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New Nanoparticle Technology developed to treat Aggressive thyroid Cancer

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Abstract
Thyroid Adenoma or Malignant Neoplasm(Thyroid Cancer) , the most forceful type of thyroid disease, has a death rate of almost 100 percent and a middle survival time. Thyroid harmful tumors are once in a while connected with hyperfunctioning thyroid. The rate of this co-occurrence is exceedingly factor.
Contextual investigation : A 45 year women who was experiencing Cancer First sentiment of biopsy report of the patient expresses that there are nodular epitomized leisions made out of unpredictable follicles. Biopsy report are herewith follicular variation and papillary carsinoma Thyroid flap HPE (Histo neurotic examination) demonstrates limpholytic thyroiditis which is aggravation of thyroid organ. Ca – 125 test measure Cancer antigen 125 in the patient blood, it is utilized to screen malignancy amid and after treatment, chemiluminiscence imuno examine (CELIA) pack is proposed for quantitative assurance of CA-125 fixation in human serum The biopsy report of Nodule on lower shaft of right projection of thyroid organ to check whether it kindhearted tumor, for example, Thyroid Adenoma or Malignant Neoplasm(Thyroid Cancer, for example, Papillary, Folicular medulary or Anoplastic Thyroid Cancer Right Thyroid Gland is amplified and FNAC is proposed even in the second supposition. Second supposition of the biopsy report says the patient experienced extraction of lone knob of right projection of thyroid organ exhorted the patient run with prescription or evacuate left flap of thyroid organ. Given little of Radio dynamic iodine and a gama camera to identify disease cell in thyroid organ tolerant demonstrates no proof of inaccessible useful metastasis

Keywords:- thyroid Cancer, Therapeutics, Inhibitors, Tumor, Immunotherapy, Clinical trial, Histo neurotic examination, chemiluminiscence imuno examine

INTRODUCTION:

Nanobiotechnology is still in its beginning periods. The multidisciplinary field of nanobiotechnology is bringing the exploration of the limitlessly little gadget consistently nearer to the real world. The effects of these improvements will sooner or later be vast to the point that they will presumably influence essentially all fields of science and innovation. Nanobiotechnology offers a wide scope of employments in medication. Advancements, for example, medicate conveyance frameworks are just the beginnings of the beginning of something new. Numerous infections that don't have fixes today might be restored by nanotechnology later on. In spite of the fact that the desires from nanobiotechnology in prescription are high and the potential advantages are perpetually enrolled, the wellbeing of nano-drug isn't yet completely characterized. Utilization of nanotechnology in medicinal therapeutics needs satisfactory assessment of its risk and wellbeing factors. Researchers who are against the utilization of nanotechnology additionally concur that headway in nanotechnology should proceed in light of the fact that this field guarantees

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extraordinary advantages, however testing ought to be completed to guarantee the wellbeing of the general population. It is conceivable that nanomedicine in future would play a urgent/unparallel job in treatment of human ailments and furthermore in improvement of typical human physiology. In the case of everything runs easily, nanobiotechnology will, at some point, turn into an unavoidable piece of our regular daily existence and will help spare numerous lives.

Nanotechnology is an up and coming innovation that may change current cancer finding and treatment techniques. Nanotechnology covers an expansive scope of themes; in this manner, it is known as a multidisciplinary field, which incorporates science, material science, chemistry and designing. The fundamental thought in nanotechnology is creation and control of material at the nanoscale. Nanotechnology has given an approach to adjusting and rebuilding matter on a nuclear scale and henceforth that we can comprehend the base of any issue. Nanoparticles are tiny particles with size in nanometers (1-100 nm).

NANOBIOTECHNOLOGY

Biotechnology and nanotechnology are two of the 21st century's most encouraging advances. Nanotechnology (now and then alluded to as nanotech) is characterized as the plan, advancement and utilization of materials and gadgets whose least useful make up is on a nanometer scale . By and large, nanotechnology manages creating materials, gadgets, or different structures having something like one measurement estimated from 1 to 100 nanometers. In the interim, Biotechnology manages metabolic and other physiological procedures of organic subjects including microorganisms. Relationship of these two advancements, for example nanobiotechnology can assume an imperative job in creating and actualizing numerous helpful instruments in the investigation of life. Nanotechnology is various, extending from expansions of ordinary gadget physical science to totally new methodologies dependent on sub-atomic self-get together, from growing new materials with measurements on the nanoscale to researching whether we can specifically control matters on/in the nuclear scale/level. This thought involves the use of fields of science as various as surface science, natural science, atomic science, semiconductor material science, microfabrication, and so on.

Propelled brilliance microscopy strategies have accomplished high resultion up to ~10nm; nonetheless, customary recoloring utilizing expansive fondness bodies doesn't give exact goals to super-goals imaging[2]. Nanomaterials likewise add to the advancement of protein clusters, permitting multiplexing of biochemical investigations on proteins, for example, protein distinguishing proof and protein-protein interaction[3]

1.4 DETECTION :

Many currently used/conventional clinical tests reveal the presence of a molecule or a disease causing organism by detecting the binding of a specific antibody to the disease-related target. Traditionally, such tests are performed by conjugating the antibodies with inorganic/ organic dyes and visualizing the signals within the samples through fluorescence microscopy or electronic microscopy. However, dyes often limit the specificity and practicality of the detection methods. Nanobiotechnology offers a solution by using semiconductor nanocrystals (also referred to as "quantum dots"). These minuscule probes can withstand significantly more cycles of excitations and light emissions than typical organic molecules, which more readily decompose[11].

1.4.1 Individual target probes :

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Despite the advantages of magnetic detections, optical and colorimetric detections will continue to be chosen by the medical community. Nanosphere (Northbrook, Illinois) is one of the companies that developed techniques that allow/ allowing doctors to optically detect the genetic compositions of biological specimens. Nano gold particles studded with short segments of DNA form the basis of the easy-to-read test for the presence of any given genetic sequence. If the sequence of interest in the samples, it binds to complementary DNA tentacles on multiple nanospheres and forms a dense web of visible gold balls. This technology allows/facilitates the detection of pathogenic organisms and has shown promising results in the detection of anthrax, giving much higher sensitivity than tests that are currently being used[12].

1.4.2 Protein chips :

Proteins play the central role in establishing the biological phenotype of organisms in healthy and diseased states and are more indicative of functionality. Hence, proteomics is important in disease diagnostics and pharmaceutics, where drugs can be developed to alter signaling pathways. Protein chips can be treated with chemical groups, or small modular protein components, that can specifically bind to proteins containing a certain structural or biochemical motif[13]. Two companies currently operating in this application space are Agilent, Inc. and NanoInk, Inc. Agilent uses a non-contact ink-jet technology to produce microarrays by printing oligos and whole cDNAs onto glass slides at the nanoscale. NanoInk uses dip-pen nanolithography (DPN) technology to assemble structure on a nanoscale of measurement[14] .

1.4.3 Sparse cell detection :

Sparse cells are both rare and physiologically distinct from their surrounding cells in normal physiological conditions (e.g. cancer cells, lymphocytes, fetal cells and HIV-infected T cells). They are significant in the detection and diagnosis of various genetic defects. However, it is a challenge to identify and subsequently isolate these sparse cells. Nanobiotechnology presents new opportunities for advancement in this area. Scientists developed nanosystems capable of effectively sorting sparse cells from blood and other tissues. This technology takes advantage of/exploits the unique properties of sparse cells manifested in differences in deformation, surface charges and affinity for specific receptors and/or ligands. For example, by inserting electrodes into microchannels, cells can be precisely sorted based on surface charge. They can also be sorted by using biocompatible surfaces with precise nanopores. The nano-biotechnology center at Cornell University (NBTC) is currently using these technologies to develop powerful diagnostic tools for the isolation and diagnosis of various diseases[15] .

1.4.4 Nanotechnology :

as a tool in imaging Intracellular imaging can be made possible through labelling of target molecules with quantum dots (QDs) or synthetic chomophores, such as fluorescent proteins that will facilitate direct investigation of intracellular signalling complex by optical techniques, i. e. confocal fluorescence microscopy or correlation imaging[16].

1.5 THERAPEUTIC APPLICATIONS :

Nanotechnology can provide new formulations of drugs with less side effects and routes for drug delivery. 1. Drug Delivery: Nanoparticles as therapeutics can be delivered to targeted sites, including locations that cannot be easily reached by standard drugs. For instance, if a therapeutic can be chemically attached to a nanoparticle, it can then be guided to the site of the disease or infection by radio or

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magnetic signals. These nanodrugs can also be designed to "release" only at times when specific molecules are present or when external triggers (such as infrared heat) are provided. At the same time, harmful side effects from potent medications can be avoided by reducing the effective dosage needed to treat the patient. By encapsulating drugs in nanosized materials (such as organic dendrimers, hollow polymer capsules, and nanoshells), release can be controlled much more precisely than ever before. Drugs are designed to carry a therapeutic payload (radiation, chemotherapy or gene therapy) as well as for imaging applications[17]. Many agents, which cannot be administered orally due to their poor bioavailability, will now have scope of use in therapy with the help of nanotechnology[18] .

Nano-formulations offer protection for agents vulnerable to degradation or denaturation when exposed to extreme pH, and also prolong half-life of a drug by expanding retention of the formulation through bioadhesion. Another broad application of nanotechnology is the delivery of antigens for vaccination. Recent advances in encapsulation and development of suitable animal models have demonstrated that microparticles and nanoparticles are capable of enhancing immunization. 2. Gene delivery Current gene therapy systems suffer from the inherent difficulties of effective pharmaceutical processing and development, and the chance of reversion of an engineered mutant to the wild type. Potential immunogenicity of viral vectors involved in gene delivery is also problematic [29,30]. To address this issue, nanotechnological tools in human gene therapy have been tested and nanoparticle-based nonviral vectors (usully 50-500 nm in size) in transportation of plasmid DNA described. Therefore, successful introduction of less immunogenic nanosize gene carriers as a substitution of the disputed viral vectors seems beneficial in repairing or replacing impaired genes in human [31].

1.5.1 Liposomes :

A liposome being composed of a lipid bilayer can be used in gene therapy due to its ability to pass through lipid bilayers and cell membranes of the target. Recent use of several groups of liposomes in a local delivery has been found to be convincingly effective [32,33]. Liposomes can also help achieve targeted therapy. Zhang et al demonstrated widespread reporter expression in the brains of rhesus monkeys by linking nanoparticle (such as polyethylene glycol) treated liposomes to a monoclonal antibody for human insulin reporter [34]. These successful trials reflect the future of targeted therapy and the importance of nanometer-sized constructs for the advancement of molecular medicine.

1.5.2 Surfaces :

In nature, there are a multitude of examples of the complicated interactions between molecules and surfaces. For example, the interactions between blood cells and the brain or between fungal pathogens and infection sites rely on complex interplays between cells and surface characteristics. Nanofabrication unravels the complexity of these interactions by modifying surface characteristics with nanoscale resolutions, which can lead to hybrid biological systems. This hybrid material can be used to screen drugs, as sensors, or as medical devices and implants. Nanosystems, owned by the Irish drug company Elan, developed a polymer coating capable of changing the surface of drugs that have poor water solubility [35].

1.5.3 Biomolecular Engineering :

The expense and time involved in traditional biomolecule designing limit the availability of bioactive molecules. Nanoscale assembly and synthesis techniques provide an alternative to traditional methods. Improvements can be

achieved due to the ability to carry out chemical and biological reactions on solid substrates, rather than through the traditional solution based processes. The use of solid substrate usually means less waste and the ability to manipulate the biomolecule far more precisely. EngeneOS (Waltham, Massachusetts) pioneered the field of biomolecular engineering. The company developed the engineered genomic operating systems that create programmable biomolecular machines employing natural and artificial building blocks. These biomolecule machines have broad range of commercial applications-as biosensors, in chemical synthesis and processing, as bioelectronic devices and materials, in nanotechnology, in functional genomics and in drug discovery.

1.5.4 Biopharmaceuticals :

Nanobiotechnology can develop drugs for diseases that conventional pharmaceuticals cannot target. The pharmaceutical industry traditionally focuses on developing drugs to treat a defined universe of about five hundred confirmed disease targets. But approximately 70 to 80 percent of the new candidates for drug development fail, and these failures are often discovered late in the development process, with the loss of millions of dollars in R&D investments. Nanoscale techniques for drug development will be a boon to small companies, which cannot employ hundreds of organic chemists to synthesize and test thousands of compounds. Nanobiotechnology brings the ability to physically manipulate targets, molecules and atoms on solid substrates by tethering them to biomembranes and controlling where and when chemical reactions take place, in a fast process that requires few materials (reagents and solutions). This advance will reduce drug discovery costs, will provide a large diversity of compounds, and will facilitate the development of highly specific drugs. Potentia Pharmaceuticals (Louisville, Kentucky) is an early-stage company that is attempting to streamline the drug development process with the use of nanotechnologies (Harvard Business School 2001).

1.5.5 Nanotechnology in cardiac therapy :

Nanotechnology is currently offering promising tools for applications in modern cardiovascular science to explore existing frontiers at the cellular level and treat challenging cardiovascular diseases more effectively. These tools can be applied in diagnosis, imaging and tissue engineering [36]. Miniaturized nanoscale sensors like quantum dots (QDs), nanocrystals, and nanobarcodes are capable of sensing and monitoring complex immune signals in response to cardiac or inflammatory events [20]. Nanotechnology can also help detect and describe clinically-significant specific mechanisms implicated in cardiac disorders. In addition, it is useful in designing atomic-scale machines that can be incorporated into biological systems at the molecular level. Introduction of these newly designed nanomachines may positively change many ideas and hypotheses in the treatment of critical cardiovascular diseases. Nanotechnology could also have great impact in tackling issues like unstable plaques and clarification of valves. Thus, this approach could be a real milestone of success in achieving localized and sustained arterial and cardiac drug therapy for the management of cardiovascular diseases .

1.5.6 Nanotechnology In Dental Care :

Nanotechnology will have future medical applications in the field of dentistry. The role of nanodentistry by means of the use of nanomaterials, biotechnology, and nanorobotics will ensure better oral health. Millions of people currently receiving poor dental care will benefit from such remarkable breakthrough in the science of dental health. Moreover, nanodental techniques in major tooth repair may also

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evolve. Reconstructive dental nanorobots could be used in selective and precise occlusion of specific tubules within minutes, and this will facilitate quick and permanent recovery. The advantage of nanodentistry in natural tooth maintenance could also be significant. Covalently-bonded artificial materials like sapphire may replace upper enamel layer to boost the appearance and durability of teeth].

1.5.7 Nanotechnology in orthopedic applications :

Nanomaterials sized between 1 and 100 nm have role to play as new and functional constituents of bones being also made up of nanosized organic and mineral phases [45,46]. Nanomaterials, nanopolymers, carbon nanofibers, nanotubes, and ceramic nanocomposites may help with more efficient deposition of calcium-containing minerals on implants. Based on these evidences and observations, nanostructure materials represent a unique realm of research and development that may improve the attachment of an implant to the surrounding bone matters by enhancing bone cell interactions, and this will indeed aid in improving orthopedic implant efficacy while drastically minimizing patientcompliance problems. Future prospects of nanobiotechnology There is much debate on the future implications of nanobiotechnology. It could create and suggest implementation of a choice of various new materials and devices potentially useful in the field of medicine, electronics, biomaterials and energy production. Nevertheless, this approach raises many of the same issues as any new technology, including problems with toxicity and environmental impact of nanomaterials [47] and their potential effects on global economics, as well as speculation about various doomsday scenarios.

These concerns have accounted for a debate among advocacy groups and governments on whether special statutory regulation of nanobiotechnology is warranted. Despite the existence of some disputes, this technology renders immense hope for the future. It may lead to innovations by playing a prominent role in various biomedical applications ranging from drug delivery and gene therapy to molecular imaging, biomarkers and biosensors. One of these applications being the prime research objective of the present

time would be target-specific drug therapy and methods for early diagnosis and treatment of diseases. Two types of medical applications are already emerging, both in clinical diagnosis and in R&D. Imaging applications, such as quantum dot technology are already being licensed and applications for monitoring cellular activities in tissue are coming soon. The second major type of application involves the development of highly specific and sensitive means of detecting nucleic acids and proteins.

By 2015 to 2020, we will see that products being tested in academic and government laboratories will be creeping into commercialization. Sparse cell isolation and molecular filtration applications should, by then, make it to market. Some of the drug delivery systems should be commercialized or in advanced clinical trials. For example - drug delivery systems have been developed by NanoSystems or by American Pharmaceutical Partners, which is testing the encapsulation of Taxol, a cancer drug in a nanopolymer called paclitaxel. Most medical devices and therapeutics are a decade or more away from market.

1.6 CHALLENGES FOR NANOBIOTECHNOLOGY

No single person can provide the answers to challenges that nanotechnology brings, nor can any single group or intellectual discipline. The five main challenges are to develop instruments to assess exposure to engineered nano-materials in the air and

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water. It is fairly understood that exposure of humans and animals to the environment potentially contaminated with nano-materials may need to be monitored for any adverse consequence. The challenge becomes increasingly difficult in more complex matrices like food. The second challenge would be to develop applicable methods to detect and determine the toxicity of engineered nano-materials within next 5 to 15 years. Then again, proposing models for predicting effects of these nano-materials on human health and the environment would be an inevitable issue. The next challenge would be to develop reverse systems to evaluate precise impact of engineered nano-materials on health and the environment over the entire life span that speaks to the life cycle issue. The fifth being more of a grand challenge would be to develop the tools to properly assess risk to human health and to the environment. Commercialization challenges of nanobiotechnology include uncertainty of effectiveness of innovation, scalability, funding, scarce resources, patience etc.

A broad majority of company recognizes a These have been studied in vitro and in animal models and the effect on human system is difficult to extrapolate from such studies. Their use in humans requires further research and much needed caution.

1.7 NANOTECHNOLOGY:

Nanotechnology (sometimes shortened to "nanotech") is the study of manipulating matter on an atomic and molecular scale. Generally, nanotechnology is deals with the structures and sized in between 1 to 100 nanometer at least one dimension, Nanoscience and nanotechnology are the study and application of extremely small things and can be used across all the other science fields, such as chemistry, biology, physics, materials science, and engineering. Nanotechnology is not just a new field of science and engineering, but a new way of looking at and studying.

NANOTECHNOLOGY IN TREATING DISEASES:

Nanotechnology is one of the most popular areas of scientific research, especially with regard to medical applications. We've already discussed some of the new detection methods that should bring about cheaper, faster and less invasive cancer diagnoses. But once the diagnosis occurs, there's still the prospect of surgery, chemotherapy or radiation treatment to destroy the cancer. Unfortunately, these treatments can carry serious side effects. Chemotherapy can cause a variety of ailments, including hair loss, digestive problems, nausea, lack of energy and mouth ulcers.

But nanotechnologists think they have an answer for treatment as well, and it comes in the form of targeted drug therapies. If scientists can load their cancer-detecting gold nanoparticles with anticancer drugs, they could attack the cancer exactly where it lives. Such a treatment means fewer side effects and less medication used. Nanoparticles also carry the potential for targeted and time-release drugs. A potent dose of drugs could be delivered to a specific area but engineered to release over a planned period to ensure maximum effectiveness and the patient's safety.

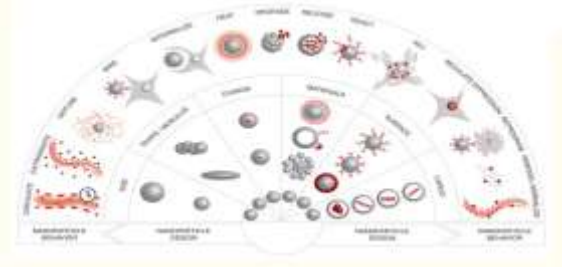

Fig Nanoparticle Behaviors. Nanoparticle designs, in terms of size, shape, modulus, charge, material, surface and cargo, as well as their interactions in the body, determine their individual behavior.

Nanoparticles with high angle extents, and particles that are rigid, have been seemed to

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total more progressively in macrophages than more diminutive, versatile particles, along these lines diminishing their room time from the blood. In conditions where take-up is fundamental, for instance, in tumor conditions, round nanoparticles have so far shown increasingly gainful. All around, the limit of nanoparticles to recognize, move and act in the body is controlled by their arrangement and correspondences with the earth. Building the direct of nanoparticles has ended up being logically possible, as a result of a creating cognizance of science and nanoparticle transport, and the astounding apparatus compartment of nanoparticle modifiers open to bioengineers. The limit of nanoparticles to react to their condition is clearly connected with their material association.[19].

NANOBIOTECHNOLOGY IN TREATING CANCER:

The application of nanobiotechnology in cancer, i.e., nanooncology, which is currently the most important chapter of nanomedicine. Several drugs in development for cancer are based on nanotechnology and a few of these are already approved. Nanotechnology based devices are in development as aids to cancer surgery. The impact of nanobiotechnology on oncology is shown schematically in Fig. 1.

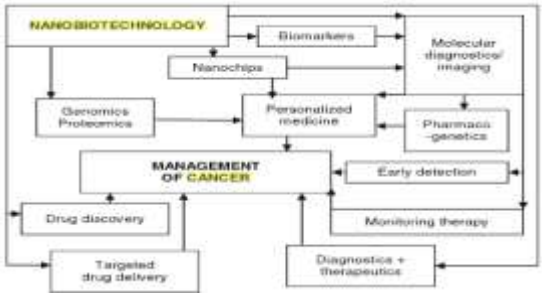

Fig 1 Role of Nanobiotechnology in the management of Cancer. Various Nanobiotechnologies have a direct as well as indirect effect on the diagnosis and management of cancer. Many of these technologeis interact with each other

1.11 NANOTECHNOLOGY FOR DETECTION OF CANCER BIOMARKERS

Basic of Cancer Biomarkers

Any measurable specific molecular alteraction of a cancer cell either on DNA, RNA, protein, or metabolite level can be referred to as a Cancer Biomarker. The expression of a distinct gene can enable its identification in a tissue with none of the surrounding cells expressing the specific biomarker. Cancer cells themselves may be difficult to detect at an early stage but they leave fingerprint, i.e., a patter of change in biomarker proteins that circulate in the blood. There may be 20-25 biomarkers, which may require as many as 500 measurements, all of which should be made from a drop of blood obtained by pinprick. Miniaturized techniques such as nanotechnology are useful for the discovery of Cancer biomarkers.

Silicon nanowires incorporated into arrays provide label-free, multiplexed electrical detection of cancer protein biomarkers such as prostate specific antigen at femtomolar concentrations with high sensitivity in clinically relevant serum samples. Real-time assys of the binding, activity, and small-molecule inhibition of telomarase could be performed with this technique using unamplified extracts from a few as 10 tumor cells. This opens up substantial possibilities for diagnosis and treatment of cancer.

1.12 NUCLOPROTIEN NANODEVICES FOR DETECTION OF CANCER BIOMARKERS

DNA Y-junctions have been used as flurescent scaffolds for EcoRIi methyltransferasase thioredoxin fusion proteins and covalent links were formed between DNA scaffold and the methyltransferase at preselected sites on the

scaffold containing 5FdC. The resulting thioredoxin targeted nanodevice was found to bind selectively to certain cell lines but not to others. The fusion protein was constructed so as to permit proteolytic cleavage of the thioredoxin peptide from the nanodevice. Proteolysis with thrombin or enterokinase effectively removed the thioredoxin peptide from the nanodevice and extinguished cell line-specific binding measured by flurescence. Potential applications for device of this type include the ability of the fused protein to selectively target the nanodevice to certain tumor cell lines and not others, suggesting that this approach can be used to probe cell surface receptors as biomarkers of cancer and may serve as an adjunct to immunohistochemical methods in tumor classification.

1.13 NANOPARTICLE FOR COMBIND CANCER DIAGNOSIS AND THERAPY

Nanoparticles have refined molecular diagnostics and enabled early detection of tumors and discovery of biomarkers of Cancer. Nanoparticles are also therapeutic agents as well as carriers for targeted drug delivery. Main advantage of using nanoparticels in cancer is combining diagnosis with therapy. Important among the several nanoparticles used for this purpose are quantum dots(QDs) dendrimers, nanotubes and gold or silver nanoparticles. Details of the basic Characteristics and comparative advantage as well as drawbacks are discussed.

1.13.1 Gold Nanoparticles :

Photoacoustic flow cytometry has been used for real-time detection of circulating cells labeled with gold nanorods and the threshold sensitivity is estimated as one cancer cell in the background of 107 normal blood cells. An additional applicaiton of this technique is selective nanophotothermolysis of metastatic squamous cells. Gold nanoparticles could play an important role in efficient drug delivery and biomarking of drug-resistant leukemia cells. This could be explored as a novel strategy to inhibit multidrug resistance in targeted tumor cells and as a sensitive method for the early diagnosis of certain cancer. Interaction between the functionalized gold nanoparticles and biologically active molecules on the surface of leukemia cells may also contribute to the obseved enhancement in cellular drug uptake. The strong plasmon resonance absorption and photothermal conversion of gold nanoparticles has been exploited in cancer therapy through the selective localized photothermal heating of cancer cells.

Silver Nanoparticles :

Silver nanoparticles are bright enought to be seen by eye using optical microscopy but unlike fluorophores, fluorescent proteins, or quantum dots, silver naopartiles do not photodecompose during extended illumination. Thefore, they can be used as a probe to continuously monitor dynamic events in living cells during studies that last for weeks or even months and detect early changes in malignancy. Further development of Silver Nanoparticle based probes and assays may enable detection and diagnosis of cancer using ony a single cell from the patient.

Quantum dots :

Quantum dots(QDs) are crystalline semiconductors composed of a few hundred or a few thousand atoms that emit different colors of light when illuminated by a laser. Stable QDs are made from cadmium selenide and Zinc sulfide. Because of these probes are stable, they have the ability to remain in a cell's cytoplasm and nucleus without fading out much longer than conventional fluorescent labels. Their longevity has also made QDs a molecular label, allowing scientists to study the earliest signs of cancer and track the effectiveness of pharmaceuticals that target

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the cellular underpinnings of disease. Conjugation of QDs with biomolecules, including peptides and antibodies, could be used to target tumor in vivo.

1.14 THYRIOD GLAND

The Thyroid gland is a butterfly-shaped organ located interiorly to the trachea at the level of the second and third tracheal rings. Its name originates from the Greek term "thyroes," which means shield (named after the laryngeal thyroid cartilage). It consists of two lobes connected by the isthmus in the midline. Its bilaterality is important because the presence of malignant cells on one or both sides can significantly alter the management of the patient. Eg. Requiring more extensive surgery such as bilateral neck dissections, if there is local extension of tumor. Each lob is about 3-4 cms long, about 2cms wide, and only a few millimeter thick. Because of its very close anatomic relationship to the rounded trachea, nodules arising from the posterior aspect of the gland are usually inaccessible to the examining fingers and therefore often missed on a routine clinical examination. The isthamus is 12-15 mm high and connects the two lobes. Occasionally, a pyramidal lobe is located in the midline, superior to the Isthmus(fig. 1.1). It represents a remnant of the thyroglossal duct, as the primitive thyroid gland descends from the base of the tongue to its final location in the neck during embryonic development. Anatomic variation of the thyroid gland occur and are encountered in clinical practice; one of the more common is thyroid hemiagenesis. With only one lobe and an isthmus to the same abnormalities as are normal thyroid glands, including nodules and thyroid cancer.

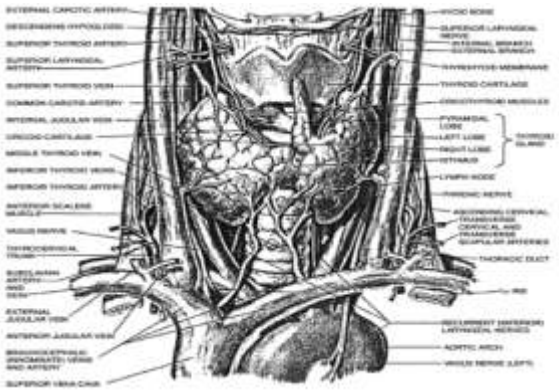

Fig 1: Thyroid Anatomy. Thyroid relations with surrounding cervical structures

A fibrous capsule overs the thyroid gland. Nodules within the parenchyma of the gland may also have a capsule or pseudo capsule. Surgical pathology reports may refer to tumor invasion "through the capsule," and for staging purposes, prognosis and management, it is important to know if this represents extension through the capsule of the gland into the surrounding perithyroidal tissue .

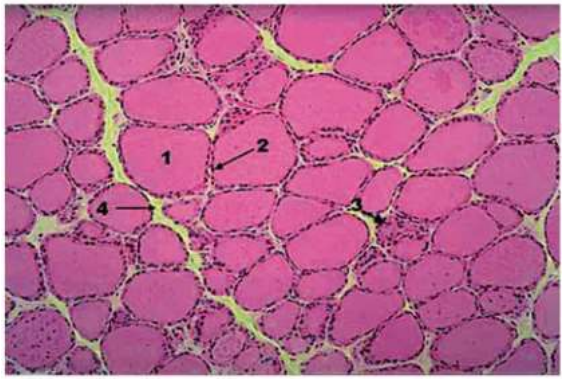

Fig 2 Histology of normal adult thyroid gland : Colloid of a thyroid follicle; (2) Follicular cells. Single layer cells forming a follicle; (3) parafollicular cells (C. cells); (4) connective tissue spectrum

The gland's blood supply comes from two sets of arteries on each side. The superior thyroid arteries orginate from the external carotid arteries. The descend to the superior poles of Thyroid gland and are accompanied by the superior laryngeal nerve. The nerve orginates from the inferior

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vagus ganglion. The thyroid gland has a characteristic histology and distinction between benign and malignant thyroid tissue are important to appreciate.

1.15 THYRIOD CANCER

Thyroid cancer is a rare tumor and represents only 1% of all human cancers; nevertheless it is the most common endocrinological malignancy. According to the WHO histological classification [1], thyroid tumors are classified as follows:

a) Papillary thyroid carcinoma (PTC);
b) Follicular thyroid carcinoma; and Poorly differentiated thyroid tumors;
c) Anaplastic thyroid carcinoma;
d) Medullary thyroid carcinoma (MTC);
e) Other rare thyroid tumors (i.e., lymphomas, sarcomas, hemangiosarcomas and mucoepidermoid, among others).

PTC and follicular thyroid carcinoma are defined as 'differentiated thyroid carcinomas' (DTCs) since they maintain the most important specific features of follicular normal cells, such as the ability to take up iodine, to produce thyroglobulin and to be dependent on thyroid stimulating hormone (TSH). PTC is the most common endocrine malignancy (Figure 1) and its incidence has increased in the last three decades in 2012 it has been estimated to reach 56,460 new cases annually in the USA [2,101]. Fortunately, the mortality rate is stable and approximately 95% of patients affected by PTC have long survival, up to 35–40 years.

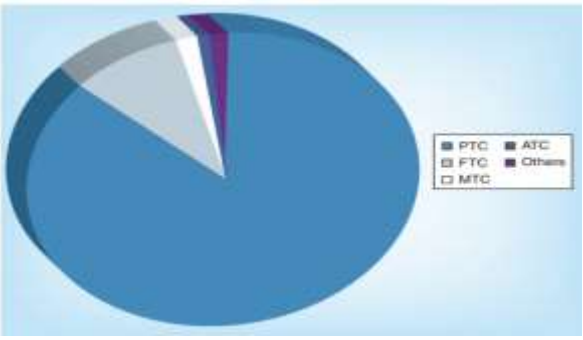

Figure 1. Distribution of thyroid cancer by histology. ATC: Anaplastic thyroid carcinoma; FTC: Follicular thyroid carcinoma; MTC: Medullary thyroid carcinoma; Others: Lymphomas, sarcomas, hemangiosarcomas, mucoepidermoid carcinoma; PTC: Papillary thyroid carcinoma.

CHAPTER THREE
MATERIALS AND METHODS

1.1.1. CLINICAL DATA

Ten patients with thyroid cancer were selected randomly from those who were treated from April 2017 to October 2019. All the patients were given total thyroidectomy combined with central neck lymph node dissection by the same surgeon. Five patients (5 males mean age: 36.4±2.5 (23–65) years) who received nano-carbon suspension during the operation were included in the experiment group and all were diagnosed with papillary thyroid carcinoma pathologically. Five patients (5 males, mean age: 44.5±5.8 (18–59) years) who did not use nano-carbon suspension were included in the control group, in which 3 cases were diagnosed with papillary carcinoma and 2 cases were diagnosed with follicular thyroid carcinoma pathologically. There were no statistically significant differences in age or sex between the 2 groups. Nano-carbon suspension was provided Informed consent for all the materials and methods involved in the paper was obtained from the patients, and the study was in one of the Hyderabad hospital and a case study of one of the Patient has been given.

3.2 NANOBIOTECHNOLOGY AND CANCER DETECTION

One of the most important factors in effective cancer treatment is the detection of cancerous tumor cells in an early and perhaps curable stage. Thus, the detection time frame has an enormous effect on a patient's prognosis. Nanobiotechnology brings new hope to the arena of cancer

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detection research, owing to nanoparticles' unique physical and chemical properties, giving them the potential to be used as a synthetic scaffold for imaging probes in the detection and monitoring of cancer. Nanoparticles' surface properties are tunable, meaning injectable solutions of them can be made without using toxic organic solvents to attach water-insoluble anticancer agents. This, along with nanoparticles' ability to do passive or active tumor targeting, makes them an excellent platform to use for diagnostic imaging and treatment. Thus, Nanobiotechnology-based imaging modalities have made a significant entry into cancer research with their potential of highly sensitive probes for cancer detection.

Quantum Dots

Over the past few decades quantum dots (QDs) have been an area of intense research due to their unique physical properties that can be exploited for cancerous tumor detection. QDs usually consist of an inorganic transition metal core/shell system, and the majority of QDs are made up of cadmium selenide (CdSe), cadmium telluride (CdTe), indium phosphide (InP), and indium arsenide (InAs) as core elements inside a shell, usually zinc sulfide (ZnS). The major reasons that these inorganic-organic composite nanoparticles are extremely efficient agents for cancer detection *in vivo* are their small size, which gives them unhindered access to the systemic circulation, and at the same time their ability to conjugate targeting molecules that direct specific accumulation in neoplastic sites. Additionally, similar to other nanoparticles, QDs have sufficient surface area to attach therapeutic agents and tumor-specific moieties for simultaneous drug delivery and *in vivo* imaging and tissue engineering. Depending on size and the core/shell system, QDs have the ability to emit light across the visible and infrared wavelength spectrum, and thus one can choose a suitable color of light emission. The main advantage of the QDs is that with a single light source, the variously-sized QDs can be excited while preserving the narrow emission of each individual particle/wavelength. Additionally, QDs have the ability to incorporate different markers simultaneously (multiplexing), enabling numerous targets to be imaged in a single experiment.

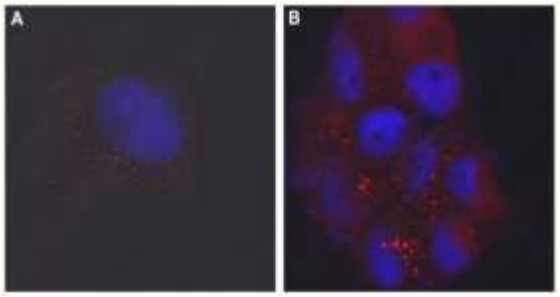

Figure 4: Confocal microscopy images showing uptake of Tetrac-PEG-QDs by Panc1 cells: (**A**) Cells were left untreated prior to incubation with QDs; (**B**) cells were pre-treated with T_4 (thyroxin, a thyroid hormone) for 2 hours prior to the addition of QDs.

A recent advancement in QDs technology is the use of QDs for near infrared (NIR) imaging (700–1000 nm wavelength range) as an imaging probe. The main advantage of NIR QDs over its counterpart, visible QDs, is that it increases the depth of tissue penetration, allowing for more accurate and sensitive detection of photons *in vivo*. Additionally, NIR QDs evade the problem of auto-fluorescence associated with optical imaging because of the naturally-occurring compounds present in animal tissue. The use of NIR QDs for *in vivo* imaging was demonstrated for lymphatic mapping in animal models, and for biological imaging, using InAs/ZnCdS as a core/shell. NIR QDs coated with PEG allowed imaging of tumor vasculature as deep as 200 um, contrary to

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the visible QDs-generated images with very poor vascular contrast.

In summary, owing to their unique properties such as photostability, size- and composition-tunable emission properties (from visible to infrared wavelengths), and their ability to deliver multiple diagnostic or targeting agents, QDs have emerged as a promising nanotechnology for cancer detection. Furthermore, utilization of NIR QDs can potentially not only maximize the depth of tissue penetration compared to conventional imaging, but also can enhance the accuracy and photon detection sensitivity in an *in vivo* systems.

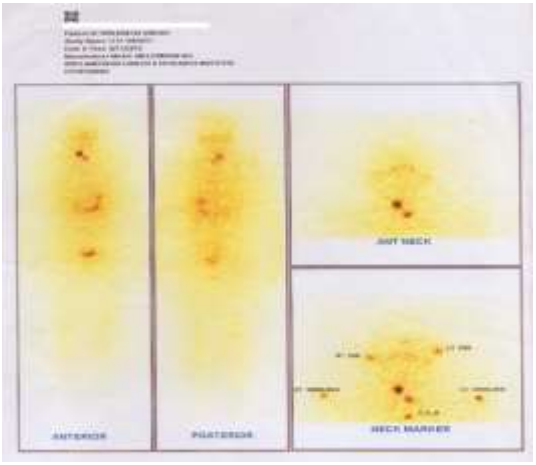

Fig : Iodine Scan Test

Iron Oxide Nanocrystals

Though there have been tremendous efforts to determine a suitable imaging tool for cancer detection, until now only magnetic resonance imaging (MRI) has been used. It is one of the most frequently-used, non-invasive imaging tools for disease diagnosis and monitoring, including cancer. However, a major problem associated with MRI is its low sensitivity. Utilization of nanotechnology to improve the sensitivity and efficacy of MRI for cancer detection and imaging is an area that researchers have focused on in the last several decades.

Magnetic nanoparticles used in biomedical applications mainly have an inorganic nanoparticle core and in most cases are coated by a suitable coating material. Suitable coatings not only increase the stability and solubility of the nanoformulation but also can be used to incorporate a targeting moiety to increase the imaging sensitivity and to do real-time monitoring. Enhanced proton relaxation is one of the most added-value properties that make magnetic nanoparticles one of the best contrast agents for biomedical applications of MRI.

Table 1: Magnetic nanoparticles in clinical trials or currently available on the market.

Product	Company Developer	Coating Agent	Application	Targeting Moiety	Use
Feridex/ Endorem	AMAG Pharma. Inc	Dextran	Liver tumors	None	Imaging
Feraheme/	AMAG Pharma. Inc	Polyacrylic acid, carboxy methyl ether	CNS tumors	None	Imaging
Resovist®	Bayer Schering Pharma AG	Carboxy-dextran	Liver metastasis, colon cancer	None	Imaging
SPION	Sun, Rangnathan, Feng 2008	PEG/Dextran	Breast cancer	Folic Acid	Imaging
SPION	Kohler et al., 2005	3-(aminopropyl) trimethoxysilane	Brain tumors	Methotrexate	Imaging and treatment
SPION	Sun, Lee, Zhang, 2008	PEG	Brain tumors	Chlorotoxin	Imaging and treatment
SPION	Wang et al., 2008	PEG	Prostate cancer	A10 RNA aptamer	Imaging and treatment
SPION	Lanchner et al., 2008	Chorionic gonadotropin	Breast cancer	LHRH	Imaging
SPION	Kikumori et al., 2009	Liposome	Breast cancer	Anti-HER2 antibody	Imaging
SPION	Chen et al., 2009	Dextran	Breast cancer	Herceptin	Imaging
USPION	Jiang et al., 2009	3-(aminopropyl) trimethoxysilane	Lung cancer	RGD	Imaging

CNS, central nervous system; PEG, poly(ethylene glycol); LHRH, luteinizing hormone releasing hormone; RGD, arginine-glycine-aspartic acid.

3.2.3 Nanobiotechnology and Cancer Treatment:

The cure for cancer remains as an elusive goal. Though there have been countless drugs coming to the market with the promise of eliminating this lethal disease, most of these drugs have proved to be too toxic or simply not as effective at extending life expectancy as originally projected. Most of these drugs have serious side effects, even resulting in death to the patient, mainly because of their non-specificity, and thereby seriously affecting normal cells along with the tumor cells. One of the major strengths

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of a nanomedicine approach is the ability to alter the pharmacokinetics and biodistribution of the drug. The idea behind targeted delivery that is now being elucidated is that chemotherapy drugs can be directed to cancer cells by exploiting the same properties of cancer cells that made their detection and targeting possible.

Table 2: Nanoparticle formulations currently available on the market.

Product	Company	Drug	Formulation/ROA	Application	Status
Abraxane	Abraxis Bioscience, AstraZeneca	Paclitaxel	Albumin-bound nanoparticles/iv	Metastatic breast cancer	Marketed
Caelyx	Schering-Plough	Doxorubicin	Pegylated liposome/iv	Metastatic breast and ovarian cancer; Kaposi sarcoma	Marketed
Myocet	ZeneusPharma Ltd	Doxorubicin	Liposome/iv	Metastatic breast cancer	Marketed
Doxil	Sequus Pharmaceutical	Doxorubicin	Liposome/iv	Kaposi sarcoma	Marketed
L-Annamycin	Callisto Pharmaceuticals	Annamycin	Liposome/iv	Children and young adults with refractory or relapsed ALL or AML	Phase I/II
Genexol-PM	Samyang Pharmaceuticals	Paclitaxel	Methoxy PEG-PLA/iv	Breast and lung cancer	Phase II
CALAA-01	Calando Pharmaceuticals	Anti-R2 SiRNA	Cyclodextrin-containing polymer (CAL 101) and targeting agent (AD-PEG-TF)/iv	Solid tumors that are refractory to standard-of-care	Phase I
Revia-G	Epeius Biotechnologies	Dominant negative cyclin G1 construct	Pathotropic nanoparticles/iv	Recurrent or metastatic breast cancer	Phase I/II
BIND Nano particle	MD Anderson Cancer Center/NCI	Pro-apoptotic Bik gene (BIBND)	Liposome/iv	Pancreatic Cancer	Phase I
Docetaxel-PNP	Samyang	Docetaxel	Polymeric nanoparticles/iv	Advanced solid malignancies	Phase I

ROA, route of administration; iv, intravenous; im, intramuscular; ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; PEG-PLA, poly(ethylene glycol)-poly(lactide); Tf, human transferring protein; HCC, hepatocellular carcinoma

Nanobiotechnology not only has the potential to conjugate the required targeting moiety, but also has the ability to carry the moiety for site-specific delivery without compromising its activity. Various polymeric materials are often used to synthesize nanoparticles loaded with conventional chemotherapy drugs such as docetaxel or doxorubicin, and then coated with polyethylene glycol to evade the patient's immune system. Additionally, nanoparticles can be conjugated with a targeted moiety such as an aptamerbioconjugate that binds, for example, to prostate-specific membrane antigens present on prostate cancer cells. This type of active-targeted delivery to the tumor by using a tumor-specific moiety can be achieved by exploiting various natural interactions like lectin-carbohydrate, ligand-receptor, and antibody-antigen interactions within the tumor cell, resulting in preferential accumulation within the cancer-bearing organ or cancerous tumor cells. Active targeting has the potential to change current cancer treatment scenarios.

3.2.4 Gold Nanoshells:

Gold nanoshells are useful in detecting tumors and metastasis in many solid tumors. The main advantage of the gold is its potential for cancer detection and treatment of cancers using near-infrared light. In a study where silica/gold nanoshells were used to treat breast cancer *in vivo*, the nanoshells were injected into the tumor site and irradiated with 820 nm, 4 W/cm^2 light pulses. The tumor site increased in temperature when irradiated with light, and thus this system had the ability to destroy the tumor cells without causing any harm to the surrounding, normal cells. In another step forward, gold nanoshells were conjugated with ligands for specific accumulation in oral squamous carcinoma cell lines (HSC 313 and HOC 3 Clone 8). Furthermore, these kinds of nanoshells have been used for targeted delivery and therapy of many cancers, including breast and prostate cancers.

3.2.5 PLGA Nanoparticles/Nanocells:

One of the most extensively used nanoparticles for cancer treatment is the poly (lactide-co-glycolide) (PLGA)-based nanoparticle. Proven biodegradability and a safe history have made PLGA nanoparticles a first choice for many researchers. Fonseca *et al.* reported encapsulation of paclitaxel in PLGA nanoparticles synthesized by interfacial deposition, and found an initial fast release profile during the first 24 hours of administration and

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later, a slower, continuous-release profile. Increased cytotoxicity of the nanoformulation was observed when it was compared to commercial formulations of free paclitaxel in an *in vitro* cell viability test in the NCI-H69 SCLC human small cell lung cancer cell line.

3.2.6 Dendrimers:

Dendrimers are a unique group of nanoparticles that are highly suitable for effective delivery of drugs, particularly for cancer treatment. Dendrimers can be synthesized by controlled, repeated polymerization reactions to engineer a desired shape and size. The main advantage of dendrimers is their exclusive branching point that is available for conjugation to multiple entities, including targeting proteins, treatment moieties, and even apoptosis factor ligands. Chemotherapy drugs, when incorporated into the core of the dendrimer, do not affect healthy cells. The dendrimer can be engineered so that when it gets into the target tumor cell, it can change its conformation, allowing the incorporated moiety to be released to the tumor site, efficiently suppressing tumor growth.

3.3.1 Synthesis of Dox-COOH

Doxorubicin hydrochloride (5 mg) was dissolved in dry dimethyl sulfoxide (DMSO) at room temperature in a dry glass bottle. Hereafter, 5 µL trimethylamine and *cis*-aconitic anhydride (1.3 mg) were added with stirring. The reaction mixture was stirred overnight and left for conjugation with SiO_2 NPs without further purification.

Preparation of Dox-loaded SiO_2 NPs (SiO_2@Dox)

3.3.2 Competitive uptake inhibition of TSH-SiO_2@Dox by blocking with free TSH

CHO/$TSHr^+$ cells were seeded in six-well plates at 0.5 million cells per well overnight. Prior to NP treatment, free TSH (10 µU/mL) was added to each well to block the surface TSHr. Thereafter, SiO_2/Dox and TSH-SiO_2/Dox at 5 µg Dox/mL were added to the wells, respectively, with PBS as a control. After 3 h, the cells were thoroughly washed by PBS three times and then trypsinized and collected before fixation by 4% paraformaldehyde. The fluorescence from Dox can be measured by flow cytometry (BD Biosciences, Franklin Lakes, NJ, USA), gated by the PBS-treated group.

CHAPTER FOUR

4.1 RESULTS

Here, we describe a silicon dioxide NP for acid-triggered release of Dox for thyroid cancer therapy. Following a well-reported strategy, Dox was firstly conjugated to *cis*-aconitic anhydride and this Doxprodrug (Dox-COOH)26 was further conjugated to a PEGylated silicon dioxide NP (SiO_2). For thyroid targeting, TSH was linked to NPs via disulfide bond formation (Scheme 1). The TSH-SiO_2@Dox thus prepared then showed excellent targeting to the thyroid cancer, with enhanced cytotoxicity and antitumor effect in vivo.

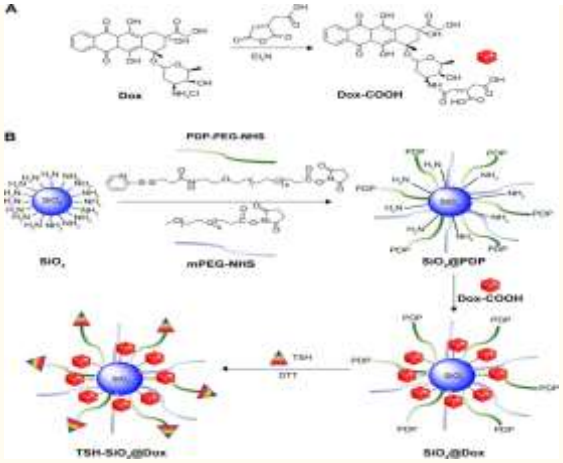

Figure 4.1: Synthesis of Doxprodrug and preparation of thyroid-targeting NPs TSH-SiO_2@Dox. Dox was firstly conjugated with *cis*-aconitic anhydride to prepare Dox-COOH (**A**). SiO_2 was PEGylated with mPEG-NHS and PDP-PEG-NHS. PEGylated SiO_2 with PDP groups (SiO_2@PDP) was further conjugated with Dox and TSH. Targeted NPs with Dox and

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TSH ligand (TSH-SiO_2@Dox) were prepared in this way (**B**).

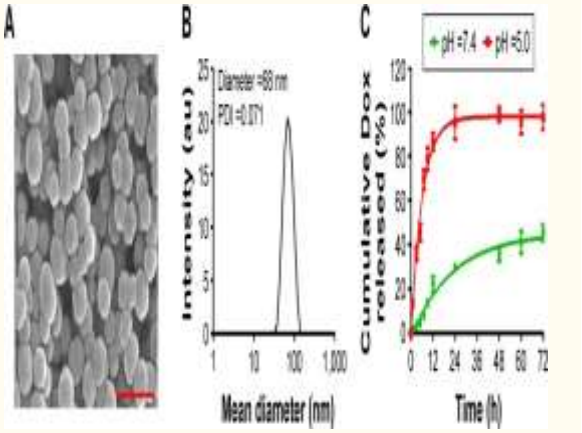

Figure 4.2: Characterization of TSH-SiO_2@Dox. Representative TEM image (**A**) and DLS curve (**B**) of TSH-SiO_2@Dox NPs. Scale bar =100 nm. Due to the presence of *cis*-aconitic linkage between the SiO_2 and Dox, release of Dox can be triggered by the acidic environment in tumor cells, which was simulated by the acid-triggered drug release as shown in (**C**).

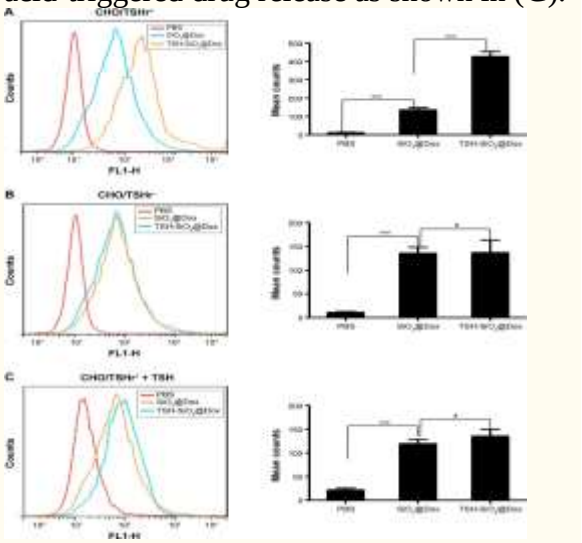

Figure 4.3: Targeting effect of TSH-SiO_2@Dox NPs. Monitoring targeting effect of TSH-SiO_2@Dox by flow cytometry as compared to SiO_2@Dox uptake by $CHO/TSHr^+$ cells (**A**) and $CHO/TSHr^-$ cells (**B**). To show the targeting effect, free TSH was added to the cells to competitively bind to the TSHr. In the presence of TSH, SiO_2@Dox and TSH-SiO_2@Dox showed minimal difference in uptake (**C**). Data are shown as mean ± SD (n=3). Significance is defined by $^{\#}P>0.05$ and $^{***}P<0.001$.

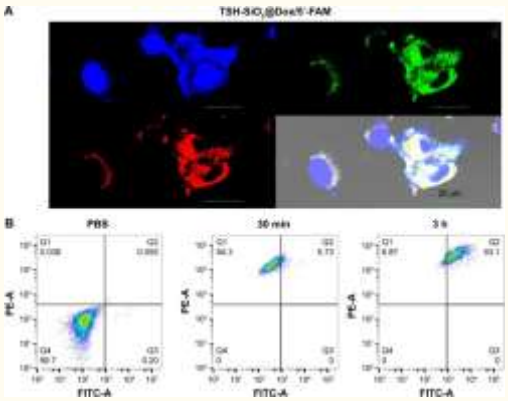

Figure 4.4: A study of the uptake of TSH-SiO_2/Dox/5′-FAM. Confocal laser scanning of cells treated with TSH-SiO_2/Dox/5′-FAM after 3 h. The targeting NPs were labeled by 5′-FAM (green). Hoechst stained the cell nucleus. Red fluorescence came from Dox. Scale bars =20 µM (**A**). To quantitatively monitor the NPs and the drug, cells were treated with TSH-SiO_2/Dox/5′-FAM, and then red and green fluorescence were monitored by flow cytometry. PBS-treated group (left), TSH-SiO_2@Dox/5′-FAM-treated group at 30 min (middle) and 3 h (right) (**B**).

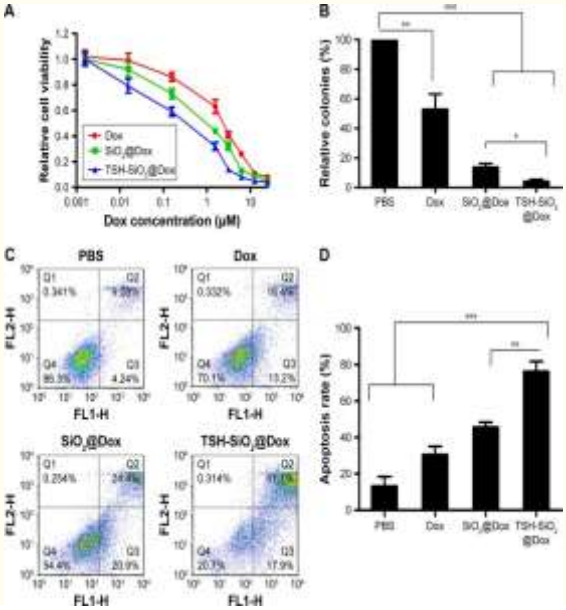

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Figure 4.5: In vitro evaluation of the anticancer efficacy of TSH-SiO_2@Dox on thyroid cancer cells. Cell viability curve of Dox, SiO_2@Dox, and TSH-SiO_2/Dox at 72 h (**A**) and relative cell colonies formation by cells treated with Dox, SiO_2@Dox, and TSH-SiO_2/Dox, respectively, at an equal Dox concentration at 0.05 μM (**B**). (**C** and **D**) Apoptosis rate of the cells treated with Dox, SiO_2@Dox, and TSH-SiO_2/Dox. Data shown as mean ± SD (n=3). Significance is defined by **P*<0.05, ***P*<0.01, and ****P*<0.001.

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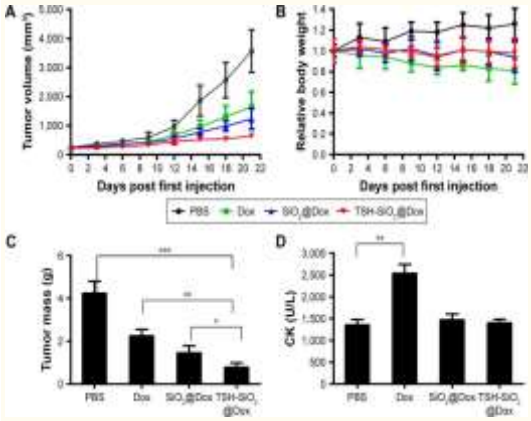

Figure 4.6: In vivo evaluation of TSH-SiO_2/Dox on FTC-133 xenograft model. Tumor shrinkage by TSH-SiO_2/Dox as compared to PBS, Dox, and SiO_2/Dox-treated mice (n=5, each group). Mice were intravenously injected with either PBS (PBS group) or an equal Dox dose of 5 mg/kg body weight (drug-treatment groups) on days 0, 6, and 12 (**A**). The body weight change of the mice is shown in **B**. At the end of this study, mice were sacrificed and tumors were collected and weighed (**C**). Cardiotoxicity as indicated by the CK is shown in **D**. Significance is defined by **P*<0.05, ***P*<0.01, and ****P*<0.001.

4.2 DISCUSSION :

Nanobiotechnology has officially had an effect on malignant growth identification and treatment. The fast interruption of this front line innovation in the present pharmaceutical industry is showed by Abraxane, a nanomedicine way to deal with treat metastasis bosom malignant growth. These aluminum-bound paclitaxel nanoparticles likewise have treatment potential for different malignancies with or without the co-nearness of other anticancer medications. Numerous nanomaterials like SPIO and USPIO nanoparticles are widely utilized under different trademarks for imaging of different sorts of malignant growths. On the site ClinicalTrials.gov, a vault of governmentally and secretly upheld clinical preliminaries led in the US and around the globe, it is uncovered that more than 70 nanomedicine methodologies are right now in clinical preliminaries for malignant growth treatment and imaging.

4.3 CONCLUSION :

Here we demonstrated the conceivable focusing of thyroid malignant growth by developing a TSH-stacked NP conveyance framework with Dox. By presenting a corrosive at risk linker among Dox and the NP, corrosive activated arrival of Dox was accomplished. TSH can be appended onto the outside of the NPs by disulfide bond development. This TSH-SiO2/Dox specially gathers in the TSHr+ cells for focusing on thyroid malignant growths. We at that point indicated disease focusing by confocal laser checking microscopy just as better in vitro anticancer viability of TSH-SiO2/Dox over free Dox and non-focused on NPs. This upgraded adequacy was additionally demonstrated by a more noteworthy capacity to hinder the malignant growth cell province arrangement examine and raised apoptosis. Further in vivo assessment of TSH-SiO2/Dox affirmed the conceivable focusing on effect of TSH-SiO2/Dox on thyroid malignant growths, with better tumor hindrance rate and lower harmfulness, which opens the entryway for the treatment of thyroid disease in the center.

REFERENCES :

[1]. Dahman, Yaser. *Nanotechnology and Functional Materials for Engineers*. Elsevier, 2017.
[2]. Roy Choudhury, S., and A. Goswami. "Supramolecular reactive sulphur nanoparticles: a novel and efficient antimicrobial agent." Journal of applied microbiology 114.1 (2013): 1-10.
[3]. Bhushan, Bharat, ed. *Springer handbook of nanotechnology*. Springer, 2017.
[4]. Dahman, Yaser. *Nanotechnology and Functional Materials for Engineers*. Elsevier, 2017.
[5]. Shatkin, Jo Anne. *Nanotechnology: health and environmental risks*. Crc Press, 2017.
[6]. Mittal, Amit Kumar, Yusuf Chisti, and Uttam Chand Banerjee. "Synthesis of metallic nanoparticles using plant extracts." *Biotechnology advances* 31.2 (2013): 346-356.
[7]. Lamish, Aharon, and Ofer Klein. "Magnetic separation of rare cells." U.S. Patent Application No. 15/406,819.
[8]. Ishikawa-Ankerhold, Hellen C., Richard Ankerhold, and Gregor PC Drummen. "Advanced fluorescence microscopy techniques—Frap, Flip, Flap, Fret and flim." *Molecules* 17.4 (2012): 4047-4132.
[9]. Guo, Zhongyi, et al. "Dielectric metasurface based high-efficiency polarization splitters." *RSC Advances* 7.16 (2017): 9872-9879.
[10]. Gupta, Ajay Kumar, et al. "Recent advances on surface engineering of magnetic iron oxide nanoparticles and their biomedical applications." (2007): 23-39.
[11]. Jain, K. K. "Targeted drug delivery for cancer." (2005): 311-313.
[12]. Vasir, Jaspreet K., Maram K. Reddy, and Vinod D. Labhasetwar. "Nanosystems in drug targeting: opportunities and challenges." *Current Nanoscience* 1.1 (2005): 47-64.
[13]. Maeda, Hiroshi, et al. "Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review." *Journal of controlled release* 65.1-2 (2000): 271-284.
[14]. Allen, Theresa M., and Pieter R. Cullis. "Drug delivery systems: entering the mainstream." *Science* 303.5665 (2004): 1818-1822.
[15]. Alyautdin, R. N., et al. "Significant entry of tubocurarine into the brain of rats by adsorption to polysorbate 80–coated polybutylcyanoacrylate nanoparticles: an in situ brain perfusion study." *Journal of microencapsulation* 15.1 (1998): 67-74.
[16]. Feng, Si-Shen, et al. "Nanoparticles of biodegradable polymers for clinical administration of paclitaxel." Current medicinal chemistry 11.4 (2004): 413-424.
[17]. Shaffer, Catherine. "Nanomedicine transforms drug delivery." (2005): 1581-1582.
[18]. Drexler, K. Eric. "Nanosystems." *Molecular machinery, manufacturing and computation.* (1992).
[19]. Cheng, Mark Ming-Cheng, et al. "Nanotechnologies for biomolecular detection and medical diagnostics." *Current opinion in chemical biology* 10.1 (2006): 11-19.
[20]. Lee, Ki-Bum, et al. "Protein nanoarrays generated by dip-pen nanolithography." Science 295.5560 (2002): 1702-1705.
[21]. NanoInk Inc: 2004. Available at http://www.nanoink.net.
[22]. NBTC (Nano-biotechnology Center, Cornell University): 2004. Available at http://www.nbtc.cornell.edu/default.htm
[23]. Guccione, Samira, King CP Li, and Mark D. Bednarski. "Vascular-targeted nanoparticles for molecular imaging and therapy." Methods in enzymology. Vol. 386. Academic Press, 2004. 219-236.
[24]. LaVan, David A., David M. Lynn, and Robert Langer. "Moving smaller in

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p-ISSN: 2348-795X
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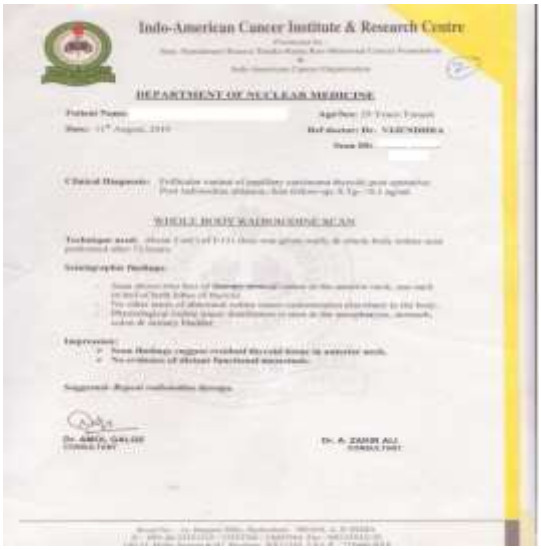
drug discovery and delivery." Nature Reviews Drug Discovery 1.1 (2002): 77.
[25]. Hu, LianDong, Xing Tang, and FuDe Cui. "Solid lipid nanoparticles (SLNs) to improve oral bioavailability of poorly soluble drugs." Journal of Pharmacy and Pharmacology 56.12 (2004): 1527-1535.
[26]. Stirling, Dale A. "History, Trends, and Future Directions." *The Nanotechnology Revolution*. Pan Stanford, 2018. 151-160.
[27]. von Maltzahn G, et al. Computationally guided photothermal tumor therapy using long-circulating gold nanorod antennas. Cancer Res. 2009;69:3892–3900
[28]. Jain, K. K. "Role of nanobiotechnology in developing personalized medicine for cancer." *Technology in cancer research & treatment* 4.6 (2005): 645-650.
[29]. Jain, Kewal K. "Nanomedicine: application of nanobiotechnology in medical practice." *Medical Principles and Practice* 17.2 (2008): 89-101.
[30]. Li, Jiahe, et al. "Nanobiotechnology for the therapeutic targeting of cancer cells in blood." *Cellular and molecular bioengineering* 8.1 (2015): 137-150.

Case Study of Thyroid Cancer
(On the request of the Patient name and Identity not disclosed)
The report has been used only for project purpose not for Commercial

Ultra Sound Scan of Thyroid Clearly shows Nodule on lower pole on Right lobe of thyroid gland of the patient which is Nacrotic at some areas suggested to refer to an endocrinologist and go for FNAC(Fine Needle Aspiration Cytology)



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Patient was given small of Radio active iodine and a gama camera to detect cancer cell in thyroid gland patient shows no evidence of distant functional metastasis.


Indo-American Cancer Institute & Research Centre