METAL OXIDE NANOPARTICLES AS ANTI-CANCER THERAPEUTIC AGENT

A

Thesis Submitted

To

Orissa University of Agriculture and Technology, Bhubaneswar

in Partial Fulfillment of the requirement of The Degree of

MASTERS OF SCIENCE IN CHEMISTRY

BY

DIBYAJYOTI DASH

Admission No.: 04 CHEM/18

DEPARTMENT OF CHEMISTRY

COLLEGE OF BASIC SCIENCE AND HUMANITIES

ORISSA UNIVERSITY OF AGRICULTURE AND TECHNOLOGY,
BHUBANESWAR- 751003

2020

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DEPARTMENT OF CHEMISTRY

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CERTIFICATE – I

This is to certify that the thesis entitled, "METAL OXIDE NANOPARTICLES AS ANTI-CANCER THERAPEUTIC AGENT" submitted in partial fulfillment of the requirements for the award of the degree of Master of Science in **CHEMISTRY** to the Orissa University of Agriculture and Technology, Bhubaneswar, is a faithful record of bonafide research work carried out by **DIBYAJYOTI DASH, Adm No: 04CHEM/18** under my guidance and supervision and that no part of thesis has been submitted for any degree or diploma or published in any form.

It is further certified that the help and sources of information availed of during the course of study have been duly acknowledged.

Place: Bhubaneswar
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CERTIFICATE – II

This is to certify that the thesis entitled, **"METAL OXIDE NANOPARTICLES AS ANTI-CANCER THERAPEUTIC AGENT"** submitted by **DIBYAJYOTI DASH** to the Orissa University of Agriculture and Technology, Bhubaneswar, in partial fulfillment of the requirements for the degree of master of science in chemistry, has been approved by the students' advisory committee after an oral examination on the same in collaboration with an External Examiner.

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ACKNOWLEDGEMENT

At the outset I take this opportunity to acknowledge all the persons whose help and support has made me complete this work successfully.

I express my sincere reverence, obligation and deepest sense of gratitude to my guide **Mr. Sirish Ranjan Panda, Department of Chemistry, College of Basic Science and Humanities, O.U.A.T, Bhubaneswar** for his keen supervision, help in every respect and encouragement throughout the period of this manuscript.

I am highly obliged to **Dr. Nandita Swain, H.O.D, Department of Chemistry, College of Basic Science and Humanities, O.U.A.T, Bhubaneswar** for his constant inspiration, guidance and encouragement during the period of work.

I express my sincere thanks to **Dr. Bikas Chandra Panda, Director, College of Basic science and Humanities, O.U.A.T, Bhubaneswar** for his guidance and encouragement.

I acknowledge, with highest sense of respect and regard to my father, mother, especially my brother for his constant inspiration and necessary help throughout the study period. I pay my heartfelt thanks to all my family members for their blessings, unwavering support, love and affection without which, I couldn't have come to this stage.

This acknowledgement would be incomplete without thanking all my seniors and my friends for their help, support and co-operation.

Last but not the least, I express my obligation to all the Faculties and staff of the **Department of Chemistry, College of Basic Science and Humanities, O.U.A.T**, for their guidance and their timely help.

At the end, I bow down my head to the Almighty whose Omnipresence has always guided and helped me to overcome all odds and inconvenience.

Place: Bhubaneswar
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CONTENTS

ABSTRACT

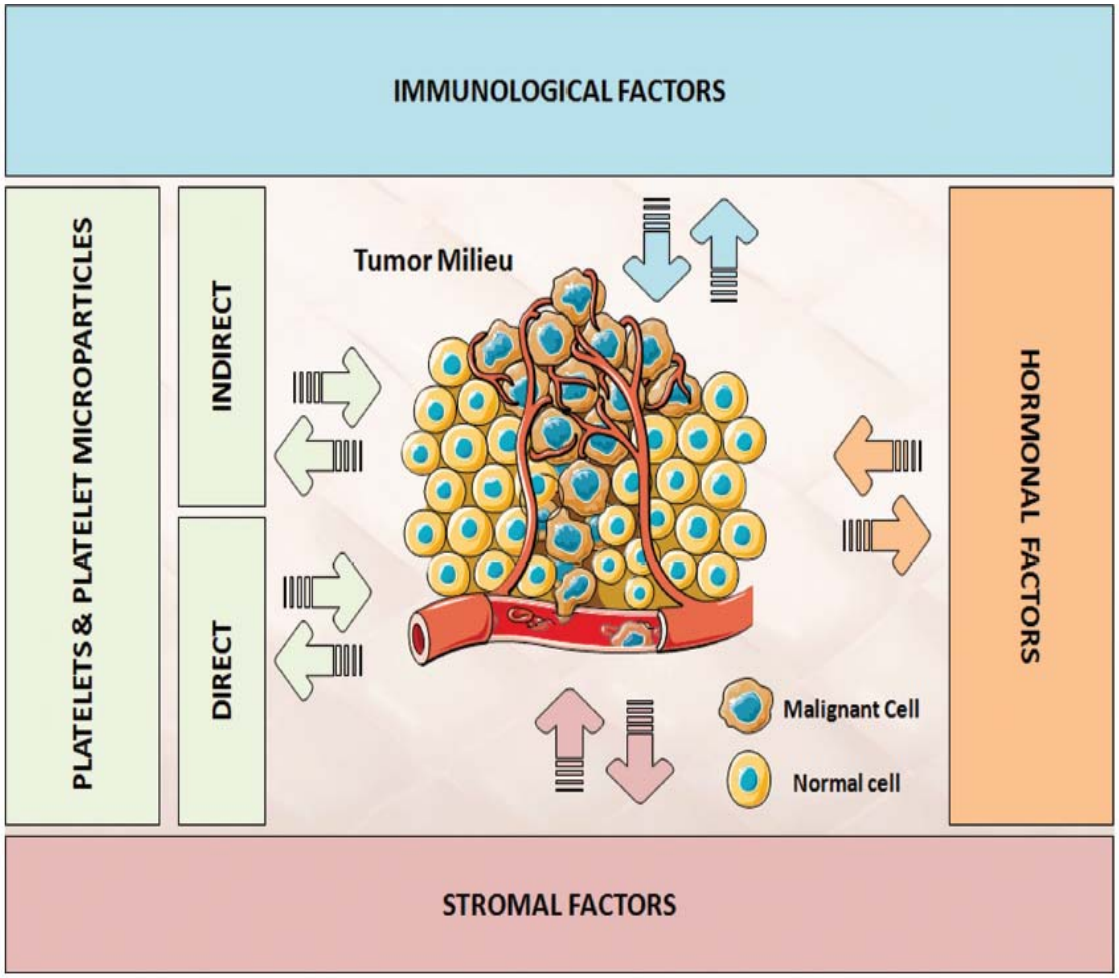
Cancer is known as one of the most notorious and deadly diseases, human kinds have ever faced on this earth. Many methods are implemented to eliminate this disease. Metal nanoparticles in recent days received significant research interest for their potential application in medical field for treatment of several deadly diseases including cancer. One of the most successful use of nanoparticle derived tools in recent years are nano-drug delivery devices. The use of such nanosized carriers to load therapeutic agents aid in overcoming their pharmacological and toxicological hurdles through site specific and controlled drug delivery. Conventional chemotherapeutics possess some serious side effects including damage of the immune system and other organs with rapidly proliferating cells due to nonspecific targeting, lack of solubility, and inability to enter the core of tumors resulting in impaired treatment with reduced dose and with low survival rate. In the other hand metal oxide nanoparticles can be programmed for recognizing the cancerous cells and giving selective and accurate drug delivery avoiding interaction with the healthy cells. Some metal nanoparticles also have differential cytotoxicity effect on normal cells and cancerous cells. They found to be toxic on cancerous cells and destroy only cancerous cells rather than normal cells. In this present thesis the implications of nanoparticles in treatment of several types of cancers is discussed. We present here about selective cancer targeting of different nanoparticles and how nanoparticles can be designed through various modification for targeting desired cells and how it succeeded in treating deadly disease like cancer.

Chapter I

Introduction

Introduction

Cancer is a deadly disease in which cell grows abnormally and divide uncontrollably causing destruction of normal body tissue. Cancer can result in tumors, damage to immune system and other impairment that can be fatal. Cancer cells do not die at the natural point in a cell's life cycle. Some types of cancer cause rapid growth while other causes cell to grow and divide at a slower rate [1-3]. Certain forms of cancer result invisible growths called tumors, while other such as leukemia does not. In 1980s many evidences began to emerge that a variety of viruses causes cancer in humans. There is now sufficient evidence of carcinogenicity in humans for human T-cell lymphotropic virus, human immune deficiency virus, hepatitis B virus, hepatitis- c virus, human papilloma virus, epestien barr virus, and human herpes virus8. According to the international agency for research on cancer (IARC) many other causes of cancer have also been identified by IARC, which include sunlight, tobacco, pharmaceuticals, hormones, alcohol, particles, fungi, bacteria, salted fish, wood dust and herbs. These carcinogenic and mutagenic stimuli, including environmental toxins, radiations and viral as well as other infections, results in cell bearing abnormal characteristics reported in a relatively important number of persons [4-6]. Tumors however can only if their complex tissue environment provides them with a suitable environment that can sustain their growth and spread. A complicated bidirectional interaction is therefore happening at the interface between the genetically unstable cancerous cell and their stable environment [7,8]. Hormone related cancers, namely breast, endometrium, ovary, prostate, testis, thyroid and osteosarcoma, share a unique mechanism of carcinogenesis. Endogenous and exogenous hormones drive cell proliferation, and thus the opportunity for accumulation of random genetic error. The emergence of malignant phenotype depends on a series of somatic mutations that occur during cell division, but the specific genes involved in progression of hormone-related cancers are currently unknown [9,10,11]. Now a day's nano particles are very much useful for the treatment of cancers [12,13]. Among them cerium dioxide and zinc dioxide are very much useful. Cerium dioxide nano particles due to its variable oxidation states between ce3+ and ce4+ act differently for normal cells and cancer cells. It has different cytotoxicity for normal cells and cancer cells. The other nanoparticles such as selenium oxide, silver oxide, gold nanoparticles etc. also used as drug delivery system in cancer treatments and can also be used for other biomedical applications [14,15].



Types of Cancer-

Cancer is the uncontrolled growth of abnormal cells anywhere in a body. There are over 200 types of cancer. Cancer symptoms and signs depends on the specific type and grade of cancer; although general signs and symptoms are not very specific and following can be found in patients with different cancers; fatigue ,weight loss, skin changes, change in bowel or bladder function ,unusual bleeding, persistent cough or voice changes, fever, lumps, or tissue masses[16,17]. There are so many types of cancers found in case of humans. These are the 10 common cancers in most humans such as- 1. Lung cancer, 2. prostate cancer. 3.Breast cancer, 4. colon cancer, 5.skin cancer 6. Bladder cancer, 7. Melanoma skin cancer, 8. Lymphoma ,9. Kidney cancer,10. Bone marrow cancer or leukemia.

What causes cancer

Cancer is caused by accumulated by accumulated damage to genes. Such changes may be due to chance or to exposure to a cancer-causing substance. The substance that causes cancer are

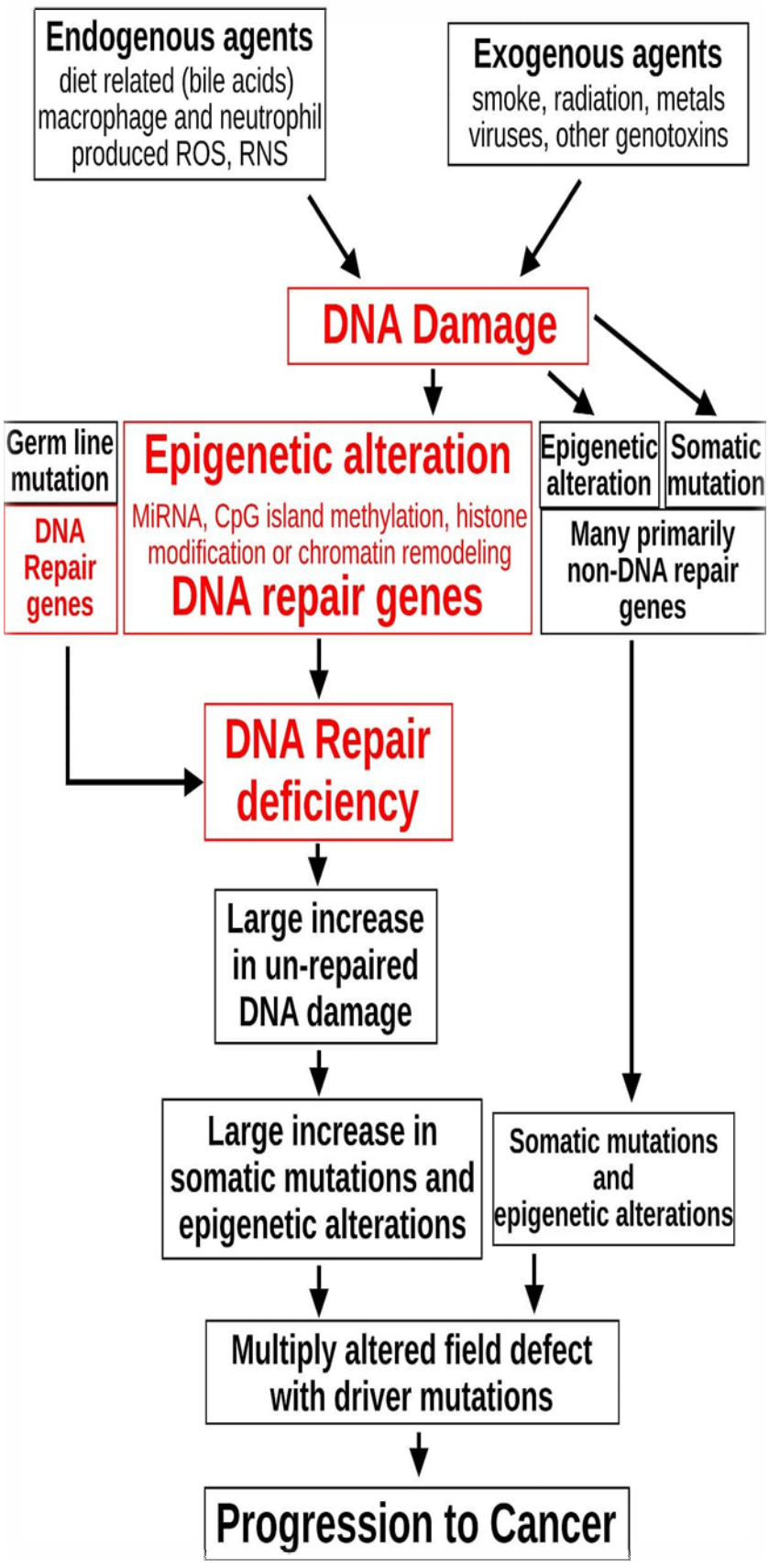
called carcinogens. A carcinogen may be a chemical substance, such as certain molecules in tobacco smoke. The cause of cancer may be environmental agents, viral or genetic factors. But the majority of cancer cases cannot be attributed to a single cause [18,19]. Cancer risk factors can be divided into following groups such as-

1. Biological or internal factors, such as age, gender, inherited genetic defects and skin type.
2. Environmental exposure, for instance to radon and UV radiation, and fine particulate matter.
3. Occupational risk factor, including carcinogens such as many chemicals, radioactive materials and asbestos.

_Biology of Cancer-

Cancer is a genetic disease. Most common cancers are caused by acquired mutation in somatic cells. In contrast, specific germline mutations account for rare hereditary cancer syndromes. In general, cancer associated genes can be divided into two groups i.e. oncogenes and tumor suppresser genes [TSGs]. Oncogenes undergo activation and are phenotypically dominant, while TSGs undergo inactivation and are phenotypically recessive. Oncogenic activation can occur by specific point mutations within the gene sequence, amplification of the number of copies of gene, or translation of DNA to sides where transcription is more active or where a new fusion gene is formed that endocodes a protein with enhanced biological activity. TSGs are inactivated by mutations that destroy the function of the protein encoded by the gene, or by silencing g the genes promoter. The biological behavior of cancer can be considered in terms of 8 specific hallmarks and two additional so-called enabling characteristics. Improved understanding of these processes has revolutionized diagnosis treatment and prognostication in cancer medicine [20].

Below the figure shows biology of cancer -

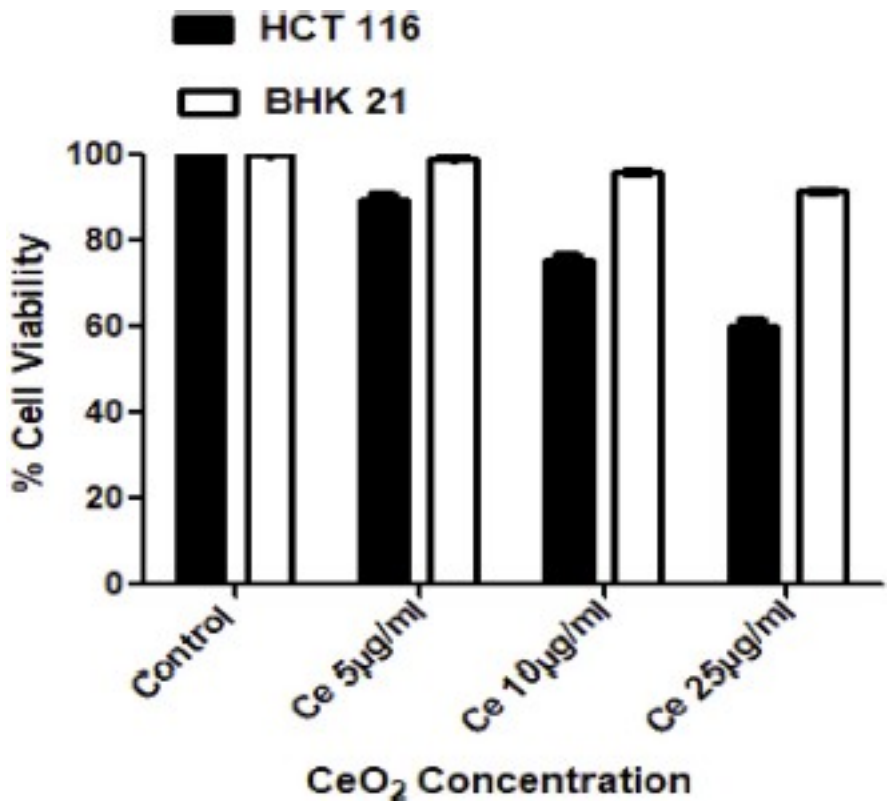

Endogenous agents
diet related (bile acids)
macrophage and neutrophil
produced ROS, RNS
Exogenous agents
smoke, radiation, metals
viruses, other genotoxins
DNA Damage
Germ line mutation
DNA Repair genes
Epigenetic alteration
MiRNA, CpG island methylation, histone modification or chromatin remodeling
DNA repair genes
Epigenetic alteration
Somatic mutation
Many primarily non-DNA repair genes
DNA Repair deficiency
Large increase in un-repaired DNA damage
Large increase in somatic mutations and epigenetic alterations
Somatic mutations and epigenetic alterations
Multiply altered field defect with driver mutations
Progression to Cancer

CHAPTER II

Treatment of cancer and use of nanoparticles in cancer therapy

Treatment of Cancer and Use of Nanoparticles in Cancer Therapy-

There are many types of cancer treatment. The type of treatment always depends upon the type of cancer and in which stage it is. Some people with cancer will have only one treatment. But most people have a combination of treatments, such as surgery with chemotherapy or radiation therapy. Recently, metal nanoparticles have drawn huge attention in cancer therapeutics and diagnostics [21,22]. Among them cerium oxide nano particles are very much effective. The cytotoxicity of CeO_2 nanoparticles was evaluated against cancerous and normal cell lines at different concentrations. Interestingly, in tested cell lines the nano particles exhibit negligible cyto toxicity in normal and significant toxicity in cancerous cells. When test was done by SR Panda and co-workers on human colon cancer cells HCT116 and BHK21 [Baby hamster kidney] cells i.e. normal cells then following results obtained at different concentrations of CeO_2 nano particles [23].



Not only cerium dioxide nano particles but also other nano particles such as gold, silver, selenium, zinc and may other nanoparticles also very much efficient in cancer treatment. They are used as drug delivery agent in cancer treatment. They are more efficient than other therapeutic methods. Nanoparticles provide a new mode of cancer drug delivery functioning as a carrier for entry through fenestrations in tumor vasculature allowing direct cell access [24,25]. These particles allow exquisite modification for binding to cancer cell membranes, the micro environment, or to cytoplasmic or nuclear receptor sites. This results in delivery of high drug concentration to the targeted cancer cell.

Nanotechnology in Cancer Targeting-

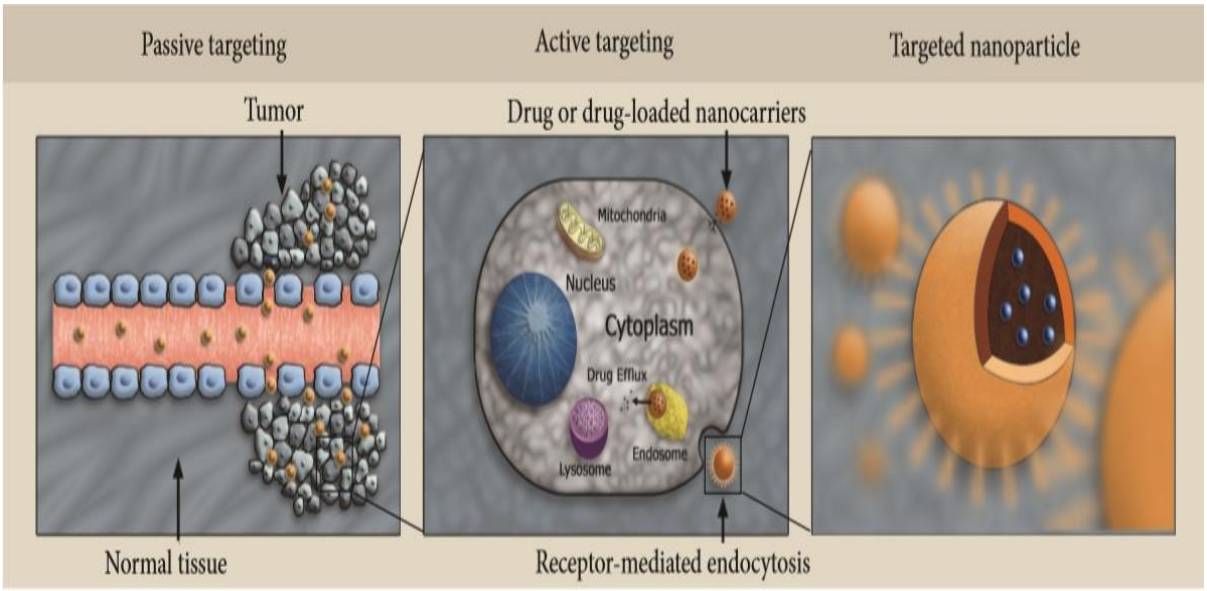
Nanotechnology has made a great revolution in selective cancer targeting. Nanoparticles can be designed through various modifications such as changing their size, shape, chemical and physical properties, and so forth, to programmed them for targeting desired cells. They can target the neoplastic cells either through active or passive targeting.

Active targeting - In case of active targeting, nanoparticles containing the chemotherapeutic agents are designed in such a way as they directly interact with the defected cells. Active targeting is based on molecular recognition. Hence the surface of nanoparticles is modified to target the cancerous cells. Usually, targeting agents are attached with the surface of nanoparticles for molecular recognition. Designed nano particles target the cancerous cells either by ligand-receptor interaction or either by antibody-antigen recognition [26]. Nanotechnology based targeted delivery system has three main components such as an apoptosis-including agent [anti-cancer drug], a targeting moiety-penetration enhancer, and a carrier. A variety of substances are used to construct nanoparticle. Commonly used material includes metals, lipids, polymers, and ceramic etc. [27]. A variety of strategies were developed to sustain the nanoparticles in blood stream one of which is the alternation of the polymeric composition of the career. Nanoparticles are coated with hydrophilic polymers to avoid washout and remain in blood stream for longer time that can sufficiently target cancerous cells. Cancerous cells have some unique properties that differentiate them from healthy cells at molecular level. Some receptors are over expressed on the surface of them that make the distinguishing feature. Attachment of the complementary ligands on the surface of nano particles makes them able to target only the cancerous cells [28,29]. Once the nano particles bind with the receptors, they rapidly undergo receptor mediated endocytosis or phagocytosis by cells resulting in cell internalization of the encapsulated

drug.

Passive targeting - Nano particles can also target cancer through passive targeting. As apoptosis is stopped in cancerous cells, they continue sucking notorious agent abnormally through the blood vessels from wide and leaky blood vessels around the cells induced by anagenesis. Leaky blood vessels are formed due to basement membrane abnormalities and decreased number of pericytes lining rapidly proliferating endothelial cells ranges from 100nm – 780nm [30,31]. Thus, nano particles bellow that size can easily pass through the pours as a result it facilitates to efflux the nanoparticles to cluster around the neoplastic cells [32]. Nano particles can be targeted to specific area of capillary endothelium to concentrate the drug within a particular organ and perforate the tumor cell by passive diffusion or convection. Lack of lymphatic drainage eases the diffusion process. The tumor interstitium is composed of collagen network and gel like fluid. The fluid has high interstitial pressure which resist the inward flux of molecules. Tumors also lack well defined lymphatic networks having leaky vasculature their fore drugs that enter the interstitial area may have extended retention time in the tumor interstitium. This feature is called the enhanced permeability and retention effect and facilitates tumor interstitial drug accumulation nano particles can easily accumulate selectively by enhanced permeability and retention effect and then diffuse into cells [33].

This figure shows active and passive targeting by nanoparticles.



CHAPTER III

REVIEW OF LITERATURE

Cerium Dioxide Nanoparticles in Treatment of Cancer-

There are so many studies on the treatment of several types of cancers using cerium dioxide as well as other nano particles. Milica Pesica and her co-workers also investigated about the anticancerous effect of cerium oxide nano particles. They used 10 nm CONP suspension which was prepared in ethanol and dispersed for 20 min by using a sanicator. Before treatment, CONP and cisplatin were freshly diluted in sterile water. Nanometric sized ceria powdered particles with fluorite type structure were obtained by applying self-propagating room temperature method using as starting materials nitrate of Ce and NaOH. Obtained powder was characterized by x-ray diffraction and by Raman spectroscopy [34]. The growth inhibition effects of CONP were studied in six different human cancer cell lines. CONP cytotoxicity in lung carcinoma cells was compared to normal fatal bronchial cells. It was shown that CONP was ineffective in normal cell lines and selective towards cancer cells [35].

From many experiments it was concluded that x-ray photoelectron spectroscopy and x-ray absorption near edge spectroscopy are used to investigate the oxidation state of cerium ions in ceria nano particles. Feng Zhang and co-workers prepared cerium oxide nano particles by mixing cerium nitrate and hexamethylene tetraamine in aqueous solution at room temperature. The prepared nano particles have been characterized by x-ray diffraction, high resolution trans mission electron microscopy, UV-visible light absorption and Raman scattering. The XPS samples were prepared by dispersing the ceria particles in a 10% poly vinyl alcohol, aqueous solution and spin coating the solution onto silicon wafers at 4000 rpm for 1 min. Xray photo electron spectroscopy was measured using an x-ray photo electron spectrometer with a monochromatic x-ray source of AlKα. In this experiment it is well accepted that 10 peaks appear for CeO_{2-x} in the Ce 3D XPS spectrum.[36] It was well known that ceria-based materials are famous for their redox properties, because of the conversion between Ce^{3+} and Ce^{4+} valence states under oxidation and reduction conditions with the help of in situ high temperature time resolved XRD studies, Rodrinuez showed the lattice parameter change of ceria based materials under oxidation and reduction. The Ce^{3+} concentration obtained from XPs core–shell model analysis is significantly larger than those obtained from other experiments. In this experiment it was also shown that the placement of ceria particles with in the XPS UV chamber and X ray radiation cause gradual reduction of Ce^{4+}. Here in, the concentration of Ce^{4+} decreased significantly after overnight storage inside the XPS chamber [37].

Ovarian cancer is the fifth most common cause of death from all cancers among women. Some experiments on these cancer cells concluded with the fact that it can be treated with nano technology and nanoceria is an amazing therapeutic modulator in treatment of ovarian cancer. S. Giri and his co-workers synthesized nano ceria by wet chemical synthesis. In this synthesis process cerium nitrate hexahydrate was dissolved in di ionized water and then filtered using a 200 nm filter paper to get rid of any freely suspending particulates. The solution containing cerium ions was then oxidized using hydrogen peroxide and ammonium hydroxide. Change in the oxidation state of the as prepared nano particles in solution was monitored using UV- visible spectrometry [38]. The oxidation states of cerium in the particles were confirmed using photo electron spectroscopy. Ros was determined using the membrane permeable fluorescent dye 6-carbonyl 2,7-di chloro di hydro fluorescin di-acetate. Cerium oxide nano particles used in this study contains individual crystallites of 3-5 nm that are loosely aggregated to 15-25 nm. As the synthesis process is free from any organic surfactant, the hard accumulation of nano particles is controlled by controlling the pH of the nano particles below 3.5 during synthesis to keep them in colloidal range. Cerium dioxide nano particles have been shown to act as free radical scavengers by inhibiting the production of reactive oxygen species. Since it is well established that ROs accumulation plays an important role in the initiation and the progression of tumorigenesis in human ovarian cancer [39]. Nano ceria treatment inhibits basal levels of oxidation stress in ovarian cancer cells but it remains un effective on the normal body cells.

Reprogramming to cancer stem cell kinetics was a very new technique in cancer therapy and many experiments were done towards this. Xvefen hao and his co-workers used an agent based cellular automata model to describe the behavior of individual cancer cell dependent on intrinsic mechanism of migration, proliferation and death. The domain is defined as a two- dimensional lattice under periodic boundary condition using a more neighborhood with radius of 1. A proliferative cell turns quiescent when it completely surrounded by other cells and can re-enter the cell cycle when a neighboring free space is available. Cancer stem and non-stem cells are considered [40]. As per the stem cell hypothesis cancer stem cells reside at the top of hierchy and give rise to progenitor cells which in turn give rise to the non-stem cancer cells. While cancer stem cells can duplicate for an indefinite amount of time, non-stem cancer cells are able to divide only a limited number of times. By monitoring the tumor population dynamics over time, it was concluded that in addition to a higher resistance, some non-stem cancer cells self-renewal was required to explain the reported non stem cancer cells function following a certain fractionated IR regimen [41].

However, emerging evidence shows that non stem cancer cells may not represent a stable cell type and that the stem like state may rises in differentiated tumor cells in certain conditions.

Due to their radical scavenging nature cerium oxide nanoparticles are used for various applications including drug delivery system and alternative chemotherapy agents. Numerous experiments are done to investigate several applications of cerium dioxide nanoparticles. Zorita Diaconeasa and her co-workers cerium dioxide nanoparticles and used it on lung carcinoma cells to investigate its effect on them [42]. CeO_2 NPs were synthesized at the room temperature in preparation method in this experiment. An aqueous cerium nitrate solution used as the cerium precursor and as precipitating reagent an excess of ammonia solution was used. The nanoparticles obtained in this experiment was studied using transmission electron microscopy (TEM). The chemical nature of the sample was estimated by Fourier transform infrared spectroscopy. The structure of CeO2 NPs was studied by X-ray diffraction. FT-IR spectroscopy was used for better understanding of the chemical nature of the nanoparticles. The obtained nanoparticles showed anti proliferative potential against lung carcinoma cells. Due to co- existence of Ce (3+) and Ce (4+) oxidation states those nanoparticles are involved in redox reactions which makes them to act distinctively against cancer and normal cells [43].

Osteosarcoma is an aggressive form of bone cancer. Nowadays many experiments are done for the treatment of osteosarcoma using cerium dioxide nanoparticles [44]. Christos Tapeinos and co- workers also did experiment on osteosarcoma cells applying pH-responsive microparticles with anti-tumoral properties as therapeutic modulators for osteosarcoma. The calcium carbonate therapeutic modulators were fabricated using a simple co precipitation method. The dispersion of CeO_2 nanoparticles and doxorubicin were added to the Na2CO3 solution and vortexed for 30s. The new dis person (Na_2CO_3+CeO_2NPs+doxorubicin) was added to the $CaCl_2$ solution under vigorous stirring and stirred for 30s. The therapeutic microparticles were collected by centrifugation at 500 rpm for 10s. Calcium carbonate microspheres has been used as a anti- cancer drug delivery system due to easy fabrication and pH sensitive properties. In this study it was explained that combination of calcium carbonate delivery system with versatile CeO_2 nanoparticles, could be used as pro oxidant or as an anti-oxidant agent depending on extracellular pH, and it can also be effective towards osteosarcoma cells as a therapeutic modulator [45].

The Multifaceted Activity of Cerium oxide Nanoparticles in Cancer Prevention and Therapy-

Cerium dioxide nanoparticles were well-known as cell protective agents, reducing oxidative stress through their unique property of scavenging reactive oxygen species. Expect the other application cerium dioxide nanoparticles could be used in treatment of several types of cancer. So many experiments prove the efficiency of cerium oxide nanoparticles on cancer cells. Francesca corsi and co-workers give some idea about the multifaceted activity of cerium dioxide nanoparticles. As a matter-of-fact, CNPs administration at the tumor site helps correcting micro environment homeostasis in animal cells. It includes restoration of a proper redox asset. Stroma changes occurring during tumor genesis include the trans differentiation of fibroblast into myofibroblast modulated by cytokinin such as tumor transforming factor betel released by tumor cells, implying on oxidative cascade [46]. CNPs toxicity issue was abundantly investigated, overall, CNPs are considered biocompatible agents, rapidly cleared from organs with very little toxicity. In fact, CNPs play a substantial role as protectors against induced damage.

Cerium oxide nanoparticles used is modulator in cancer treatment. They are used as the modifying agent for the recombinant tumor necrosis factor-alpha and recombinant tumor necrosis factor-alpha thymosin i.e. alpha-1(rh TNF and rh TNF-T). The antitumoral activity of these particles were demonstrated by O. Shydlovsk and his co-workers. In this research they used two different method of preparation of tumor necrosis factor (TNF) as model object i.e. Human recombinant tumor necrosis factor-alpha and recombinant tumor necrosis factor- alpha thymosin i.e. Alpha-1 cerium oxide nanoparticles were synthesized as an aqueous 0.1M solution [47]. The interaction of CNP with TNF and the formation of corresponding Nano bio composites should lead to an increase in the peptides hydrodynamic diameter (HD) was monitored by dynamic light scattering (DLS) method using a zeta sizer nanozs analyzer [48]. All measurements were performed at a constant temperature i.e. 25 degree Celsius and neutral media i.e. pH equal to 7.2. DLS data indicates that cerium oxide nanoparticles cause the increase of both rh-TNF-alpha and rh TNF-T hydrodynamic diameter. Investigation of the dependence of the biological activity of TNF and TNF + CeONP composites on the exposure time showed that the modification of therapeutic proteins with cerium oxide nanoparticles efficiently increase the biological activity of TNF-Alpha at various exposure times, with the most pronounced effect registered at 15minute exposure. The obtained rh-TNF+CeONP and rh TNF-T+CeONP nano bio composites have a stronger cytotoxic effect to malignant tumor cells than other

proteins [49]. The enhanced cytotoxic effect of this composites was confirmed by fluorescent microscopic study of stained cells.

In recent studies selenium dioxide nanomaterials comes out to be a very good anticancer agent and is used for treatment of many types of cancer including colorectal cancer. Olena Yu Yefilmenko and his co-workers investigate the effect of nanoceria on some rats. All rats were divided into four class as i. Control group, ii. Group which were injected 3 ml of water inter gastrically and iii. Rats which were injected 3 ml/kg stabilizing solution intra gastrically iv. Which were injected with nanoceria [50]. Rats maintained on hunger with free access to water. Motor activity of colon was registered by balanographic method in rats. In vivo studies of spontaneous gastric motility have shown that IMA was reduced by 21.1+0.2% in old rats of the control group compared with the young rats. A 10day administration of NCD increased IMA in the stomach of young rats by 9.3% relatively to the control group. Introduction of NCD also increased the mortar activity in stomach of the old rats. Thus, the effect of strengthening of IMA by NDD was almost twice higher in the old rats than in young. As NCD increase the mortar activity in colon in old rats it can prevent the accumulation of tumor and can be used as a good anti-cancer agent.

Recently many therapeutic strategies, such as chemo therapy (CHT), photo thermal therapy (PTT) and chemo dynamic therapy (CDT) have been used to fight against cancer. However single cancer treatment strategy cannot maximize therapeutic efficiency. Jiau Yan and his co- workers like many others experimented on nanoceria for synergistic tumor therapy. Silica nanospheres were synthesized by modified stobber method. Hallow CeO_2 NPs were prepared according to templet method. The product was collected by centrifugation and washed with water and ethanol for three times and dried at 50 degree Celsius for overnight cerium dioxide were deposited on the surface of silica followed by calcination. Hollow CeO_2 NPs are obtained after removing silica with sodium hydroxide solution [51]. The X-ray diffraction pattern showed that crystalline phase of CeO_2 nanoparticles could be indexed to cubic fluorite structure. The NH_4CO_3 created and Doxorubicin loaded hollow CeO_2 NPs for PTT/CDT/CHT combination therapy against cancer with excellent biocompatibility. When exposed to NIR light and convert it into heat, which can not only kill cancer cells with hyper thermia, but also stimulate NH_4HCO_3 to produce gas (CO_2, NH_3) to destroy the PDA shell. The breakage PDA shell further accelerated the drug release from hollow CeO_2. Meanwhile, the exposed surface of CeO_2 could enhance hydroxyl radical generation. As a result, PDAC NPs could provide a synergistic effect

among PTT, CDT and CHT treatments and exhibit an excellent tumor eliminating efficiency [52].

Anticancerous Activity of Some other Metal Oxide Nanoparticles-

Yttrium oxide is one of the most important compounds and it is being considered for biological applications because of its high stability. Many researches are done on the yttrium oxide and it is found to be a good anticancer drug. P.C Nag Jyothi and his co-workers after their research on yttrium oxide synthesized by green synthesis concluded that Y2O3 NPs exhibited potent anticancer activity against renal carcinoma cells. The synthesis method they used is inexpensive and eco-friendly. It also reduced harmful side-effects of other physical and chemical methods [53]. They used Fosythiae fructose fruit, which is a well-known traditional herbal medicine in Korea, for the synthesis of yttrium oxide nanoparticles. The synthesized nanoparticles were flake like flower in shape with an average size of 11nm according to them. To find the crystallographic structure of the Y_2O_3 NPs XRD was performed by them. They get different peaks [54]. The mean, crystallite size P_{hkl} was calculated using Scherrer's formula. The mean crystallite size of the Y_2O_3 NPs was found about 11 nm. SRB and flow cytometric assays were used to test the cytotoxicity of the NPs on the normal cells and cancerous cells. The results indicated that the NPs were non-toxic to normal cells but highly toxic against renal carcinoma cells at high concentration. According to the researchers the green synthesized nanoparticles proved to be a potential candidate for medical applications.

Lanthanum strontium manganese oxide (LSMO) nanoparticles are a new class of magnetic nanoparticles, which exhibit favorable magnetic and biological properties for therapeutic activities in cancer treatment. Vaishnavi Kulkarni and her co-workers experimented on these LSMO NPs due to vast biological and medical implications and got proof about its anticancerous activity. LSMO nanoparticles are manganese oxide base compounds (manganites) with the formula $R\text{-}1xAxMnO_3$ where R sites are substituted by the rare earth metal-lanthanum, and A by strontium. They synthesized these nanoparticles in bottom up approach i.e. chemical reduction of salts or decomposition base synthesis. This thermal decomposition method for synthesis of nanocrystalline LSMO nanoparticles used in cancer therapies because of their attractive magnetic properties and an inherent biocompatibility which has already been established with studies demonstrating its therapeutic efficiency. They function as MRI contrast agent as well as a heat generating source for localized hyperthermia and imaging, LSMO can also act as drug delivery agent according to the

experiment of Dr. Kulkarni and her co-workers [55].

Noble metal nanoparticles have attracted the interest of scientific community due to their fascinating application in the field of biomedical science and material science and some other field. Javed Musarat and his co-workers give a different approach to the synthesis of silver nanoparticles [56]. They synthesized those nanoparticles using extract of Nepeta deflersiana in the in method of green synthesis. The aerial part of N. deflersiana was collected and washed several times with distilled water to remove dust and was dried under shade. The air-dried plant was cut into small pieces, macerated in distilled water, filtered with gravity and the solvent evaporated under reduced pressure using a rotatory evaporator. The dried extract was kept at 4 degree Celsius, and then it was dissolved in 100 ml distilled water. The 90 ml of this mixture was added to 0.1M $AgNO_3$ solution. After 24 hours of incubation, the solution turned dark brown, which indicates the formation of Ag NPs. The black powder i.e. nanoparticles are obtained after washing thrice with distilled water and after drying overnight in an oven at 80 degree Celsius. The optical absorption of green synthesized silver nanoparticles was studied using FTIR and UV-VIS spectroscopy respectively. The crystalline nature of green synthesized NP was confirmed by XRD pattern [57]. The biosynthesized NP when applied on cancer cells, they showed a concentration dependent cytotoxicity in cervical cancer cells. ND-Ag NPs were also found to include oxidative stress as observed by the increase in ROs. It also showed that Ag NPs have the capacity of including apoptosis and necrosis cell death of cervical cancer cells through cell cycle arrest.

Gold nanoparticles [Au NPs] are used enormously in different cancer but very little is known regarding their molecular mechanism and surface charge role the process of cell death [58]. Here Dr. Sunil Kumar Surapaneni and his co-workers elucidate the molecular mechanism by which differently charged Au NPs include cytotoxicity in triple negative breast cancer cells (TNBC). There is no targeted effective therapy is available for triple negative breast cancer till date. Resistance to anticancer drugs and their side effects are the major hurdles in the treatment of TNBC. In this experiment they used different cancer cells such as MCF-10A, MDA-MB231 etc. which were obtained from cell culture. Cells were grown under standard condition of 5%CO2 and 37 degree Celsius in a controlled humidified incubator. Cytotoxicity assay (MTT) for Au NPs was carried out in MDA-MB-231 and MCF-10A cells [59]. Then cells were treated with synthesized Au NPs of various concentration. After 24 hour of Au NPs treatment, 200 ml of MTT solution was added to individual wells. Synthesized AuNPs were characterized by several means such as zeta size,

zeta potential analysis and transmission electron microscopy (TEM). TEM images showed that Au NPs were spherical in shape, having a size of around 25-30nm. Cytotoxicity assay of citrate-capped Au NP (negatively charged) was performed in human mammary epithelial (MCF-10A) and triple negative breast cancer (MDA-MB-231 and MDAMB-468) cells in different concentration range. Negatively charged Au NPs caused abrupt destruction of MDA-MB-231 cells due to increased histone H3 ser10 phosphorylation. Cell type dependent epigenetic alternations were observed with differentially charged AU NPs. For a better understanding of the potential of gold nanoparticles and its cytotoxicity against human osteosarcoma cells, Anna Malankwoska and her co-workers did research on the shape and cytotoxicity and the impact of gold nanoparticles in invitro model. They investigated the cytotoxicity in different shapes of gold nanoparticles such as Au NPS rods, Au NPS starts and Au NPs Spheres against human osteosarcoma cell lines by MTT and neutral red uptake assay. Cellular uptake of nanoparticles and ultrastructure changes were examined by transmission electron microscopy (TEM). Au NPs Spheres were obtained by mixing solution of tannic acid and hot solution of $HAuCl_4$ for 1 minute. Nano stars are prepared by adding aqueous solution of gold precursor 0.01 M $AgNO_3$ solution and 0.1 M solution. Similarly, nanorods are obtained by adding cetyl trimethyl ammonium bromide (CTAB) solution with 0.5 mm gold precursor and 0.6 ml of 0.01 M $NaBH_4$. MTT assay was used to determine cell viability. When stars, rods and Spheres in concentration 0.3, 0.6, 1.2, 2.5 and 5 mg/ml were examined on the osteosarcoma cells, it was found that Au NPS stars are mostly cytotoxic against human cell [60,61]. They observed that cancer cells are more susceptible to AuNPs cytotoxic effect. The results of this experiment proved that cytotoxicity of Au NPs is shape dependent. AuNPs stars with the highest anticancer potential are also the most cytotoxic type of tested nanoparticles whereas Au NPs spheres which appears to be the safest one had small anticancer potential [62].

A Comparison Between Particle Size and Cell Type In-vitro Cytotoxicity of Nanoparticles -

Devashri sahu and her co-workers did a research comparing between zinc oxide (ZnO) and silicon dioxide (SiO_2). They compared the effect of particle size and cytotoxic effect of both these oxides. The reduction in size of zinc oxide and silicon dioxide particles from micron to Nano micron affects unique physical characteristic as well as make them

cytotoxic [63]. They used cells types such as human lung epithelial cells(L-132) and human monocytes (THP-1). The L- 132 and THP-1 cells were exposed to nano and micron size of ZnO and SiO_2 particles with different concentrations for 24 hours, and cytotoxicity was analyzed by MTT assay. ZnO and SiO_2 particles showed concentration-dependent cytotoxicity in both cell lines. In size dependent study, ZnO particles exhibit nearly equal toxicity profile in L-132 cells while in THP-1 cells nano ZnO showed more toxicity then its micron size. The SiO_2 particles showed more toxicity in their nano size than micron size in both cell lines [64]. THP-1 cells were more sensitive towards the toxicity of both particles then human lung cells, L-132. These cells such as L-132 and THP-1 obtained from laboratory and maintained as monolayer and suspension culture flasks before exposing to the nanoparticles. Physicochemical properties of particles were analyzed using transmission electron microscopy, dynamic light scattering and Zeta potential analyzer. In this experiment, it is concluded that the small size and the relatively larger surface area of nanoparticles resulted in increased toxicity when compared to particle in micrometer size.

The use of nano sized materials offers exciting new options in technical and medical applications. Due to their versatile application Thomas R. Piber and his co-workers experimented on different nanoparticles and found how cytotoxicity of nanoparticles are independent from oxidative stress. Different types of cells cultured in laboratory were treated with subtoxic concentration of particle and positive control (hydrogen peroxide H_2O_2) to exclude and influence of the signal by cell loss. Size and surface charge of particles in the dynamic light scattering differed according to the medium in which they were suspended. In distilled water dispersion was best and smallest sizes were recorded. For screening and mode of action studies cells from human umbilical vein endothelial cells were used. For localization studies cells were seeded in chamber slides in and incubated with 25 milligram per ml carboxyl fluro sphere in medium for 30 minutes and 24 hours. After this incubation cells were labelled with organelle tracker which were all obtained from Invitrogen. This study aimed to investigate the size dependent effect of carboxyl polystyrene particles on cells to identify potential adverse effect of these particles. Particles were characterized in different solution to assess the influence of the medium on size and surface charge, viability, membrane integrity, apoptosis and necrosis. These particles generated radicals to the same degree as larger polystyrene particles. Particles were taken up into endosomes and lysosomes in a size-dependent manner [65]. Protein containing solution led to increase in particle size, decrease cytotoxicity and reduced cellular uptake. It can be

concluded that even in the absence of high surface reactivity and not linked to the generation of radical nanosized particles may cause cell damage.

The cytotoxicity of 15 nm and 46 nm silica nanoparticles was investigated by using crystalline silica as a positive control in cultured human bronchoalveolar carcinoma derived cells by Dr. Weisheng Lin and his co-researchers. Exposure to 15 and 46nm SiO_2 nanoparticles for 48 hours at dosage level between 10 and 100 microgram per ml decrease cell viability in a dose-dependent manner. Both SiO_2 nanoparticles were more cytotoxic then minimum min-u-sil5, however the cytotoxicity of 15nm and 46nm silica nanoparticles were not significantly different. To study the size effect of SiO_2 nanoparticles and the oxidative stress mechanism, 15nm and 46 nm SiO_2 nanoparticles were selected by them for their study. The SiO_2 nanoparticles used in their study were supplied by US silica company. Crystalline silica was obtained [65]. The particle sizes and distribution of SiO_2 nanoparticles were measured by transmission electron microscopy (TEM). The surface area of the particles was determined by Quanta chrome Autosorb 1-C. The result from characterization of 15nm SiO_2 and 46nm SiO_2 and 2 and Min-u-sil5 were studied and it was concluded that cell viability decreased as a function of dosage level. Cells when exposed to SiO_2 nanoparticles then due to increased ROs level and peroxidation membrane damage occurs [66]. It causes a dose dependent cytotoxicity in cultural human bronchoalveolar carcinoma derived cells that is closely correlated to increased oxidative stress.

Nanoparticles contrast agents after the potential to significantly improve existing method of cancer diagnosis and treatment. Leon Smith and his co-workers experimented on nanoparticles and how those nanoparticles used in cancer imaging and therapy [67]. They used nanoparticles as enhancement agents for radiation therapy and photodynamic therapy. They used a wide range of materials such as gold, polyacrylamide, silica and biodegradable polymers. One of their primary advantages over unencapsulated photosensitizers is their ability to preferentially accumulate in target cells, which is of particular use. Given that most photosensitizers described so far in the literature have a low solubility in water and tend to accumulate in blood cells rather than tumors. This allows similar therapeutic effects to be achieved, with lower doses of conventional photo sensitizers such as hypericin, limiting their side effects. One area that remains relatively unexplored is the concept of agents for dual mode image contrast and therapy enhancement. The concept of dual mode image contrast and therapy enhancement. The concept of dual mode enhancement agent has

been tested using traditional non-particle image contrast agent, such as iodine, for radio therapy enhancement applications. As iodine is routinely used as an image contrast agent for CT scans, a conventional CT scanner could be used to simultaneously monitor tumor progression and iodine uptake [68]. In this study it cleared that titanium oxide nanoparticles for dual mode enhancement of computed tomography [CT] imaging and kilovoltage radiation therapy. Although titanium dioxide produced noticeable image contrast enhancement in the CT scans, more sensitive detectors are needed to determine whether the nanoparticles can also produce localized dose enhancement for targeted radiation therapy.

Nano carriers have the potential to improve the therapeutic index of currently available drugs by increasing drug efficiency lowering drug toxicity and achieving steady-state therapeutic labels of drugs over on extended period. Due to this advancement in the field of nanomaterials and its efficiency Julia Bottner and her co-workers experimented in the field of nanomedicines. They studied and experimented on how citrate associated iron oxide nanoparticles reacted on metastatic and non-metastatic breast cancer cells. The association of maghemite nanoparticles with rhodium citrate (MRC complex) has the potential to increase the specificity of the cytotoxic action of the later compound, since this nanocomposite can be guided tour transported to a target by the use of an external magnetic field [69]. However, it was seen that the behavior of these nanoparticles for an extended time of exposure to breast cancer cells has not yet been explored, and nor has MRC cytotoxicity comparison in different cell lines been performed until now. In this work, the effect of MRC NPS on these cells were analyzed for up to 72 hour of exposure and they focused on comparing nanoparticle's therapeutic effectiveness in different cell lines to effect the most responsive modal, Here according to this experiment data MRC embassy complex exhibited broad cytotoxicity on tumor cells mainly in the past 24 hour. However, while MRC include cytotoxicity in MDA MB 231 in a time dependent manner [70]. Progressively decreasing the required dose for significant reduction in cell viability at 48 and 72-hour MCF7 appears to recover its viability after 48 hours of exposure. Results of this experiment suggest that MRC nanoparticles are a promising nano material that can provide a conventional route for tumor targeting and treatment mainly in metastatic cells.

Drug Delivery by Nanoparticles-

In this experiment Rupinder Singh and his team incubated tumor cells in the presence of chitosan alone or drug delivery system (DDS) containing chitosan-niasome-peclitaxel-BODIPY564/570, which prominent granular accumulation on their surface when compared to normal cell. Chitosan was dissolved in 0.1 M HCL to render its free amino groups readily available for cross linking with beta glycerol phosphate. This in turn results in a pH increase to the physiological range of 77.4. This procedural step also allows for controlled hydrogel formation when temperature increases to human body temperature of 37 degree Celsius. Therefore, in this study the Chitosan beta glycerophosphate system remained a liquid at room temperature of 25 degree Celsius, but it formed a gel when placed in the tissue culture incubator set at body temperature. This property of chitosan allowed it to be dispersed as a liquid into the outer chamber of glass bottom culture dishes surrounding the inside chamber that content growing adherent cells [71]. The Mattek's plates were placed in the tissue culture incubator at 37 degree Celsius for 3 minutes facilitating cross linking of chitosan and resulting in chitosan forming gel in the outer chamber. Based on the observation of the DDS pre preferentially targeting tumor cells, there is a potential implication for the localized delivery of the therapeutic drug doses to solid tumor or post-surgical solid tumor cavities containing residual tumor cells.

Nanotechnology is a frequent treatment for cancer. Nano metals are used as the vehicles which deliver drugs in smaller but equally effective quantities. L.Perez and his team members experimented on nanoparticles [72]. They tried reducing the effective dose of cisplatin using gold nanoparticles as carrier. In this experiment the Au NPs poses characteristic spectrum when visualized in the UV visible spectrophotometer. In this case the Au NPs had a peak at 519nm, Au NP PEG at 523nm and Au NP PEG cisplatin at 525nm. They used transmission electron microscopy i.e. TEM to estimate the size and shape of the different nanoparticles, showing that the NPs have additional diameter of 8.6 + 1.97 nm, Au NP PEG of 9.5 + 1.24nm and Au NP PEG cisplatin of 10 + 1.76 nm. All the nanoparticles synthesized have a spherical shape. They also determined the hydrodynamic size zeta potential and polydispersity index of nanoparticles, nanoparticles being immersed either in H_2O and DMEM medium without fetal bovine serum, tended to form agglomerates, and zeta potential was used to 1 mu. Also, when nanoparticles were immersed in DMEM medium supplemented with fetal bovine serum at 10%, they also tended to form agglomerates although of smaller size, zeta potential being close to 1mv

[73]. In this way, they succeed in reducing the effective dose of cisplatin using gold nanoparticles as carrier.

Kevin Affram and his co-workers did a comparative study on contrast enhancement of magnevist and magnevist loaded nanoparticles (MLNPs) in pancreatic cancer cells. They formulated MLNPs by thin film hydration and extrusion and these nanoparticles were characterized for the particle size and zeta potential. A 21.1T vertical magnet was used for all MRI. The magnet was equipped with a Brker Advance console and para vision 6.1 acquisitions software. MLNPs were prepared and imaged with a 10mm bid cage coil. For in vivo imaging, animals were sedated and injected with a single dose. 4 mg/kg of Mag or MLNPs with Mag equivalent dose using a 33 mm inner diameter bid cage coil, T1 maps were acquired, and signal to noise ratio (SNR) measured for 2hr. MLNPs showed a remarkable augmentation in contrast with Mag increment. However, in in vivo imaging, no significant difference in contrast was observed between these two. While MLNPs was observed to have fairly Tumor/Muscle ratio in the first 30 min, free Mag exhibit higher T/M ratio over the time period between 30 and 120min [74]. Overall, there was no statistically significant difference between Mag and MLNPs in rating MR image quality. Low payload of Mag entrapment by MLNPs and restricted access of water to MLNPs may have affected the performance of Mag-LNPs as an effective contrast agent.

Modern chemotherapeutics are challenged with the difficult task of maintaining superior pharmaco-kinetic efficiency by narrowing their targeting windows while simultaneously preventing their toxic side effects. Nanoparticles now a days are very much efficient drug delivery vehicles used in Cancer therapy as well as other medical applications. Danmenasco and his co-workers did research on nanoparticles as efficient drug delivery vehicles (DDV) [75]. Nanoparticle DDV are manufactured with great precision to exact nanoscale specification composed of polymer, lipid, silicate or other amphipathic materials. The core of DDV is designed to act as a repository where chemotherapeutics, DNA/RNA, or an imaging agent can be stored. Whereas the core is the cargo hold of the DDV system, the exterior is responsible for in vivo navigation and avoiding both innate and adaptive immune detection. The ultimate destination through systematic delivery of the DDV is realized by presenting multiple targeting ligands such as antibodies, peptides or other substances specific for cell surface proteins or epitopes, to the surface of nanoparticles. DDV have been used to combat some the most challenging hurdles of modern cancer therapies [76]. Their modular design bearing functionalities have improved upon the

pharmacological action of clinical therapeutic through extending their systematic circulation, refining their targeting and implemented programmed payload delivery through environmental sensing and remote actuating components. These technologies driven by the amalgamation of cancer biology and nanomaterials engineering, have proven valuable in advancing significant breakthroughs in both the biology of cancer and therapies.

Lysosomes have become an important target for anti-cancer therapeutics because lysosomal cell death bypasses the classical caspase-dependent apoptosis pathway enabling the targeting of apoptosis and drug resistant cancers. Marta Siek and his co-workers researched on how mixed charged nanoparticles in lysosomes induces selective death of cancerous cell. They used d=5.3 + 0.7nm gold nanoparticles functionalized with positively charged in N, N, N trimethyl ammonium chloride (TMA) and negatively charged 11mer captoun decanoic acid [MUA] ligands Nick with surface ligand ratios of 100:0, 91:9, 80:20, 61:39 and 0:100. These nanoparticles exhibit dependent aggregation. In water supplemented with 10% fetal bovine serum [FBS], all nanoparticle types were un aggregated at pH 7.4 but gradually aggregated when pH was lowered into 50 to 100 nm cluster at pH equal to 5.5 to 6.5 and then into dominant 2 micro meter super particles at pH less than 5.5. They take 50 to 100 nm cluster size as it is compatible with cellular uptake [77]. Through endocytes, while assembly of larger super particles occurs at pH values characteristic of endosomes, lysosomes. They took two sets of cancer and normal cell pairs i.e. 1080 fibrosarcoma versus mouse embryonic fibroblast and MDA MB 231 breast cancer carcinoma versus MCF 10A normal epithelial cells. Continuous exposure of cells to nanoparticles resulted in dose and time dependent killing of cancerous cell while the cytotoxicity towards the non-cancerous cell was marginal. The effectiveness of Cancer cell killing dependent on the nanoparticle monolayer composition [78].

Joan Raitano and his co-workers did research about the response of cells exposed to nanoparticles with regard to toxicity and how can cells be protected by some specific nanoparticles. It was shown that nanoparticles composed of cerium dioxide or yttrium oxide protect nerve cells from oxidative stress [79]. The ceria and yttria nanoparticles act as direct anti- oxidants to limit the amount of reactive oxygen species required to kill the cells. These group of nanoparticles could be used to modulate oxidative stress in biological system. Here the lung cells HTT22 are taken into consideration for the study of oxidative stress. The particles examined in this study varied in size and composition. Cerium dioxide was chosen because it may act as a free radical scavenger. This metal oxide possesses a

cubic fluorite structure, and is characterized by fairly mono disperse particles that are single crystals with few twin boundaries or stacking faults and with an expanded lattice parameter relative its bulk counterpart [80]. Yttrium oxide is noteworthy because the free energy of oxide formation from elemental yttrium is among the highest known. It is characterized by only small deviations from stoichiometry under normal conditions of temperature and pressure and by absorption of water and carbon dioxide from the atmosphere. CeO2, Y2O2 nanoparticles are relatively non- toxic to HTT22 cells rather it decreased the oxidative stress by reducing formation of ROs in cancer cells. So, it can be concluded that cerium and yttrium oxide nanoparticles are neuro protective in nature.

Nanoceria: A Promising Anti-Cancer Therapeutic Reagent-

S.R Panda and co-workers synthesized nano- ceria using 1 gm of $(NH_4)_2(Ce\ (NO_3)_6)$ (ceric ammonium nitrate) and 0.52 gm of glycine which was added in stoichiometric amounts, according to oxidizer/ fuel ratio, in order to obtain CeO_2 composition [81]. The mixture obtained was heated with microwave radiation in an oven at a frequency of 2450MHZ and high power of 800 W for 3min. During this duration of heating, the mixture solution boiled, dehydration occurred and the internal heating lead to ignition, as a result of which an exothermic reaction occurred with a flame continuing firmly for 2 to 4 sec. This method occurs instantly and residue obtained was in powder form and crystalline in nature. The characterization of the sample was done by XRD and by FTIR. The crystal structure was determined by XRD with CuKα source of radiation. And the pattern was measured in the range of 10^O to 100^O at a step size of 0.05^O. Evaluation of crystallite size was carried out using XRD peaks. Human colon cancer cells HCT116 and BHK21 cell lines were obtained from NOCs, Pune, India. The cells were cultured in presence of 10% FBS, penicillin and L-glutamine. The cytotoxicity of CeO_2 nanoparticles in HCT116, and BHK21 cells was conducted using MTT reagent having concentration of 0.1µg/ml ,10000 cells were plated in 200µl of MTT solutions were included to the cells and incubated for 4h. After incubated the insoluble formazan crystal of purple color was formed [82]. Media was removed carefully. To investigate the nuclear integrity HCT116 cells were treated with CeO_2 nanoparticles for 24 hr. After 24 hr., the control (without treatment) and the treated cells were analyzed under fluorescence microscope and images were taken for further analysis.

In this experiment M. Atif and co-workers used high grade chemical salts of Merck and sigma- Aldrich for the synthesis of Mn-doped CeO2 nano composite the soft chemical route

was employed to synthesize $Mn_xCe_{1-x}O_2$[where x = 0,3,5,7 and 9 %] nano composites. Cerium Nitrate ($CeNO_3.6H_2O$) and Manganese chloride ($MnCl_2.4H_2O$) were used as starting materials. Five different molar samples were prepared in distilled water. Each sample solution was placed on a magnetic stirrer while maintaining 700 rpm with temperature kept in the range of 100- 150^oC for 2 hrs. to obtain homogeneous solutions. An acidic agent (2ml of CH_3COOH) was used as the capping agent and was added drop wise into the parent solution, along with 8 g/100 ml of NaOH base solution to reach PH 10. The precipitate was then allowed to settle the initial step for the purification of the solution was to remove the supernatant from the solution using a centrifugation process. The reaction mixture prepared from the chemicals were kept for one day at room temperature for stabilization and subsequently centrifuged at 10000 rpm for 30 min to obtain a clear supernatant and pure nano particles. The final product of the calcined materials was analytically studied to obtain different characterization as well as the anti- bacterial and the anti-cancer properties [83]. For the anti-bacterial activity experimentation some multi drop resistant tuberculosis (MDR) bacterium of MRSA, E. coli and P. aeruginosa were obtained from clinical isolates of patient affected by urinary tract, throat and ear functions collected at a micro biology lab. The nano composite susceptibility patterns of the bacterium were determined by disc diffusion on Muller-Hinton agar (MHA) plates. Discs containing different concentrations of nano composite were placed on the surface of the bacterium – inoculated plates. The Zone of inhibition was then measured in millimeters after the plates were incubated for 24 hr. at 37^oC. Colonies of pathogens were cultured in agar. This widely used rich medium is popular because it permits the fast growth of many species. All ingredients were mixed in 200 ml of distilled water with 1 hr. of continuous stirring. 4N NaOH was added to maintain a PH of 7.5, before 300 ml of the volume was adjusted followed by autoclave. Crystallographic analysis shows the XRD profiles of synthesized undoped CeO_2 and doped $Mn_xCe_{1-x}O_2$ nano composites. In the absence of impure peaks, the cubic fluorite single phase structure for un doped CeO_2 showed the presence of several brag peaks. The crystallite size of the un doped CeO_2 nano composite was 8.2 nm. These were calculated using peak broadening and Debye Scherer's approximation [84].

CHAPTER IV

Conclusion

Conclusion

Nanotechnology has already revolutionized cancer therapy in many aspects and is radically changing the treatment pattern. It has made a great impact on selective recognizing of the cancerous cells, targeted drug delivery, and overcoming limitations of the conventional chemotherapies. The side effects of traditional chemotherapies can greatly be removed by these novel active or passive targeting which can substantially increase the survival rate. As cancer is one of the most serious lethal disease, the contribution of nano technology in precise treatment avoiding the life-threatening side effects can potentially contribute to a great movement in biomedical field as well as in the field of chemical engineering. In this technique nano particles are used as drug delivery systems and for selective targeting. The nano particles modified according to the cancerous cells by chemical engineering. The change in shape and size of nanoparticles is very much useful in cancer treatment. The differential cytotoxic effect of nano particles helps them to distinguish between normal and cancerous cell. Nanoparticles can also be used in diagnosis and bio imaging of cancer. The killing of cancerous cell by nanoparticles may include induction of apoptotic and necrotic cell death and decreased proliferation. In this way nanotechnology emerges as a very efficient method in biomedical as well as chemical engineering field.

CHAPTER V

References

Reference

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