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A review of the emerging nanotechnology applications in medicine treatment

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Abstract
Current modalities of determination and treatment of different diseases, especially cancer have significant impediments, for example, poor affectability or specificity and Medicine toxicities separately. Fresher and enhanced techniques for cancer detection in light of nanoparticles are being produced. They are utilized as contrast agents, fluorescent materials, molecular research tools and Medicines with targeting antibodies. Paramagnetic nanoparticles, quantum dabs, Nano shells and Nano some are few of the nanoparticles utilized for diagnostic purposes. Meds with high dangerous potential like cancer chemotherapeutic Medicines can be given with a superior security profile with the utility of nanotechnology. These can be made to act particularly at the objective tissue by dynamic and additionally aloof means. Different modalities of therapy, for example, warm prompted removal of cancer cells by Nano shells and gene therapy are likewise being produced. This review discusses the different stages of nanotechnology being utilized as a part of various perspectives of medicine like diagnostics and therapeutics. The potential toxicities of the nanoparticles are likewise portrayed notwithstanding speculative plans, for example, responds and micro biomes. The safety of Nano medicine isn't yet completely characterized. In any case, it is conceivable that Nano medicine in future would assume an essential part in the treatment of human diseases and furthermore in improvement of ordinary human physiology.

Keywords: Nanotechnology, Applications, Medicine Treatment, diseases, limitations, improved, nanoparticles, cancer cells, therapeutics.

Introduction
Nano medicine includes use of nanotechnology for the benefit of human health and wellbeing. The utilization of nanotechnology in different areas of therapeutics has changed the field of medicine where nanoparticles of measurements running between 1 - 100 nm are outlined and utilized for diagnostics, therapeutics and as biomedical tools for research. It is presently conceivable to provide therapy at a sub-atomic level with the assistance of these apparatuses, in this way treating the disease and aiding investigation of the pathogenesis of disease. Conventional Medicines experience the ill effects of real constraints of unfriendly impacts happening because of non-specificity of Medicine action and absence of viability because of dishonorable or ineffectual measurements detailing (e.g., cancer chemotherapy and ant diabetic operators). Outlining of Medicines with more noteworthy level of cell specificity improves viability and limits adverse effects. Diagnostic methods with more noteworthy level of affectability help in early identification of the disease and give better prognosis. Nanotechnology is being connected widely to give focused on Medicine therapy, diagnostics, tissue regeneration, cell culture, biosensors and different devices in the field of molecular biology. Various nanotechnology stages like fullerenes, nanotubes, quantum dots, Nano pores, dendrites, liposomes, magnetic Nano probes and radio controlled nanoparticles are being developed.

Review of Literature
The major factors impacting the treatment outcome in a patient are the adequacy and safety profile of the Medicine all the more so when utilized for cancer chemotherapy. These Medicines have poor cell specificity and high lethality like bone marrow suppression, gastric erosion, hair loss, renal toxicity, cardiomyopathy, and a few impacts on other systems. Correspondingly treatment for diabetes faces challenges with the course of conveyance and deficient glycemic control. Accessibility of non-parenteral measurements types of insulin would be an achievement and improvement of a suitable Medicine delivery device can help in this approach. Much of the time, the affectability and specificity of different diagnostic methods as in radio imaging and different examines for discovery of harm are not sufficiently adequate for early identification and treatment.

Nanotechnology and Medical Applications
Development of fresher Medicine delivery frameworks in view of nanotechnology methods is being striven for conditions like cancer, diabetes, fungal infections, and viral infections and in gene therapy. The main advantages of this methodology of treatment are focusing of the Medicine and upgraded wellbeing profile. Nanotechnology has additionally discovered its utilization in diagnostic medicine as complexity operators, fluorescent colors and magnetic nanoparticles (Table 1).

Table 1: Some nanoparticles used for medical applications

Study phase	Product	Description	Use	Manufacturer
Preclinical	MRX 952	Nanoparticle preparation – to encapsulate camptothecin analogues	Tumours	IMA Rx Therapeutics
Preclinical	Targeted Nano Therapeutics (TNT)™ system	TNT with polymer coated iron oxide magnetic particle	Solid tumours	Triton Biosystems
Preclinical	AuroLase™	Gold nanoshell	Head and neck cancer	Nanospectra Biosciences Inc
Preclinical	Dendrimer-Magnevist®	PAMAM dendrimer	MRI imaging agent	Dendritic Nanotechnologies Inc
Phase 1	VivaGel®	Dendrimer based microbicide gel	HIV prevention	Starpharma Pty Ltd
Phase 1	INGN 401	Nanoparticle formulation of tumour suppression gene FUS1	Lung cancer	Introgen Therapeutics Inc
Phase 1&2	Cyclosert-Camptothecin – IT 101	β-Cylcodextrin polymer drug delivery system	Solid tumours	Calando Pharmaceuticals
Phase 2	VivaGel®	Dendrimer based microbicide gel	HSV prevention	Starpharma Pty Ltd
Phase 2	MRX 815	Nanobubble technology	Treatment of intravascular clot	IMA Rx Therapeutics
Phase 3	Combidex® / Ferumoxtran 10	Iron oxide nanoparticle	MRI contrast agent	AMAG Pharmaceuticals
Marketed	Abraxane®	Albumin bound taxane particles	Non small cell lung cancer	Abraxis Oncology
Marketed	AmBisome®	Liposomal preparation of amphotericin B	Fungal infection	Astellas Pharma US
Marketed	Doxil®	Liposomal doxorubicin	Ovarian tumour	Ortho Biotech

Liposomes: Liposomes discovered in mid 1960s were the first models of Nano scaled Medicine delivery devices. They are round nanoparticles made of lipid bilayer layers with a watery inside however can be Unilamellar with a solitary lamella of film or multilamellar with multiple membranes. They can be utilized as viable Medicine delivery frameworks. Cancer chemotherapeutic Medicines and different toxic Medicines like amphotericin and hacking, when utilized as liposomal Medicines produce much better viability and security when contrasted with customary arrangements. These liposomes can be stacked with Medicines either in the watery compartment or in the lipid membrane. Usually water soluble Medicines are stacked in watery compartment and lipid soluble Medicines are joined in the liposomal membrane. The major limitation of liposome is its quick corruption and leeway by the liver macrophages, hence diminishing the length of activity of the Medicine it conveys. This can be decreased to a specific degree with the appearance of stealth liposomes where the liposomes are covered with materials like polyethylene which avoids of the liposome and their take-up by macrophages. Different methods for dragging out the dissemination time of liposomes are consolidation of substances like cholesterol, polyacrylamide lipids and high transition temperature phospholipids.

Nano pores: Nano pores composed in 1997 by Desai and Ferrari comprise of wafers with high density of pores (20 nm in diameter). The pores permit passage of oxygen, glucose and different items like insulin to go through. In any case, it doesn't allow immunoglobulin and cells to go through them. Nano pores can be utilized as devices to protect transplanted tissues from the host immune framework, in the meantime, using the benefit of transplantation. β cells of pancreas can be encased inside the Nano pore device and embedded in the recipient's body. This tissue sample gets the supplements from the surrounding tissues and in the meantime stays undetected by the immune system and consequently don't get rejected. This could fill in as a fresher methodology of treatment for insulin subordinate diabetes mellitus. Nano pores can likewise be employed in DNA sequencing. Brinton's group at Harvard University has been taking a shot at changed Nano pores that can separate DNA strands in view of contrasts in base pair

sequences. Nano pores are additionally being produced with capacity to separate purines from pyrimidines. Further, fuse of electricity conducting electrodes is being intended to enhance longitudinal resolution for base combine distinguishing proof. Such a technique could read a thousand bases for every second per pore. These can be utilized for minimal effort high throughput genome sequencing which would be of extraordinary advantage for application of pharmacogenomics in Medicine development process.

Nanotubes: Carbon nanotubes found in 199134 are tubular structures like a sheet of graphite moved into a cylinder capped at one or the two finishes by a Bucky ball. Nanotubes can be single walled carbon nanotube (SWCNT) or multiwall carbon nanotube (MWCNT) in concentric design. Single walled nanotube has an internal measurement of 1-2 nm and multiwall nanotube has a diameter of 2-25 nm with 0.36 nm distance between layers of MWCNT. These change in their length extending from 1 µm to a few micrometers. These are described by more prominent quality and solidness henceforth can be utilized as steady Medicine carriers. Cell specificity can be accomplished by conjugating antibodies to carbon nanotubes with fluorescent or radiolabelling. Passage of nanotubes into the cell may be mediated by endocytosis or by addition through the cell membrane. Carbon nanotubes can be made more solvent by fuse of carboxylic or ammonium gatherings to their structure and can be utilized for the vehicle of peptides, nucleic acids and different Medicine molecules. Indium-111 radionuclide named carbon nanotubes are being researched for killing cancer cells selectively.

An Amphotericin B nanotube has demonstrated expanded Medicine delivery to the inside of cells thought about to amphotericin B organization without nanotubes. The adequacy of amphotericin B nanotubes was more noteworthy as an antifungal specialist contrasted with amphotericin B alone and it was powerful on strains of fungi which are typically safe to amphotericin B alone. Further, there was lessened lethality to mammalian cells with amphotericin B nanotubes. The capacity of nanotubes to transport DNA across cell membrane is utilized as a part of studies including gene therapy. DNA can be joined to the tips of nanotubes or can be consolidated inside the tubes. Prato *et al*. indicated more noteworthy articulation of the β galactocidase marker gene through nanotubes compared to exchange of naked DNA. This gives the preferred standpoint of non-immunogenicity in difference to viral vectors utilized for gene transfer. Gene silencing contemplates with little interfering RNA (siRNA) have been done as a methodology of cancer therapy where tumors cells will be specifically adjusted. Functionalized single walled carbon nanotubes can be utilized with siRNA to hush focused on gene expression.

Nano shells: Nano shells were developed by West and Halas45 at Rice University as a new modality of targeted therapy. Nano shells consist of nanoparticles with a core of silica and a coating of thin metallic shell. These can be targeted to desired tissue by using immunological methods. This technology is being evaluated for cancer therapy. Hirsh *et al.* used Nano shells which are tuned to absorb infra-red rays when exposed from a source outside the body to demonstrate the thermo ablative property of Nano shells. The Nano shells when exposed to NIR region of the electromagnetic spectrum get heated and cause destruction of the tissue. This has been studied in both in vitro and in vivo experiments with HER 2 expressing SK-BR-3 human breast carcinoma cells. The control cells did not lose their viability even after treatment with Nano shells with non-specific anti IgG or PEG and NIR ablation.

Nano shells can also be embedded in a hydrogel polymer containing the Medicine. After directing the Nano shells to the tumour tissue by immunological methods, with an infrared laser, these can be made to get heated up, melting the polymer and releasing the Medicine at the tumour tissue. Targeting the Medicine release avoids the toxicity of cancer chemotherapy Medicines. Nano shells are currently being investigated for micro metastasis of tumours and also for treatment of diabetes. Nano shells are also useful for diagnostic purposes in whole blood immunoassays. Gold Nano shells can be coupled to antibodies and the size can be modulated so that it responds to NIR wavelength, which has the ability to penetrate whole blood specimens. With this method it is possible to detect immunoglobulins at a concentration range of Nano grams per millilitre in plasma and whole blood.

Nano bubbles: Cancer therapeutic Medicines can be incorporated into nanoscale bubble like structures called as Nano bubbles. These Nano bubbles remain stable at room temperature and when heated to physiological temperature within the body coalesce to form microbubbles. These have the advantages of targeting the tumour tissue and delivering the Medicine selectively under the influence of ultrasound exposure. This results in increased intracellular uptake of the Medicine by the tumour cells. It also provides an additional advantage of enabling visualisation of the tumour by means of ultrasound methods. Rapaport *et al.* have demonstrated the utility of Nano bubbles in delivery of Medicines like doxorubicin based on in vitro and in vivo experiments using breast cancer cells MDA MB231 and mice with breast cancer xenograft respectively. On administration of Nano bubble loaded doxorubicin, these reach the tumour tissue through leaky vasculature and get accumulated at the site of tumour. This is followed by formation of microbubbles by coalescing of Nano bubbles which can be visualized by ultrasound techniques. When the site is focused with high intensity focused ultrasound (HIFU), it causes disruption of the microbubbles resulting in release of the Medicine. The microbubbles retained the Medicine in a stable state until stimulated by HIFU. This results in attainment of higher levels of Medicine in the target cells and hence reduced toxicity and increased efficacy. This method needs further exploration for its utility in treatment of various malignancies. Liposomal Nano bubbles and microbubbles are also being investigated for their role as effective non-viral vectors for gene therapy.

Nano-Technology in Gene Therapy: Gene therapy is a more up to date methodology of approach for treatment of numerous genetic disorders including diabetes mellitus, cystic fibrosis, and alpha 1 antitrypsin inadequacy. Viral vectors utilized for gene transfer have the impediments of security concerns and incitement of immune system with generation of

antibodies against the viral vectors. Further, bare DNA cannot cross the contrarily charged cell membrane as these are likewise negatively charged. Thus, there is a requirement for different methods of exchange of genetic material such as nanoparticle based gene therapy. Liposomes measuring less than 100 nm can be utilized for conveyance of genetic material into cells. Liposomes incorporated with polyethylene glycol and galactose target liver cells effectively because of their fast take-up by liver Chuffer cells. Hence gene therapy might be attempted with such liposomal nanoparticles for different liver disorders, for example, Wilson's disease and inherited hemochromatosis. Niu *et al.* utilized human insulin gene in chitosan nanoparticles to transfect STZ diabetic rat through gastrointestinal tract. They found a noteworthy abatement in fasting blood glucose level, increment in plasma insulin levels and articulation of human insulin gene mRNA in the investigation rats. This investigation may prompt the improvement of a more up to date methodology of therapy for sort 1 diabetes mellitus. A "mixture Nano device" outlined by laborers of Northwestern University and Argonne National Laboratory comprises of a titanium dioxide (TiO2) semiconductor nanoparticle of measurement 4.5 nm connected covalently to oligonucleotide DNA. The oligonucleotide sequence can guide the half breed Nano device to the comparing DNA segment inside the cell nucleus. At the point when fortified with light or X beams, TiO2 incites nucleic acid endonuclease which separates off the particular DNA fragment. This gadget is yet to be tried in a laboratory model. In any case, it might have a potential utility in treatment of different malignancies in the future.

Regulatory Challenges with Nano Medicines: Regulatory issues assume a noteworthy part in the development of Nano formulation Medicines. These incorporate, the kind of Nano Medicine created and the different administrative necessities that the makers must take after amid the assembling of Nano Medicines. A Nano formulation of a Medicine which depends on a formerly approved Medicine in micro formulation can experience a shorter endorsement pathway by methods for contracted new Medicine application if bioequivalence can be exhibited to its micro formulation Medicine. However, if bioequivalence cannot be illustrated, it would require endorsement of the considerable number of stages of new Medicine application. Further, when a Nano Medicine is designed as another chemical entity, the assessment technique turns out to be more stringent.

Nano Medicine manufacturers must consent to FDA's Current Good Manufacturing Practices (CGMP) and Quality System Regulations (QSR). Noncompliance with these regulations would warrant authorization activities by the FDA. For example, 21 CFR 211.25 of FDA's CGMP requires that the faculty associated with the manufacturing process, in giving preparing to the workers and the staff directing the manufacturing process have satisfactory training, education and experience. Further, the preparation must be led at satisfactory frequency and there must be sufficient number of qualified staff for the relegated obligations. A Nano Medicine manufacturer must contribute significant measure of financial resources to have such qualified faculty in the working unit. Maintenance of hardware for manufacture of Nano Medicines and control of pollution are additionally administrative necessities for manufacturers. The Medicine products are refined by the utilization of channels and CGMP requests that the channels don't release fibers. Be that as it may, when liquid filtration is utilized, Nano Medicine manufacturers will not have the capacity to agree to CGMP; since the littlest filtration level accessible is around 15 nm and Nano Medicines could be at the scope of 5 to 6 nm long. The FDA centers in particular, the Center for Medicine Evaluation and Research (CDER), the Center for Devices and Radiological Health (CDRH) and the Center for Biologics Evaluation and Research (CBER) regulate Medicines, devices, and biologics respectively and are in charge of managing Nano medical products. FDA arranges medicinal products as Medicine, device or biologics according to their essential method of activity to allot middle for their primary jurisdiction amid the evaluation process. In the event of a Nano Medicine it is hard to order it as a Medicine, device or biologics since it has a tendency to have a blend of the above. Thus, the assignment of the Center winds up noticeably troublesome. Further, the Medicine has to go through every one of the Centers of FDA owing to its complexity. This result in more noteworthy day and age for endorsement of the Medicine The staff of FDA should likewise be adequately instructed and prepared in nanotechnology in the field of medicine to evaluate Nano Medicine products.

Nanotechnology in Health and Medicine:

Even today various disease like diabetes, cancer, Parkinson’s disease, Alzheimer’s disease, cardiovascular diseases and multiple sclerosis as well as different kinds of serious inflammatory or infectious diseases (e.g. HIV) constitute a high number of serious and complex illnesses which are posing a major problem for the mankind. Nano medicine is an application of nanotechnology which works in the field of health and medicine. Nano-medicine makes use of nano materials, and nano electronic biosensors. In the future, nano medicine will benefit molecular nanotechnology. The medical area of nano science application has many projected benefits and is potentially valuable for all human races. With the help of nano medicine early detection and prevention, improved diagnosis, proper treatment and follow-up of diseases is possible. Certain nano scale particles are used as tags and labels, biological can be performed quickly, the testing has become more sensitive and more flexible. Gene sequencing has become more efficient with the invention of nano devices like gold nano particles, these gold particles when tagged with short segments of DNA can be used for detection of genetic sequence in a sample. With the help of nanotechnology, damaged tissue can be reproduced or repaired. These so called artificially stimulated cells are used in tissue engineering, which might revolutionize the transplantation of organs or artificial implants. Advanced biosensors with novel features can be developed with the help of Carbon nano tubes. These biosensors can be used for astrobiology and can throw light on study origins of life. This technology is also being used to develop sensors for cancer diagnostics. Though CNT is inert, it can be functionalized at the tip with a probe molecule. Their study uses AFM as an experimental platform.

i. Probe molecule to serve as signature of leukemia cells

identified. ii. Current flow due to hybridization will be through CNT electrode to an IC chip. iii. Prototype biosensors catheter development.

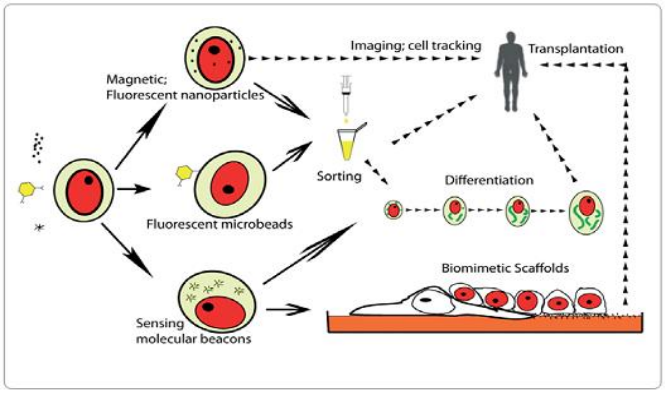

Fig 1: Nanotechnology applications in stem cell biology and medicine

Nanotechnology has made excellent contribution in the field of stem cell research. For example, magnetic nanoparticles (MNPs) have been successfully used to isolate and group stem cells. Quantum dots have been used for molecular imaging and tracing of stem cells, for delivery of gene or Medicines into stem cells, nano materials such as carbon nano tubes, fluorescent CNTs and fluorescent MNPs have been used. Unique nanostructures were designed for controllable regulation of proliferation and differentiation of stem cells is done by designed unique nano structures. All these advances speed up the development of stem cells toward the application in regenerative medicine [3]. The recent applications of nanotechnology in stem cell research promises to open new avenues in regenerative medicine. Nanotechnology can be a valuable tool to track and image stem cells, to drive their differentiation into specific cell lineage and ultimately to understand their biology. This will hopefully lead to stem cell-based therapeutics for the prevention, diagnosis and treatment of human diseases [4]. Nano devices can be used in stem cell research in tracking and imaging them. It has its applications for basic science as well as translational medicine. Stem cells can be modulated by mixing of nano carriefrs with biological molecules (Figure 6). Nano devices can be used for intracellular access and also for intelligent delivery and sensing of biomolecules. These technologies have a great impact in stem cell microenvironment and tissue engineering studies and have a great potential for biomedical applications [5].

Conclusion

Although the desires from nanotechnology in medicine are high and the potential advantages are interminably enrolled; the security of Nano medicine isn't yet completely characterized. Utilize of nanotechnology in medical therapeutics needs sufficient assessment of its hazard and wellbeing factors. Notwithstanding, it is conceivable that Nano medicine in future would assume a vital part in treatment of human diseases and furthermore in improvement of ordinary human physiology. With concurrent application of nanotechnology in different fields, its utility is probably going to broaden promote into diagnostics, molecular research techniques and devices. Nano materials have expanded surface region and Nano scale impacts, henceforth utilized as a promising apparatus for the headway of Medicine and gene delivery, biomedical imaging and diagnostic biosensors. Nano materials have novel physicochemical and biological properties when contrasted with their larger counterparts. The properties of Nano materials can incredibly impact their connections with biomolecules and cells, because of their exceptional size, shape, chemical composition, surface structure, charge, dissolvability and agglomeration. For example, nanoparticles can be utilized to create exceptional images of tumor destinations; single walled carbon nanotubes, have been utilized as high-productivity conveyance transporters for biomolecules into cells. There is a brilliant future to nanotechnology, by its converging with other technologies and the consequent development of perplexing and inventive hybrid technologies. Biology based technologies are interweaved with Nano technology is as of now used to control genetic material, and Nano materials are now being assembled utilizing biological components. The capacity of Nano technology to design matter at the littlest scale is altering zones, for example, information technology subjective science and biotechnology and is prompting new and interlinking these and different fields. By additionally look into in Nano technology; it can be helpful for each part of human life. Medicine, regenerative medicine, stem cell research and nutraceuticals are among the main parts that will be changed by Nano technology innovations.

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