemotherapeutic or radiation methods, oncolytic therapy can be used to prolong the life of cancer patients or may even be helpful in providing a complete cure.

**REFERENCES:**
- medscape.com
- classic.the-scientist.com
- www.canceractive.com

---

**30. C-REACTIVE PROTEIN (CRP) AND CANCER**

**Dr. Aruna Jadhav**, Akhila Menon, Sharole Manjrekar, & Poonam Chaudhary,

*Bharati Vidyapeeth’s College of Pharmacy, Sector-8, C.B.D., Belapur,
Navi Mumbai - 400 614*

**KEYWORDS:** “CRP, cancer, inflammation”

**OBJECTIVE:** The objective is to study role of CRP in development of cancer is leading cause of death worldwide. Cancer is caused due to disruption to the DNA of the cell, the genetic code that directs the life of the cell. Cancer can be reduced and controlled by implementing evidence based strategies for cancer prevention, early detection of cancer and management of patients with cancer. Inflammation is the latest buzzword in medical science, implicated in everything from asthma and arthritis to heart disease and cancer. Inflammation is a protective attempt by the organism to remove the injurious stimuli and to initiate the healing process. Inflammation is not a synonym for infection, even in cases where inflammation is caused by infection. Without inflammation, wounds and infections would never heal. Similarly, progressive destruction of the tissue would compromise the survival of the organism. But the type of inflammation causing a stir among scientists and doctors is the chronic (long-term), systemic inflammation which nobody can see or feel, but leaves a trail of markers, including something called C-reactive protein (CRP), which shows up on a simple blood test. CRP is a protein found in the blood, the levels of which rise in response to inflammation (i.e. C-reactive protein is an acute-phase protein). Its physiological role is to bind to phosphocholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system via the C1Q complex. CRP is synthesized by the liver in response to factors released by fat cells (adipocytes). It is a member of the pentraxin family of proteins. It is not related to C-peptide or protein C. CRP molecules, such as this cluster below, are measured to diagnose or confirm the presence of
inflammation or infection. CRP levels in the blood rise in response to an inflammation or injury, and fall after healing or during periods of remission. Some research suggests that patients with chronic inflammation (prolonged elevated levels of CRP) are at an increased risk for heart disease, stroke and cancer. CRP measures general levels of inflammation in your body. But a CRP test cannot show where the inflammation is located or what is causing it.

**C-reactive protein**

Normal concentration of CRP in healthy human serum is usually lower than 10 mg/L, slightly increasing with aging. Higher levels are found in late pregnant women, mild inflammation and viral infections (10–40 mg/L), active inflammation, bacterial infection (40–200 mg/L), severe bacterial infections and burns (>200 mg/L). CRP is a more sensitive and accurate reflection of the acute phase response than the ESR. The half-life of CRP is constant. Therefore, CRP level is mainly determined by the rate of production (and hence the severity of the precipitating cause). In the first 24 h, ESR may be normal and CRP elevated. CRP returns to normal more quickly than ESR in response to therapy. CRP is the most widely tested marker for inflammation. CRP tests have been in use for more than 20 years, mainly for rheumatoid arthritis and bloodstream infections. Lately, the test had piqued interest among cancer researchers. A large 2009 Danish study, found that people with high blood levels of CRP and a predictor of heart disease risk - have a 30 percent greater risk of developing any cancer later in life, and were associated with the risk of developing lung and possibly colorectal cancers, compared with people with low CRP levels. Researchers also found that among people with cancer, those with high CRP levels prior to their diagnosis were 80 percent more likely to die sooner than people with cancer who did not have elevated CRP. Some organs of the body show greater risk of cancer when they are chronically inflamed. Blood samples of persons with colon cancer have an average CRP concentration of 2.69 mg/L. Persons without colon cancer average 1.97 mg/L. The difference was statistically significant. These findings concur with previous studies that indicate that anti-inflammatory drugs could lower colon and lung cancer risk. The human papillomavirus (HPV) causes cervical cancer and people with hepatitis C or hepatitis B have a much greater risk of liver cancer than the general population. Inflammation has also been shown to play a role in development of prostrate, pancreatic as well as digestive system cancers. Chronic irritation and inflammation, resulting from factors such as long-term exposure to cigarette smoke, asbestos or silica, can also greatly increase cancer risk.

**CONCLUSION:** Chronic infections, a cause of inflammation, are associated with nearly 15 percent of cancers. Chronic inflammation is often an indolent, slow process where there is ongoing tissue injury and repair. This constant repair work affects the rate of cell turnover, increasing the risk of DNA mutations including cancer. CRP testing may play a part in early cancer detection. The CRP test help distinguish illnesses requiring antibiotics from those that don't. A high-sensitivity version of the test (hsCRP) is available for people at risk of heart problems. Recent research has indicated that statins, the drugs usually taken to control cholesterol levels, may also be able to reduce the risk of heart attack and stroke in people who have normal cholesterol levels but suffer chronic inflammation. Natural anti-inflammatory nutrients like omega-3 have been shown to reduce the risk of colorectal and
Cancer - Comprehensive Approaches in Drug Discovery and Development 2011 63

other cancers. Future research work in this area may have profound influence in chemoprevention.

REFERENCES:

31. A NEW TARGET FOR CANCER DRUGS

Akshaya Pathare¹, Nupur Joshi¹, Dr. Dnyanesh Limaye².
1. Final year B. Pharm, ². Prof. &HOD- Dept. of pharmacology. Bharati Vidyapeeth College of Pharmacy. C.B.D. Belapur, Navi Mumbai, Maharashtra, India - 400 614

ABSTRACT: Suppressing cancer cells’ ability to cope with damage to their DNA could enhance dramatically the effectiveness of chemotherapy drugs such as Cisplatin, according to a research study published in the (PNAS), Proceedings of the National Academy of Sciences of the United States of America November 2010. In studies of mice, the researchers found that slowing down a specific system for tolerating DNA damage in cancer cells not only prolonged the lives of the mice, but also prevented relapsed tumors from becoming resistant to chemotherapy, and made tumors much less likely to spread to other parts of the body. Two enzymes that play key roles in tumor cells’ response to DNA damage could be an enticing target for new cancer drugs, according to Michael Hermann and Graham Walker, senior authors of the published study. Many cancer drugs, including Cisplatin, attack cancer cells by damaging their DNA. This DNA damage can prevent cells from copying their DNA, which they must do before dividing. If they can't, they usually commit suicide. However, cancer cells can use enzymes known as translation DNA polymerases to copy over DNA damage, allowing them to survive. This type of DNA copying can be highly prone to mistakes, introducing mutations into the DNA. Those newly acquired mutations make cancer cells that survive chemotherapy much more drug-resistant and aggressive. This means that if the first round of chemotherapy fails to completely destroy the tumor, the patient is usually much worse off than before the treatment. If the tumor fails to respond to initial therapy, the likelihood of clinical success is very low upon repeated rounds of treatment. In these studies, the researchers controlled Rev1 and Rev3 levels using a technique called RNA interference, which employs short strands of RNA to block specific genes from being expressed. Researchers are now trying to develop ways to effectively and safely use RNA interference to treat many diseases, but no such therapies have been approved. Another option is to find molecules that would disrupt the action of these polymerase enzymes. Walker is now looking for such drugs, which might be able to shut down the translation DNA polymerase system more thoroughly than RNA interference. Such drugs, used in combination with traditional chemotherapy, could provide a better way to treat cancers that don't respond well to the usual treatments.

REFERENCE:
ABSTRACT: For decades, researchers have been working to develop nanoparticles that deliver cancer drugs directly to tumors, minimizing the toxic side effects of chemotherapy. However, even with the best of these nanoparticles, only about 1 percent of the drug typically reaches its intended target. A team of researchers from MIT, the Sanford-Burnham Medical Research Institute and the University of California at San Diego have designed a new type of delivery system in which a first wave of nanoparticles homes in on the tumor, and then calls in a much larger second wave that dispenses the cancer drug. Nanoparticles can be engineered to communicate with each other in the body, and that these capabilities can improve the efficiency with which they find and treat diseases like cancer. The MIT team’s approach is based on the blood coagulation cascade - a series of reactions that starts when the body detects injury to a blood vessel. Proteins in the blood known as clotting factors interact in a complex chain of steps to form strands of fibrin, which help seal the injury site and prevent blood loss. In a study of mice, one system of communicating nanoparticles delivered 40 times more doxorubicin than non-communicating nanoparticles. The researchers also saw a correspondingly amplified therapeutic effect on the tumors of mice treated with communicating nanoparticles. To pave the path for potential clinical trials and regulatory approval, the MIT researchers are now exploring ways to replace components of these cooperative nanosystems with drugs already being tested in patients. For example, drugs that induce coagulation at tumor sites could replace the signaling particles tested in this study. Researchers have mentioned that the new strategy is a clever way to improve drug delivery to tumor sites. “Instead of targeting the tumor itself, it’s targeting a microenvironment that they’ve created,” By developing these nanosystems in a two-step approach that could be used in combination with a lot of other strategies.”

REFERENCE:

33. AZURIN: A GREAT HOPE TO TREAT CANCER
Hindlekar .D, Padte .P, Salunkhe .S.Zine S.P., Vivekanand Education Society’s College of Pharmacy, Chembur, Mumbai, Email: dhindlekar217@gmail.com

KEYWORDS: “Antitumor, azurin, Pseudomonas aeruginosa, cupredoxin, apoptosis”

OBJECTIVE: Azurin as Antitumor Protein obtained from Pseudomonas putida and its effect on cancer cell lines

INTRODUCTION: Cancer harms the body when damaged cells divide uncontrollably to form lumps or masses of tissue called tumors. Tumors can grow and interfere with the digestive, nervous, and circulatory systems and they can release hormones that alter body function. Cancer is ultimately the result of cells that uncontrollably grow. Normal cells in the body
follow orderly path of growth, division, and death whereas programmed cell death is called apoptosis, and when this process breaks down, cancer begins to form. P. aeruginosa groups tend to form biofilms, which are characterized by “attached for survival” because once they are formed; they are very difficult to destroy. Azurin a low molecular weight redox protein was elaborated from the biofilm of pathogenic bacteria Pseudomonas Aeruginosa used in the treatment of tumors. P. aeruginosa preferentially enters human melanoma and breast cancer cells, triggering apoptotic cell death by forming a complex with the well-known tumor suppressor protein p53, stabilizing it, and activating caspases that induces apoptosis in cancer cells.

**DISCUSSION & CONCLUSION:** The cytotoxic effect of the recombinant azurin was successfully tested against human breast cancer cell line, human hepatocellular carcinoma cell lines, human colon carcinoma cell line and human normal melanocytes cell line. The study showed that when the concentration of azurin was increased, the proliferation of colon carcinoma cell line was strongly inhibited. The proliferation of breast cancer cell line decreased whereas the proliferation of hepatocellular carcinoma cell line gave a fluctuation result and no effect was detected on human normal melanocytes, making it a promising anti-tumor drug. Azurin is not only a potential anticancer drug candidate, but it also forms complexes with many surface proteins, thereby interfering in their entry to the host cells and significantly suppressing their growth.

**Future prospects:** Pseudomonas aeruginosa is known to secrete the protein azurin as a weapon against invaders as cancers, parasites and viruses. The production of such weapons by pathogenic bacteria could provide important insights into how a pathogen responds in the post colonization state to impede other intruders for its own survival. These molecules might find use in the pharmaceutical industry as next-generation therapeutics and offer a new route to cancer therapy and a good vehicle for cancer-targeted chemotherapy

**REFERENCE:**

**34. ROLE OF CAVEOLIN-1 IN CANCER**
Deweshri Kerzare¹, Roopesh Tiwari, Prarthana Rewatkar, Nikhil Amnerkar, Vaishali Potnis
Corresponding address, Kamla Nehru College of Pharmacy, Borkhedi (Gate), Butibori, Dist.- Nagpur - 441 108, Email-id: kerzarepritee@gmail.com
**ABSTRACT:** Caveolin-1 is a ubiquitously expressed integral membrane protein and essential for formation of so called caveolae, small invaginations of the plasma membrane. It is involved in major physiological functions of the mammalian cells, including endocytosis, transcytosis process, signal transduction and cholesterol homeostasis. Caveolin-1 places a key role in cancer progression and metastasis. Caveolin-1 is implicated in the oncogenic transformation of cells as a tumor suppressor. Caveolin-1 activity is regulated by cellular localization, oligomerization, tyrosine 14 phosphorylation, serine 80 phosphorylation, and palmitoylation. Major sites of expression for Caveolin-1 is with high expression in fat, lung and smooth muscle and low expression in liver. Caveolin-1 regarded as a prognostic marker in cancer such as lung cancer, prostate cancer, blood cancer, breast cancer and provides the basis for development of new anticancer treatment.

**KEYWORDS:** “Cancer, Caveolin-1, Cell biology:”

---

**35. STUDIES ON SOME NOVEL POTENTIAL ACRIDONE ANALOGUES**

Velingkar V.S., Ghumare R. A., Gadkari Y.*
Prin. K. M. Kundnani College of pharmacy, Cuffe Parade, Colaba, Mumbai

**KEYWORDS:** “Acrid one, Intercalation Ullman’s Condensation, SRB Assay”.

**OBJECTIVE:** As structural building block in many natural products, the acridine or acrid one ring is one of the most commonly encountered heterocyclic in medicinal chemistry. To confer the antitumor activity the chromophore (acrid one ring) should carry at least one basic side chain. Considering above rationale, the aim of present research work was to develop newer Acridone analogs exhibiting potential anticancer activity.

**INTRODUCTION:** Cancer, the uncontrolled, rapid, and pathological proliferation of abnormal cells, is the leading cause of human death, after cardiovascular diseases. Cancer-related deaths are estimated to reach 12 million world-wide, by the year 2015.

There has been increasing interest in the development of synthetic antitumor agents belonging to the broad class of DNA binding agents. The most well-known subclass of these compounds are DNA intercalating agents where much of the binding energy is obtained by insertion of flat aromatic portion of the molecule between base pairs of DNA double helix e.g.: *mitoxantrone, bisanthrene, ametantrone*. All these compounds contain a fused linear tricyclic nucleus that possesses the necessary area widely accepted to be needed for efficient intercalative binding. Acridine and acrid one-based derivatives have been mostly studied as anticancer agents, which are believed to express their activity through binding or intercalation of DNA. The planar area of the tricyclic acridine and acrid one nuclei aid in targeting DNA by intercalating between nucleotide base pairs in the helix.
In-vitro Biological Activity Testing: In-vitro anti-neoplastic activity testing of synthesized compounds was carried out at ACTREC (Advanced Centre for Treatment Research and Education in Cancer), Kharghar, Navi Mumbai by measuring the percent inhibition of cell growth on MCF7 Breast cancer cells at various concentrations of the synthesized compounds.

RESULTS:

DISCUSSION:
- Spectral analysis of all the compounds confirms formation of all the title compounds.
- Cell line studies shows that compound 1 and compound 7 are active against MCF-7 breast cancer cells

REFERENCES:
RAPID AND QUANTITATIVE ASSESSMENT OF CANCER TREATMENT RESPONSE USING IN VIVO BIOLUMINESCEENCE IMAGING

Bhatt K., Savant N., Kambli S., Vivekanand Education Society's College Of Pharmacy,
E-mail: khushubhatt92@yahoo.co.in

KEYWORDS: “bioluminescence, MR Imaging, luciferase, in vivo, brain tumor”

INTRODUCTION AND OBJECTIVE: Current assessment of orthotropic tumor models in animals utilizes survival as the primary therapeutic end point. However, quantitative measurements of therapeutic-induced changes in tumor growth requires large numbers of animals to be killed at multiple time points to determine the average course of tumor development and growth to overcome variability between animals. The aim of the present study was to determine whether bioluminescence detection offers advantages (e.g. increased sensitivity or reduced number of animals required to demonstrate an effect) for quantitative assessment of anticancer therapies directed against brain tumor. We report on the noninvasive, in vivo imaging of the intraperitoneal growth of luciferase-transfected tumor cells in the brain of the rats. This new method of monitoring the kinetics of tumor growth was compared with MR Imaging of the tumor cells and with post-mortem scoring of tumor load after intraperitoneal treatment with 1, 3-bis (2-chloroethyl)-1-nitrosourea (BCNU), a chemotherapeutic agent. It is based on the expression of luciferase, the light-emitting enzyme of the firefly Photinus pyralis. This photon emission can be detected by a cooled charge-coupled device (CCD) camera, minutes after the administration of the substrate.

Using human tumor cell lines constitutively expressing luciferase, the kinetics of tumor growth and response to therapy have been assessed in intraperitoneal, subcutaneous, and intravascular cancer models. In this report, the ability of BLI to noninvasively quantitate the growth and therapeutic-induced cell kill of orthotropic rat brain tumors derived from 9L gliosarcoma cells genetically engineered to stably express firefly luciferase (9L\textsuperscript{Luc} gene) was investigated through in vivo measurements of both the tumor volume from MRI and photon emission from BLI and post-mortem quantification of tumors from the same group of animals over time. Quantitation of therapeutic efficacy was accomplished on a group of rats with intracerebral 9L\textsuperscript{Luc} tumors, which were treated with the chemotherapeutic agent BCNU. MR and BL images of a representative animal from this experiment are shown in Figure 2A and B, respectively. A plot of tumor volume and detected photon counts versus time for this animal is shown in Figure 2C along with an exponential fit of the tumor regrowth data. Rats were killed at respective time instances to find the actual size of tumor by doing their post-mortem.

The MR images revealed that the tumor continued to expand up to 8 days after treatment followed by regression and subsequent regrowth. The corresponding BL images revealed parallel changes in detected photon emission over this same time period. A quantitative comparison of tumor cell kill determined from serial MRI volume measurements and BLI photon counts following BCNU treatment revealed that both imaging modalities yielded statistically similar cell kill values ($P=.951$). The bioluminescence signal correlated well with post-mortem assessment of tumor load by visual inspection of the peritoneal cavity at specific follow-up times.
RESULTS AND DISCUSSION: An advantage of BLI approach for preclinical evaluation of therapeutic interventions over direct measurements of tumor volume using MRI or calipers is that it provides a quantitative surrogate measure of the number of metabolically active tumor cells which could be detected well before the appearance of the common end points of weight loss, palpable tumors or death, reasonable equipment costs, short scanning times of only 1 to 5 minutes, simultaneous scanning of multiple animals in a single image acquisition, and minimal post processing requirements, significantly reducing the cost of preclinical drug discovery. Tumor nodules of 2–3 mm could be detected in the peritoneal cavity, providing thick, pigmented organs, like the liver, did not shield them. The tumor load from deeper parts of the body will be relatively under-represented in the integrated images and small tumors that are shielded by bulky, pigmented organs may well be missed.

REFERENCES:

37. RIBOZYME MEDIATED CANCER GENE THERAPY
WAGHMARE ASHWINI (2009ashwinwi@gmail.com), KAREKAR NEHA (2009nehak@gmail.com), MUMBAI EDUCATIONAL TRUST, BANDRA RECLAMATION, BANDRA (WEST)

KEYWORDS: “ribozyme, gene therapy, surviving, angiogenesis”

ABSTRACT: Ribozymes are involved in a variety of cellular processes, but their most interesting property from the standpoint of cancer therapy is their ability to cleave messenger RNA (mRNA) molecules. When an mRNA is cleaved, it can no longer be translated to produce protein. By targeting the mRNAs encoding proteins with pathological roles in cancer, ribozymes can slow or inhibit cancerous growth. Ribozymes can combat specific stages of cancerous growth, including cell proliferation, drug resistance, and metastasis.

INTRODUCTION: Ribozymes are RNA molecules with the capacity to effect sequence-specific cleavage of other transcripts. Ribozymes were initially discovered as the intervening sequence of the RNA Group I intron which catalyzes its own excision, and this has been called self-splicing. Several naturally occurring ribozymes, such as RNA se P, Group I1 intron, hammerhead ribozymes, hairpin ribozymes, and hepatitis delta virus ribozymes have also been identified. Due to their catalytic potential, ribozymes have been investigated as agents to block genetic information. A crucial role of ribozymes as therapeutic agents would be to down regulate a specific gene by interfering with the information from the nucleic acid to the protein, i.e. mRNA. Hammerhead ribozymes have demonstrated the ability to inhibit the expression of specific genes by targeting their mRNAs Because of their small structure,
simple cleavage mechanism, and specificity, hammerhead ribozymes have been extensively investigated for potential therapeutic application.

**STRUCTURE AND CLEAVAGE MECHANISM OF HAMMERHEAD RIBOZYME**

A schematic structure of a hammerhead ribozyme and its substrate, i.e., the complex of a designed ribozyme with its target mRNA, is shown in Fig. 1. The numbering system has been proposed for simplifying the data comparison from different laboratories. The secondary structure of the ribozyme-substrate complex consists of 3 helices, a catalytic core region, and a loop sequence. The ribozyme binds to its target mRNA through helix I and helix 11, and the cleavage occurs at the 3' site. A part of the non-helical catalytic core, i.e. C3 to A9, is demonstrated to form a sharp turn using three-dimensional analysis. This turn or catalytic pocket is identical in sequence and structure to the uridine turn found in the anticodon loop of tRNAphe. This catalytic pocket of the hammerhead ribozyme requires divalent metal ion for catalytic activity. Several mutational analysis of nucleotides within the hammerhead ribozyme substrate mRNA have been investigated. Nucleotides, C3 to A6, G8 to G10, and C11 to A14 are essential for catalytic reaction. For the mRNA substrate, a nucleotide triplet at position 16.2, 16.1, and 17 is also essential for cleavage reaction, and the nucleotide at position 16.1 must be U. Although all natural hammerhead ribozymes are found to have a nucleotide G at position 16.2, it remains that any nucleotides can be substituted depending on the surrounding sequence. Also, any nucleotides are allowed at position 17 depending on the surrounding sequence, but nucleotide G at this position has demonstrated poor cleavage activity. In general, a XUN triplet (X being any nucleotides, and N being A, C, or U) is required for cleavage. The GUC, GUA, GUU, UUC, and CUC triplets have been shown in many experimental systems to be preferable targets for efficient cleavage. Hammerhead ribozymes can be designed to bind and cleave their RNA substrates in an enzymatic trans reaction. Divalent metal ions, such as Mg²⁺ and Pb²⁺, are required for catalytic cleavage. Cations neutralize the charge of the folded ribozyme-substrate molecule, by binding within a specific region of this complex and allow the transfer of a proton from the -OH group of the phosphorus grasp at the cleavage site. The intermolecular attack of the OH catalysis a trans esterification reaction breaking the 3',5'-phosphodiester bond between nucleotides 17 and 1, and generate a 2'-3'-cyclic phosphate of nucleotide 17 and a free 5'-OH products of nucleotide 1.

**APPLICATIONS OF RIBOZYMES TO CANCER GENE THERAPY:** Ribozymes are applicable to any disease process caused by the undesirable expression of mRNA. However, the selection of a suitable target is absolutely crucial. The molecular basis of the targeted disease should be at least partially identified, and modulation of the targeted gene must alter or eradicate the undesired cellular phenotype. Several mRNAs have been chosen and investigated as targets for ribozyme-mediated cancer gene therapy; these include oncogenes, growth factors, metastatic factors and drug resistance genes.

1. Survivin is a new member of the inhibitor of apoptosis protein (IAP) family that is implicated in the control of cell proliferation and the regulation of cell life span. To down-
regulate a human survivin expression as a strategy for cancer gene therapy, two hammerhead ribozymes (RZ-1, RZ-2) targeting human survivin mRNA. RZ-1 and RZ-2 efficiently cleaved the human survivin mRNA at nucleotide positions +279 and +289, which was identified by in vitro cleavage assay using in vitro transcribed ribozymes and truncated survivin mRNA substrate. To investigate the function of the ribozymes in cells, the sequences of the ribozymes were cloned into replication-deficient adenoviral vector and transferred to breast cancer cell. The cloned ribozymes resulted in a significant reduction of survivin mRNA (74% and 73%, respectively) and protein. As revealed by nuclear condensation/fragmentation and flow cytometry analysis, inhibition of survivin gene by ribozymes increased apoptosis. The results suggest that the designed hammerhead ribozymes against survivin mRNA are good candidates for feasible gene therapy in the treatment of cancer.

2. ANGIGENESIS: Clinical and experimental evidence suggests that spreading of malignant cells from a localized tumor (metastasis) is directly related to the number of microvessels in the primary tumor. This tumor angiogenesis is thought to be mediated by tumor-cell-derived growth factors. Herein we use ribozyme targeting of pleiotropic (PTN) in metastatic human melanoma cells to assess the significance of this secreted growth factor for angiogenesis and metastasis. As a model we used human melanoma cells (1205LU) that express high levels of PTN and metastasize from subcutaneous tumors to the lungs of experimental animals. In these melanoma cells, they reduced PTN mRNA and growth factor activity by transfection with PTN-targeted ribozymes and generated cell lines expressing different levels of PTN. In nude mice, however, tumor growth and angiogenesis were decreased in parallel with the reduced PTN levels and apoptosis in the tumors was increased. Concomitantly, the metastatic spread of the tumors from the subcutaneous site to the target was prevented. These studies support a direct link between tumor angiogenesis and metastasis through a secreted growth factor and identify PTN as a candidate factor that may be rate-limiting for human melanoma metastasis.

3. In the field of urology, efficient tumor inhibition of an anti-H-ras oncogene ribozyme in bladder cancer has been demonstrated. Ribozyme strategy has also been investigated in prostate cancer, and the use of a PSA promoter may make this strategy more specific and efficient.

**CONCLUSIONS:** Ribozymes have the ability to modulate specific gene expression by their site-specific cleavage activity, and are being extensively investigated for their therapeutic applications in the field of cancer gene therapy. They can be targeted to any disease in which a specific protein has been linked to its etiology, and oncogenes are obvious targets for ribozyme strategies. Many studies have demonstrated the efficacy of anti-oncogene ribozymes to modulate the malignant phenotype. Critical issues that need to be overcome include delivery systems possessing efficient cellular uptake, specific gene targeting, long term expression, and safety. The development of an effective delivery system with minimal toxicity may advance ribozymes as therapeutics for cancer treatment.

**REFERENCES:**
- www.nature.com
- www.onlinelibrary.wiley.com
- www.pubmed.com
ANTI-ANGIOGENESIS AS AN ANTI CANCER
Shirkar Pranav, Shinde Swapnaja, Walavarkar Mandar
Mumbai Educational Trust Bandra Reclamation, Bandra west

KEY WORDS: vascular endothelial growth factor - VEGF; CRC: Colo rectal cancer; MBC: metastatic breast cancer; HCC: hepatocitic cell cancer; RCC: renal cell cancer; IFL- 5-fluorouracil (5-FU)/ leucovorin (LV)/irinotecan

INTRODUCTION: Cancer chemotherapy is used as final line of defense against stage -4 metastatic cancer .But this chemotherapeutic treatment comes with handful of side effects (nausea , vomiting, hair loss etc. ) as they interfere the DNA replication process of normal cells, this creates narrow therapeutic index. Research have been made in order to tackle this problem .The anti- angiogenic agents efficacy of chemotherapy is optimized by administrating comparatively low doses of drugs on a frequent or continuous schedule . Cancer cell needs nutrients and oxygen for its survival as they lack normal supply of blood from normal blood vessels; this is done by angiogenesis promoter vascular endothelial growth factor (VEGF). Drugs interfering this process are called as anti angiogenic agents and are used in treating metastatic stage-4 solid tumor.

OBJECTIVE: Study of anti angiogenic drug (avastin) in CRC in combination chemotherapy with 5-FU and LV

EXPERIMENTAL METHODS: The addition of Avastin 5mg/kg every 2 weeks to first-line bolus 5-FU/LV results in consistent improvements in response rates and progression-free survival .Combined data from three trials shows a significant improvement in overall survival. In phase II, multicentre, double-blind, randomised, controlled trial was designed to evaluate the efficacy and safety of Avastin 5mg/kg every 2 weeks combined with 5-FU/LV versus 5-FU/LV alone in patients with previously untreated metastatic CRC who were not optimal candidates for first-line irinotecan.1 Two hundred and nine patients were randomised in a 1:1 ratio to two treatment arms: Avastin 5mg/kg plus 5-FU/LV (n=104); and placebo plus 5-FU/LV (n=105).5-FU/LV was administered via i. v. bolus weekly for the first 6 weeks of each 8-week cycle (Roswell Park regimen) and continued until study completion or until disease progression. Avastin 5mg/kg or placebo was given every 2 weeks until progression. Patients in the Avastin arm with a confirmed complete response or unacceptable toxicity due to chemotherapy treatment were eligible to discontinue chemotherapy and continue receiving Avastin in the first-line setting. The primary objectives of the study were to evaluate: the efficacy of Avastin plus 5-FU/LV versus 5-FU/LV alone in metastatic CRC, as measured by duration of survival; and the safety of Avastin plus 5-FU/LV versus 5-FU/LV alone. The secondary objectives were to evaluate the efficacy of Avastin plus 5-FU/LV versus 5-FU/LV alone in metastatic CRC, as measured by: time to disease progression; objective response rate; duration of response; change in quality of life.

RESULT: Anti-VEGF therapy has been shown to inhibit endothelial cell proliferation and migration, and to suppress new vascular sprouting within 24 hours of administration is shown below.
CONCLUSION: Avastin is the first anti-angiogenic agent for the treatment of cancer to demonstrate survival benefit in a phase III trial in first-line metastatic CRC, adding Avastin to IFL or bolus .5-FU/LV increases survival, progression-free survival and overall response rate. Avastin also improves survival when combined with FOLFOX. Avastin-based therapy is well tolerated and has a favourable and manageable toxicity profile. Combining Avastin with other regimens first line (e.g. FOLFOX, XELOX, and FOLFIRI) is likely to be effective. This has shown a promising effect in treating CRC, MBC, HCC, and RCC. Side effects like hypertension, proteinuria, arterial thrombosis, affects wound healing, bleeding severe is G.I perforation observed for avastin.

<table>
<thead>
<tr>
<th>Phase III trial of IFL ± Avastin in metastatic CRC (AVF2107g): efficacy in arm 3 (5-FU/LV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm 1</td>
</tr>
<tr>
<td>IFL + placebo</td>
</tr>
<tr>
<td>(n=101)</td>
</tr>
<tr>
<td>Median overall survival (months)</td>
</tr>
<tr>
<td>Median progression-free survival (months)</td>
</tr>
<tr>
<td>Response rate (%)</td>
</tr>
<tr>
<td>Length of response (months)</td>
</tr>
</tbody>
</table>

39. FABRICATION AND OPTIMISATION OF POLYMERIC PLGA NANOPARTICLES FOR TREATMENT OF GLIOBLASTOMA MULTIFORME
Jain Darshana S.*, Bajaj Amrita N#, C. U. Shah college of pharmacy, S.N.D.T. Women’s University, Santacruz (w) Mumbai - 400 049, SVKM's Dr. Bhanuben Nanavati College of Pharmacy, V.M. Road, Vile Parle (w), Mumbai- 400 056,
Email ID: darshanaj_cup@yahoo.com

INTRODUCTION: Nanoparticles affect the bio distribution of drugs in organ specific manner. Biocompatible macromolecules adsorbed onto biodegradable nanoparticles prevent the rapid uptake of intravenously injected particulate drug carriers by the cells of reticuloendothelial system. Such of nanoparticles can selectively delivery drugs to tumor due to “leaky” tumor vasculature, the enhanced permeability and retention (EPR) effect thus crossing the Blood brain barrier. The primary brain tumors are thought to be derived from glial cells or their progenitors and are generically classified as gliomas. Most solid tumors possess unique features and defects of their associated vasculature, such as extensive angiogenesis, defective vascular architecture, and increased vascular permeability, all of which can be used for delivering therapeutics. Drugs like paclitaxel, irinotecan, and methotrexate are being used for treatment of tumors.

AIM: To fabricate and optimize polymeric PLGA nanoparticles (NP’s) with excipients suitable for intravenous administration. Fabricated PLGA nanoparticles would be used for treatment of brain tumors.
OBJECTIVE:
- To develop drug loaded (MZT) stealth PLGA nanoparticles by adsorbing hydrophilic molecules onto the particles.
- Studying the effect of altering the formulation parameters on particle size and PI.
- Optimizing the process parameter and selection of selection of suitable cry protectants thus formulating a suitable intravenous formulation for tumors.

METHODOLOGY: Preformulation studies: A suitable HPLC method was developed and validated to estimate the concentration of drug in prepared formulations.

Formulation studies: Drug (MZT) loaded nanoparticles were prepared by solvent emulsification- evaporation method. Stabilizers were selected based upon their suitability to emulsify the formed nanoparticles and also impart stealth property. Optimization of formulation parameters in terms of 1) Organic solvent, 2) Hydrophilic surfactants, 3) Ratio of Aqueous to organic phase, 4) Polymer concentration and 5) Drug concentration was carried out. Nanoparticles were lyophilized with various cry protectants. Cry protectant and its concentration were optimized to overcome the problem of size increment.

Characterization: Developed formulations were characterized through SEM, X-RD, DSC and IR studies.

RESULTS AND DISCUSSION: Polymeric PLGA nanoparticles with long circulating property for systemic administration were prepared. Parameters like polymer concentration, drug concentration, organic solvent and ratio of water to solvent were optimized in terms of particle size (200nm ±10 nm) and PI (0.15±0.03). Increase in the particle size after stabilizer adsorption indicated that the developed nanoparticles have long circulating properties. X-RD studies reveal that the drug was entrapped in developed nanoparticles. DSC and IR studies indicated entrapment of drug in the NP’s during formation of nanoparticles. Thus, polymeric PLGA nanoparticles for treatment of brain tumors were prepared and optimized.

![Fig1: Effect of solvent on particle size](image1)

![Fig2: Effect of Polymer conc. on particle size and PI](image2)

![Fig3: Effect of drug loading on Entrapment efficiency](image3)

![Fig4: Effect of cryoprotectant on particle size](image4)

![Fig5: X-RD data particle size](image5)
CONCLUSION: Only few drugs can penetrate the BBB and enter the CNS, so various systems are developed for drug delivery. It emerges that through the nanotechnology technique drug can penetrate the BBB efficiently. Further the modified colloidal particles enhance exposure of the BBB due to prolonged blood circulation, which favors interaction and penetration into brain endothelial cells. This feature would help in efficiently delivering anti-cancer agents to tumor site and thus its treatment. Nanoparticles were thus prepared and optimized and studies are in progress to investigate the potential of the developed nanoparticles for treatment of brain tumors.

REFERENCES:
3) Pilar calvo et al. pharmaceutical research, 18:1157-1161(01)

Acknowledgement: Authors thank CIPLA PVT LTD for their support.

40. THIAZOLIDINEDIONE: UPCOMING POTENT ANTICANCER AGENT
Meenu D. Jain*, Harshada P. Bhosale, Wahid Abdul Ambekar, P.D.V.V.P. F’s College of Pharmacy, Vilad Ghat, Ahmednagar

ABSTRACT: The PPAR-gamma (PPAR-γ) activating thiazolidinedione (TZD) medications are a class of drugs used to improve lipid and glucose metabolism in type-2 diabetes. In addition to their known insulin sensitization action, these drugs have been shown to suppress tumor development in several in vitro and in vivo models. A large proportion of the literature studies indicate that TZD-induced PPAR-γ activation promotes anti-tumor actions through apoptosis induction, differentiation, and growth (proliferation) arrest. Two PPAR-γ isoforms exist that are derived from the alternate promoters, PPAR-γ1 and PPAR-γ2. The PPAR-γ2 isoform is 30 amino acids longer than PPAR-γ1 and is less abundant. PPAR-γ2 is predominantly expressed in adipose tissue where it exerts pleiotropic effects on metabolism, insulin sensitization, and inflammation. PPAR-γ2 is also expressed in vascular endothelium, suggesting a role for this protein in vascular biology as well as in alveolar macrophages. PPAR-γ has been detected in cancer cells. Several reports have demonstrated that PPAR-γ activation has anti-cancer properties. For example, TZDs suppress tumor development in several animal models, and PPAR-γ activation arrests malignant cell growth. In addition, treatment of cancer cells with PPAR-γ-activating TZDs induces cell differentiation and apoptosis. TZD’s are currently used against lung cancer, breast cancer, colon cancer, neoplastic etc. in vivo and invitro studies. One of the example like TZD against lung cancer: Proliferation of A549 lung cancer cells was significantly inhibited by ciglitazone in a dose- and time-dependent manner both in vivo and in vitro, and PPAR-γ expression was markedly up regulated by ciglitazone treatment. Troglitazone induced PPAR-γ expression and apoptosis in two human lung cancer cell lines, but not in normal cells. These results suggest the potential for TZDs to target malignant cells without affecting normal cells (the goal of anti-cancer chemotherapy). In nude mice, direct injection of ciglitazone into A549-induced tumors suppressed the rate of tumor growth by 36%. Thus we got the driving force from all these facts for the synthesis of heterocyclic thiazolidinedione through a novel synthetic
scheme staring from the basic nucleus. Finally the objective and plan of the present work was:

1. The primary objective of the present work was to successfully develop most convenient and economical route of synthesis of a variety of TZDs then the available synthetic routes and also to utilize such synthetic route to obtain a series of new TZDS.
2. Synthesized a new series of 5-[4-(N-(substituted amino) ethoxy) benzyl]-2, 4-thiazolidinedione derivatives having structural similarities to clinically useful thiazolidinedione’s (Pioglitazone and Rosiglitazone).
3. Explored the possibility of replacing the ethoxy moiety of Rosiglitazone with sulphonamide moiety or with alkoxy moiety, which seriously showed anticancer activity.
4. Biological evaluation of the synthesized compounds in respect of antitumor activity and any potential toxicity is done.
5. Characterization of the synthesized compounds was done by using UV, IR, NMR, CMR, Mass, elemental analysis, and also through Chromatography.

Finally I conclude that my present work has shown a promising synthetic scheme as well as anticancer activity. Future prospective of are to develop QSAR model, Pharmacophore Study as well as docking using V-Life software.

**KEYWORDS:** “Apoptosis, breast cancer, colon cancer, growth/cell cycle arrest, PPAR-γ, tumor suppression, TZDs, lung cancer”.

41. HERBAL APPROACH IN THE CANCER TREATMENT
Padate S. Mazgaonkar L., Pawar P., Shri. D.D. Vispute College of Pharmacy and Research Center, Gut No. 104, Devad, Vichumbe, Taluka - Panvel. District Raigad, Email id: latika_mazgaonkar@yahoo.com

**INTRODUCTION:** Cancer is a term used for diseases in which abnormal cells divide without control and are able to invade other tissue. Cancers may be caused in one of three ways, namely incorrect diet, genetic predisposition, and via the environment. According to a report of World Health Organization, more than 80% of world’s populations depend on traditional medicine for their primary health care needs. Plants have a long history of use in the treatment of cancer. Herbals have been screened for anticancer activity and many patients with cancer take plant extracts in addition to chemotherapy.

**Curcumin: Biological Source:** Curcumin, a yellow coloring ingredient derived from *Curcuma longa* L. (Family: Zingiberaceae) the most extensively investigated and well-defined chemo preventive phytochemicals Curcumin, is one of the most extensively investigated and well-defined chemo preventive phytochemicals. Curcumin has been shown to protect against skin, oral, intestinal, and colon carcinogenesis and also to suppress angiogenesis and metastasis.
**Mechanism of action:** Curcumin has a capability to inhibit carcinogen bio activation via suppression of specific cytochrome P450 isozymes, as well as to induce the activity or expression of phase II carcinogen detoxifying enzymes. It also inhibits the proliferation of cancer cells by arresting them in the various phases of the cell cycle and by inducing apoptosis. Curcumin has been shown to elicit vital cellular responses such as cell cycle arrest, apoptosis, and differentiation by activating a cascade of molecular events.

**Composition of turmeric:** Turmeric contains a wide variety of phytochemicals, which includes curcumin, demethoxy curcumin bisdemethoxycurcumin, zingiberene, curcumeno1, curcumol, eugenol, tetrahydrocurcumin, triethylcurcumin, turmerin, turmerones, and turmeronols. Among these curcumin has been highlighted for its anticancer activity.

**Cancer therapy using Curcumin:** Curcumin are used in various types of cancer such as skin, oral, esophageal, intestine, colon, breast, liver, brain, and blood. Here we have focused on skin cancer. Skin cancer is a disease in which cancer (malignant) cells are found in the outer layers of skin. Most skin cancers are classified as non-melanoma, usually occurring in either basal cells or squamous cells, and melanoma, cancer that begins in the melanocytes. Curcumin was previously described as a good ant angiogenesis agent. Curcumin has inhibitory effects against VEGF, angiopoietins1 and 2, tyrosine kinase Flk-1/KDR (VEGF receptor-2).

**CONCLUSION:** A wide variety of natural compounds appear to possess significant cytotoxic as well as chemo preventive activity. Naturally occurring compounds that are included in the diet are non-toxic and may partially regulate programmed cell death in several tissues and organs. The use of natural products holds promise for the effective targeting to cancer cells specifically of highly while avoiding toxicity to normal cells.

**REFERENCES:**

**42. OPPORTUNITIES IN DISCOVERY AND DELIVERY OF ANTICANCER DRUGS TARGETING MITOCHONDRIA**

Katare P.B., Bhusnure O.G., Poul B.N., Mulje S. S., Rathod A.V., Maharashtra College of Pharmacy, Dept. of Pharmaceutical Chemistry, Nilanga, Dist -Latur, M. S., India

**ABSTRACT:** Mitochondria are often described as the powerhouse of the cell. It also plays a central role in apoptosis, or programmed cell death, which is closely related to the loss of physiological functions of tissues. Mitochondrial processes play an important role in tumor initiation and progression. Alterations in cellular bioenergetics are an emerging hallmark of cancer. The mitochondrion is the major organelle implicated in the cellular bioenergetics and biosynthetic changes accompanying cancer. These bioenergetics modifications contribute to the invasive, metastatic and adaptive properties typical in most tumors. Moreover, mitochondrial DNA mutations complement the bioenergetics changes in cancer. In connection of this, three critical processes by which mitochondrial function may contribute to
cancer: through alterations in glucose metabolism, the production of reactive oxygen species (ROS) and compromise of intrinsic apoptotic function. Many distinct differences in mitochondrial structure and function between normal cells and cancer cells offer the potential for the clinical use of mitochondria as targets for novel and site-specific anti-cancer agents. Tumor cells are more prone to mitochondrial perturbations than normal cells due to extensive metabolic reprogramming. There are active research programs investigating drugs that specifically target the mitochondria. The unique structural and functional characteristics of mitochondria provide a number of primary targets for xenobiotic-induced bioenergetics failure, which also provide opportunities for selective delivery of drugs to the mitochondrion. The world of mitochondrial medicine can be open up by using intrinsic properties of mitochondria (a motor of cell-death), which are essential for efficient production of energy by this powerhouse of the cell. Since desired effect of any targeted drug or gene delivery can be achieved only if bioactive molecule is delivered to the destined organ and/or cell type, and also to the desired location within the cell. To achieve specificity of target, more efficient and selective delivery vehicle should be constructed so that they can transport bioactive molecule to the desired site of mitochondria. Engineering of such mitochondria selective homing devices is now a subject of current interest for controlled delivery of bio actives to mitochondria. Mitochondrial therapy may be successful by constructing such vehicles and/or carrier systems which deliver the drug/DNA to the mitochondria of specific cell that is in pathological state. An important point for future drug discovery resides in the fact that many of the known agents that target mitochondria are derived from natural compounds and have been identified by serendipity rather than by systematic screening methods. This implies that a systematic global screening approach aimed at specifically identifying mitochondria-targeting drugs from large libraries of natural substances will most likely present a treasure trove for anticancer drug discovery. This review provides an overview of the potential anticancer agents that act by targeting cancer cell mitochondria, and also brings us face to face with the emerging opportunities in cancer therapy

**KEYWORDS:** “Mitochondrial medicine, Drug discovery, Drug Delivery, Anticancer strategies”

**43. DIABETES AND ITS RELATION WITH CANCER**

Nalavade V., Patel D., Mhatre A., Rao S.,
Vivekanand Education Society’s College of Pharmacy, E-mail: dhararp@gmail.com

**KEYWORDS:** Hyperinsulinemia, Hyperglycemia, metformin, sulfonylurea, pioglitazone, DPP - 4 inhibitor, SGLT2 inhibitor

**OBJECTIVES:** Numerous studies have identified an increased risk of cancer in type 2 Diabetes. We have explored the association between anti-diabetic therapies and cancer related mortalities in patients with Type 2 Diabetes, postulating that agents that increase insulin level can cause cancer. For the 200 million diabetics worldwide, the past few years have brought some disturbing findings about risks that may be associated with certain diabetes drugs. Diabetes doubles the risk of liver, pancreas, and endometrial cancer. It increases the risk of colorectal, breast, and bladder cancer by 20% to 50%. A common thread for many of these risk factors is hyper insulinemia. Insulin induces cell proliferation.
Hyperinsulinemia, insulin resistance, and obesity are associated with increased estrogens, endometrial hyperplasia, and breast and endometrial cancers. Hyperglycemia may be responsible for excess glucose supply to these glucose-hungry cells, resistance to apoptosis, oncogenes, and tumor cell resistance to therapy. Moreover, hyperglycemia correction has yet to show reduction in cancer incidence in people with type 2 diabetes. Hyperglycemia and hyperinsulinemia are associated with endothelial proliferation and neovascularization (in the retina). Vascular growth is essential to the fuel supply required for malignancy maintenance. Therefore, it is conceivable that vascular growth is stimulated in people with type 2 diabetes, thus promoting cancers. Metformin, the most commonly used diabetes drug, seems to lower cancer risk. Metformin, the most commonly used diabetes drug, seems to lower cancer risk. But there's also evidence from some studies -- contradicted by others -- that insulin, particularly long-acting insulin glargine (Lantus), may increase cancer risk. 25% reduced risk for developing cancer when patients with type 2 diabetes used metformin. Pioglitazone (insulin sensitizers) is a prescription drug of the class thiazolidinedione (TZD) with hypoglycemic (ant hyperglycemic, anti-diabetic) action. Pioglitazone is used for the treatment of diabetes mellitus type 2. The US FDA announced that pioglitazone use for more than one year may be associated with an increased risk of bladder cancer. Dapagliflozin- Nine cases of bladder cancer occurred in male patients who took dapagliflozin. Breast cancer occurred in nine patients who took dapagliflozin, and one patient in the control group. Dapagliflozin would be the first in a new class of treatments called SGLT2-inhibitors that work by letting patients excrete excess blood sugar in their urine. Sulfonylurea- These diabetes pills lower blood sugar by stimulating the pancreas to release more insulin. Patients with type 2 Diabetes exposed to sulfonylurea and exogenous insulin had a significantly increased risk of cancer-related mortality compared with patients exposed to metformin Sulfonylurea leads to hyperinsulinemia which is a risk factor for cancer. Dpp-4 Inhibitors of dipeptide peptidase 4, also DPP-4 inhibitors or gliptins, are a class of oral hypoglycemic that block DPP-4. They can be used to treat diabetes mellitus type 2. Although one in vitro study found that DPP-4 inhibitors, together with GLP-2, increased proliferation and migration of colon cancer cells, which might encourage cancer cells to metastasize.

REFERENCES:
1. British Medical Journal
2. Michels KB, Solomon CG, Hu FB, Rosner BA, Hankensen SE, Manson GE: Type 2 Diabetes and subsequent incidences of Breast Cancer in nurses.
3. CA Cancer J Clin 2010; 60: 207-221 by the American Diabetes Association and American Cancer Society

44. ONCOPROTEOMICS: NEW TRENDS IN ANALYTICAL TECHNIQUES

ABSTRACT: Disease incidence of cancer and its associated mortality are increasing globally, indicating an urgent need to develop even more effective and sensitive sets of techniques that could help in early diagnosis and consequent intervention. Oncoproteomics is the study of proteins and their interactions in a cancer cell by proteomic technologies and
has the potential to revolutionize clinical practice, including cancer diagnosis and screening based on proteomic platforms as a complement to histopathology, individualized selection of therapeutic combinations that target the entire cancer specific protein network, real-time assessment of therapeutic efficacy and toxicity, and rational modulation of therapy based on changes in the cancer protein network associated with prognosis and drug resistance. Technology is also applied to the discovery of new therapeutic targets and to the study of drug effects. The study of oncoproteomics provides mankind with a better understanding of neoplastic. Considerable progress has been made during the past decade in the refinement of proteomic technologies and their application for understanding the disease's pathological mechanisms, discovery of biomarkers and diagnosis. Proteins can be identified from the blood or directly from the tumor tissue by laser capture micro dissection (LCM) and tissue microarrays. Protein biochips can be used for diagnosis as well as monitoring in clinical trials. Nano biotechnology has refined the use of proteomics and Nano proteomics and has improved most current protocols including protein purification/display and automated identification of protein traces in minute samples. Due to some limitations, proteomics alone is not enough to provide a complete picture of cancer. Other "-omics" technologies such as genomics are used in integrated approaches. An immediate goal of proteomic studies is the understanding of proteins including their expression, function, interaction and structure with an endpoint of discovery of protein biomarkers. Such biomarkers can be used in detection, prognostication and treatment of many diseases. A new sub discipline named clinical proteomics, concomitant with new molecular technologies, which are developed, demonstrates promise to discover new cancer biomarkers. The present review focuses on the role of antibody microarrays in oncoproteomics and its potential to provide a truly proteome-wide analytical approach.

KEYWORDS: “Oncoproteomics, Analytical approach, Biomarkers, Diagnosis”.

45. PLANT-DERIVED CANCER VACCINES: A NEW APPROACH TO INTERNATIONAL PUBLIC HEALTH


ABSTRACT: With the advent of modern molecular biology techniques in the 1980s, new strategies were developed for the production of subunit vaccines. These are vaccines comprised of proteins derived from pathogenic viruses, bacteria or parasites; in general the proteins are produced not by the pathogens themselves, but by expression of the gene encoding the protein in a "surrogate organism." In the last decade we have learned that green plants also be used as the "surrogate production organism" to produce antigens of human pathogens (including HBsAg), and that these proteins can elicit priming and boosting immune response in humans when given orally. In addition, unlike almost all other cell lines used for production of vaccines, components of plant cells have always been an important part of the normal human diet. Plants, therefore, offer significant new opportunities for making safe and effective oral cancer vaccines. The vaccines must address the need for lower costs, oral-activity, heat stability, and mucosal effectiveness, and they must include combination vaccines and those that protect against diseases. An exciting vision is to use transgenic plants as very low cost, highly-efficient production systems, especially suitable for
initial development and production in developing countries, of orally-active antigens that will be prepared for oral administration, controlled to meet appropriate regulatory requirements, and supplied as safe and effective vaccines. The continuing, intensive efforts are under way to develop effective vaccines for AIDS, cancer, malaria, tuberculosis, dengue, leishmaniasis, and enteric diseases, among others and to adapt new technologies to improved formulation and delivery. Plant-derived Vaccine development proceeds through discovery, process engineering, toxicology and animal studies to human Phase I, II, and III trials. The results of the pre-clinical and clinical trials of plant-derived vaccines and therapeutic proteins described in this review hallmark the potential of plants to become oral delivery vehicles for vaccines. This review will address issues relating to the commercial development of plant-derived vaccines, and especially their usefulness in preventing infectious diseases.

**KEYWORDS:** “Edible vaccine, transgenic plant, Therapeutic value”

---

**46. SYNTHESIS AND ANTI-MICROBIAL ACTIVITY OF 2-PHENYL QUINAZOLINE -4(3H)-ONE FUSED SCHIFF BASES**

Omprikash G. Bhusnure1, Yeshwant B.Vibhute2, Bhagwat N.Poul1, Shaikh P.H.1  
1Dept.of Pharmaceutical Chemistry, Maharashtra College of Pharmacy, Nilanga - 413 521, Dist. Latur (MS), India, 2P.G. Department of Chemistry, Yeshwant Mahavidyalaya, Nanded-431 602 (MS) India

**ABSTRACT:** A series of Schiff base of 2-phenyl-quinazolin-4(3H)-one have been synthesized from novel quinazoline, 3-[4-(4-aminobenzenesulfonyl)phenyl]-2-phenylquinazolin-4(3H)-one. The novel quinazolinone were prepared by reacting 2-phenyl-4H-3,1-benzoxazin-4-one with dapsone. The prepared quinazoline, 3-[4-(4-aminobenzenesulfonyl)phenyl]-2-phenylquinazolin-4(3H)-one was condensed with various substituted aromatic aldehyde in DMF in the presence of glacial acetic acid as a catalyst under conventional heating and microwave irradiation to yield the Schiff bases respectively. The microwave assisted reaction was remarkably successful with higher yield less reaction time as well as environmental friendship reaction in organic synthesis compared to conventional heating method. Spectral data (IR, NMR and Mass spectra) confirmed the structures of the synthesized compounds. All the synthesized products are screened for their in vitro antibacterial and antifungal activity. The results indicated that the synthesized compounds have potent antimicrobial activity with reference to their appropriate standard.

**KEYWORDS:** “2-phenyl-4H-3,1-benzoxazin-4-one, Conventional heating, Microwave irradiation method, Anti-microbial activity”.

---

**47. NANOROBOTS: NOVEL TECHNOLOGY FOR CANCER THERAPY**


**ABSTRACT:** Human knowledge, with all its growth and development, is still in its initial stages of finding efficient ways to treat cancer. The elevated number of cancer patients puts cancer treatment amongst the top priority of scientific research facilities. The advent of nanotechnology opens new windows that promise effective ways in locating the chemical
sources, tracking them, controlling the cancerous cells, and finally terminating them. Due to the fast growth of the cancer cells, the healthy cells cannot compete for adequate nutrients, and will eventually be replaced by tumor cells. After a tumor develops, only the cells in the outer surface will have access to nutrients, so the inner ones will perish. At some point the tumor growth rate will reach a steady state where the rate of cell death will equal the rate of cell proliferation, and stay in steady state until the tumor finds better access to the circulatory system. A decisive factor in determining the patient’s chance of survival is how early the cancerous cells are detected. A Nano robot capable of performing these tasks needs to have certain tools and technologies, such as sensors, actuators, data transmitters, power supply, etc. As a result, the hardware architecture for Nano robots in cancer therapy has evolved into an innovative field of engineering, where the goal is to fit the most capable of sensors and actuators within the least amount of space possible. The main manufacturing technique in early Nano robot sensor design takes advantage of the high precision technology of CMOS (Complementary Metal Oxide Semiconductor) VLSI (Very Large Scale Integration) system design. CMOS-based biosensors use nanowires as material for their circuit assembly. They can detect minimal chemical changes, such as E-cadherin and beta-catenin gradients, which can serve as chemical targets for detection of early metastatic phases. The most important benefit of using Nano robots to treat cancer is the smart drug delivery. The major cancer treatment cycle for chemotherapy can take up to several months, with two-week radiation cycles needed to treat small tumors. In these sessions, even the healthy cells surrounding the tumor are exposed to radiation, which brings numerous chemotherapy side effects. Nano robots will be able to detect the cancerous cells within one week and perform localized drug delivery once they encounter the tumor cells. As nanotechnology further shrinks the size of these Nano robots while adding on to their technical capacity, it is not far from reality that these agents will soon replace chemotherapy. These smart robots will browse through the human body, search for the tumor cells, and either labels the target cells and transmits the proper signals to the surgeon, or deliver the drug preinstalled in them, and thus eliminate the tumor.

**KEYWORDS:** Nano robots, Smart drug deliver, Detection of cancer

48. DETERMINATION OF THE MOLECULAR STATUS BY bcr-abl RT-PCR IN CHRONIC MYELOID LEUKEMIA PATIENTS ON IMATINIB MYESELATE

Geeta Sadani *, Purvish Parikh, Pratibha Amre, Nandini Negi, Amish Vora, Balkrishna Mishra, P S R K Sastry and Hari Menon, *Department of Biotechnology, G N Khalsa College, Matunga, Mumbai 19, Department of Medical Oncology, Tata Memorial Hospital, Parel, Mumbai 12.

**ABSTRACT:** Chronic myeloid leukemia (CML) is a myeloproliferative clonal disorder of the primitive hematopoietic stem cells characterized by the accumulation and expansion of white cells. CML is characterized by balance reciprocal translocation t (9; 22), the Ph chromosome. This translocation results in the fusion of the bcr gene on chromosome 22 with the c-abl gene on chromosome 9 giving rise to a novel chimeric bcr-abl gene whose fusion protein has deregulated tyrosine kinase activity. This plays an important role in the pathogenesis of CML. The standard treatment for CML so far has been myleran, hydroxyurea, interferon and bone marrow transplantation. The discovery of Imatinib
myeselate in 2001 as a specific drug targeted towards the inhibition of tyrosine kinase activity has revolutionized the treatment of CML. This results in sustained hematological as well as molecular response, and hence has a potential to cure CML.

**KEYWORDS:** CML, PCR, Imatinib mesylate, MRD.

**OBJECTIVES:** During the last decade, a large number of studies have shown that the detection of very low numbers of malignant cells i.e. detection of minimal residual disease (MRD) significantly correlates with the clinical outcome in hematological malignancies. Thus the detection of MRD was taken up for 75 CML patients treated with Imatinib myeselate at the intervals of 1 year, 1 ½ years, 2 years and 2 ½ years. The number of malignant cells post treatment are very low hence a nested PCR was standardized for its high sensitivity and specificity to detect bcr –abl. The comparison of PCR method with the conventional cytogenetic was undertaken for evaluating its use in determining the molecular status in CML.

**INTRODUCTION:** Chronic myeloid leukemia (CML) is a myeloproliferative clonal disorder of the primitive hematopoietic stem cells characterized by the accumulation and expansion of white cells. In India, it accounts for 20% of all leukemia’s. It is seen between the ages of 35-45 years. The disease commonly presents in the initial chronic phase (CML-CP), there is often an intervening period of relative resistance to therapy called accelerated phase (CML-AP) and will terminally develop plastic crisis (CML-BC). The formation of Philadelphia (Ph) chromosome is either the first or second change in the evolution of CML-CP. Very little is known about the subsequent genetic changes that are acquired during the evolution of CML-BC. CML was the first acquired disease in which a consistent chromosomal abnormality was detected. The cytogenetic hallmark of CML Ph chromosome formed by a reciprocal translocation between chromosome 9 and 22 t(9;22)(9q34.1;22 q11.21). The translocation results in the fusion of the abl gene on chromosome 9 with the bcr locus on chromosome 22 to generate the hybrid bcr-abl oncogene were elucidated by molecular cloning. The bcr-abl gene transcribes into p210 transcripts (b2a2 and b3a2) of different sizes. The gene encodes a 210 KD oncoprotein (p210 bcr/abl) that exhibits unregulated and constitutive abl kinase activity. The protein by phosphorylation leads to the activation of signal transduction cascades affecting growth and differentiation. This results in enhanced cell proliferation, transformation and prevention of apoptosis. The conventional treatment of CML is busulfan, hydroxyurea the dosages used needs to be titrated according to the WBC count. Interferons are biological response modifiers that have changed the outlook for patients with CML. They can reduce and even eliminate the Ph positive clone to induce complete remission. The standard curative therapy for CML is allogeneic bone marrow transplantation. The identification of the role played by bcr-abl in the pathogenesis of CML at the molecular level paved the way for successful therapy by rational drug designing. After a painstaking research in this area, an inhibitor of Abl kinase named STI -571 (Gleevec) was identified as promising candidate which revolutionized the treatment of CML in early 1999. This drug was found to be highly lethal to CML cells while sparing normal cells. After clinical trials showing it to be remarkably effective in treating CML despite some side effects it was approved by FDA in 2001. It is the first cancer drug targeted to a signal transduction protein unique to tumor cells. Imatinib myeselate a derivative of 2-phenylamino pyrimidine, acts as an antagonist to the tyrosine kinase activity by occupying the ATP binding pocket of the SH domain in the chimeric protein, thereby preventing the phosphorylation of tyrosine residues
on substrate in the signal transduction pathway. This results in sustained hematological as well as molecular response, and hence has a potential to cure CML. The goals of successful therapy are to achieve complete hematological response, cytogenetic response and molecular remission. During the last decade, a large number of studies have shown that the detection of very low numbers of malignant cells i.e. detection of minimal residual disease (MRD) significantly correlates with the clinical outcome in hematological malignancies. MRD detection is now being routinely implemented in several treatment protocols and is increasingly used for guiding therapy. As imatinib myeselate acts at the molecular level, the detection of \textit{bcr- abl} serves as a good marker for determining molecular remission. Post treatment the amounts of \textit{bcr-abl} present are very low hence the need for a sensitive and specific method is of utmost value. Conventional karyotyping has been used to monitor residual disease. The advantage is unambiguous identification of Ph positive cells. However metaphase analysis by conventional banding techniques is a laborious and time consuming. Also the success depends on the number of metaphases that can be examined and on the proliferative rate of the leukemic cells. An experienced Cytogenetic is required for analysis. RT-PCR is the most sensitive method and can discriminate closely related mRNAs. The sensitivity of detection can be increased with nested primers making it a highly useful in detection of MRD post imatinib myeselate treatment in patients with CML. Thus the detection of MRD was taken up for 75 CML patients treated with Imatinib myeselate at the intervals of 1 year, 1 ½ years, 2 years and 2 ½ years by nested PCR. The nested PCR and conventional cytogenetic was also carried out in parallel to compare the efficiency of detection by the two techniques.

**EXPERIMENTAL METHODS:**

1) **Samples:** BM/ PB samples of CML patients treated with imatinib misrelate at different time intervals were as follows:

<table>
<thead>
<tr>
<th>TIME INTERVAL (yrs.)</th>
<th>1</th>
<th>1.5</th>
<th>2</th>
<th>2.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>CML-CP</td>
<td>34</td>
<td>16</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>CML-AP</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>37</td>
<td>22</td>
<td>13</td>
<td>3</td>
</tr>
</tbody>
</table>

2) **Techniques:** *Nested PCR:* RNA was extracted by TRIZOL and cDNA was prepared by Superscript II with random primers. The cDNA was then subjected to two rounds of PCR with the primers to yield the transcripts b2a2 and b3a2 which were detected by agarose gel electrophoresis. A house keeping gene GAPDH was also determined by PCR to check the quality of cDNA synthesized.

*Cyto genetic:* BM aspirates was inoculated in 5 ml complete medium containing 0.5 \( \mu \)g/ml colcemid and incubated at 370 C for 30' in CO2 incubator. It was then centrifuged and 5 ml hypotonic KCl was added to the cell and incubates at 370 C for 15' & centrifuge at 1000 RPM for 10'. The cells were then fixed with Carnoy’s fixative. The step was repeated till a white pellet is obtained. Slides were then prepared & stain with conventional Giemsa. The metaphases were then scored for presence of Ph chromosome.
RESULTS:

- **NESTED BCR-ABL PCR**
- **HOUSE KEEPING GENE PCR**

### RESULTS:

**NESTED BCR-ABL PCR**

<table>
<thead>
<tr>
<th>PCR+ cytgen+</th>
<th>TIME INTERVAL (yrs.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>CML-CP</td>
<td>22</td>
</tr>
<tr>
<td>CML-AP</td>
<td>3</td>
</tr>
<tr>
<td>TOTAL</td>
<td>26</td>
</tr>
</tbody>
</table>

**HOUSE KEEPING GENE PCR**

<table>
<thead>
<tr>
<th>PCR + cytogen -</th>
<th>TIME INTERVAL (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>CML-CP</td>
<td>3</td>
</tr>
<tr>
<td>CML-AP</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>3</td>
</tr>
</tbody>
</table>

**DISCUSSION:** 64 cases were positive and 11 cases negative by PCR while 57 cases were positive and 18 cases negative by cytogenetics. The bcr –abl positive cases were found to be 85.4% with PCR and 76% by cytogenetics method. 70.6% cases were found to be positive for bcr-abl by both the methods. Bcr abl detection by PCR was comparable to the conventional method of cytogenetics used for determining MRD. Overall the performance of PCR was obviously better due to its high sensitivity and specificity and justifies its use in MRD. Our results indicate that the majority of our patients (64/75) continue to show molecular disease (by Nested PCR for bcr – c.abl) in spite of treatment with full doses of imatinib myeselate - being 68%, 91% , 100% and 100% respectively. Quantitation of bcr-abl transcripts by real time PCR more informative. It may also be useful in determining the base line values for MRD.

**CONCLUSION:** The present study highlights how the discovery of Philadelphia chromosome, the identification of critical bcr abl oncogene and its molecular action, resulting in development of a powerful new drug therapy and PCR technique as a sensitive and specific molecular tool for monitoring MRD in CML to achieve better disease management and enhance the potential of cure.
REFERENCES:

FEEDBACK
“C-CADD was a wholesome source of information about cancer, its nature, at molecular level as well as physiological and the various approaches studied and taken to curb it. It provided a foundation for us to learn and witness the various unthinkable scientific approaches studied to prevent this dreadful disease. The seminar has definitely created an impact of thought processes in our minds to face the challenge of making earth ‘cancer-free’.”

Ashok Ramakrishnan
(T. Y. B. Pharm.)

“The two day DST sponsored C-CADD conference was extremely useful and informative. The eminent speakers shared a lot of their research work and knowledge. I am glad that I was a part of the volunteering team and to be involved in its various activities. I was entrusted with the responsibility of escorting Dr. Saraf who was the chief guest of honor. So he shared his valuable knowledge and experiences on the way to college. The poster competition that was organised was very informative and a good opportunity to meet innovative minds.”

Sita Ganpathy
(First Year M. Pharm.)

“It was a privilege to attend C-CADD 2011. By attending the conference, we could update ourselves with the latest developments in the field of cancer research. Also, the poster competition that was held was really helpful as we could interact with some of the experienced people in cancer research and was a learnful experience throughout.”

Grishma Pawar
(Final Year B. Pharm.)
“Overall C-CADD was a great learning experience. It gave students a platform to showcase their technical skills via the poster presentation competition. It gave students a great deal of knowledge about the developments and progress in the field of cancer research.”

Ruchi Singh
(T. Y. B. Pharm.)

“Two days national conference on C-CADD was extremely informative and useful. It was a platform for updating ourselves with the current researches taking place in the field of cancer. I was a part of the Registration Committee. The response for the conference was overwhelming and it was a good opportunity to meet new researchers.”

Chaitali Surve
(First Year M. Pharm.)

“Cancer is a leading cause of deaths worldwide. This makes it very important to create platforms to connect scientists, researchers, doctors and students to discuss the latest developments in the field. C-CADD 2011 provided this platform. It was comprehensively informative and was a great learning experience. Also, the seminar was well-organised and acted a bridge between the Pharma students and Academia and the Researchers and Doctors in the field of Cancer.”

Swasti Pandey
(T. Y. B. Pharm.)
PHOTOGRAPHS
Coordinator welcoming the Chief Guest Dr. Saraf

Registration Desk
Dignitaries on the Dias during Inaugural Function

Lighting of lamp by Chief Guest Dr. Saraf
Key-note address by Dr. Kalpana Joshi, Nicholas Piramal

Lecture being delivered by Dr. Sharmila Bapat, NCCS Pune
Welcoming Dr. Girish Maru, Scientist, ACTREC

Inauguration of Poster Competition by Dr. Khale
Poster Evaluation by Dr. Girish Maru

Delegates enjoying the breakfast
Lecture being delivered by Dr. R. P. Gude, ACTREC

Delegates
Lecture being delivered by Dr. Supriya Mahajan, SNDT
Cancer-Comprehensive Approaches in Drug Discovery and Development

Lecture being delivered by Dr. Ramdasan Kuttan, Kerala

Lunch Break
Poster on Herbal anticancer agents

Poster Evaluation by Dr. R. P. Gude
Poster Evaluation Dr. R. Bajpai, Hinduja Hospital

Best Poster Award Distribution to the delegates
## GLOSSARY

2. Abhishek Rahim *Et Al.* 24 - 25
3. Santosh G. Jadhav *Et Al.* 25 - 26
4. Aniket Jadhav *Et Al.* 27
5. Priyanka Gandhi *Et Al.* 27 - 28
6. Parpiani Jaya *Et Al.* 29 - 30
7. R. Saiprasanth *Et Al.* 30 - 32
8. Karnik R.N. *Et Al.* 32 - 33
9. Sandbhor P. S. *Et Al.* 33 - 34
10. Sridhar V. *Et Al.* 34 - 36
11. Radhakrishnan R. *Et Al.* 36 - 37
12. Mehta Mitisha *Et Al.* 37 - 38
14. Shendge S. *Et Al.* 40 - 41
15. Hake D. *Et Al.* 41 - 42
17. Chaudhari B.N. *Et Al.* 43 - 44
18. Ramakrishnan. A. *Et Al.* 44 - 45
19. Pandey S. *Et Al.* 45 - 47
20. Ruchi .S. *Et Al.* 47 - 48
21. Anaita L. *Et Al.* 48 - 49
22. Anjana Viswanathan *Et Al.* 49 - 50
23. Harkal Kailas M. *Et Al.* 50 - 52
25. Rao A. *Et Al.* 53 - 54
27. Gupte Somesh *Et Al.* 56 - 57
<table>
<thead>
<tr>
<th></th>
<th>Authors</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>Hingane N. Et Al.</td>
<td>57</td>
</tr>
<tr>
<td>29</td>
<td>Shetty A. Et Al.</td>
<td>58-59</td>
</tr>
<tr>
<td>30</td>
<td>Dr. Aruna Jadhav Et Al.</td>
<td>59-61</td>
</tr>
<tr>
<td>31</td>
<td>Akshaya Pathare Et Al.</td>
<td>61</td>
</tr>
<tr>
<td>32</td>
<td>Nupur Joshi Et Al.</td>
<td>62</td>
</tr>
<tr>
<td>33</td>
<td>Hindlekar D. Et Al.</td>
<td>62-63</td>
</tr>
<tr>
<td>34</td>
<td>Deweshri Kerzare Et Al.</td>
<td>63-64</td>
</tr>
<tr>
<td>35</td>
<td>Gadkari Y. Et Al.</td>
<td>64-65</td>
</tr>
<tr>
<td>36</td>
<td>Bhatt K. Et Al.</td>
<td>66-67</td>
</tr>
<tr>
<td>37</td>
<td>Waghmare Ashwini Et Al.</td>
<td>67-69</td>
</tr>
<tr>
<td>38</td>
<td>Shirkar Pranav Et Al.</td>
<td>70-71</td>
</tr>
<tr>
<td>39</td>
<td>Jain Darshana S. Et Al.</td>
<td>71-73</td>
</tr>
<tr>
<td>40</td>
<td>Meenu D. Jain Et Al.</td>
<td>73-74</td>
</tr>
<tr>
<td>41</td>
<td>Mazgaonkar L. Et Al.</td>
<td>74-75</td>
</tr>
<tr>
<td>42</td>
<td>Katare P.B. Et Al.</td>
<td>75-76</td>
</tr>
<tr>
<td>43</td>
<td>Patel D. Et Al.</td>
<td>76-77</td>
</tr>
<tr>
<td>44</td>
<td>Sabnis C.D. Et Al.</td>
<td>77-78</td>
</tr>
<tr>
<td>45</td>
<td>Korale G.D. Et Al.</td>
<td>78-79</td>
</tr>
<tr>
<td>46</td>
<td>Omprakash G. Bhusnure Et Al.</td>
<td>79</td>
</tr>
<tr>
<td>47</td>
<td>Shaikh I.A.S. Et Al.</td>
<td>79-80</td>
</tr>
<tr>
<td>48</td>
<td>Geeta Sadani Et Al.</td>
<td>80-84</td>
</tr>
</tbody>
</table>
Courses Offered:
1. B. Pharm.
2. M. Pharm. in Pharmaceutics
3. M. Pharm. in Quality Assurance

REACH TO US
Hashu Advani Memorial Complex, Behind Collector Colony, Chembur (E), Mumbai - 400 074
Tel. 022- 6114 4144/ 25543600, Fax: 022- 2554 3925
vespharm@yahoo.co.in / vescop@gmail.com, www.vesip.org

In the pursuit of academic excellence....