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Nanobiotechnology in Understanding Cancer Biology

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Abstract

The biosynthesis of nano particles with a great deal of effort by using a 'Green technology' that gives an innocuous, inexpensive and environmental friendly approach has been widely used. The technology also leads to fabricate wonder materials for biomedical applications. The in vitro green approaches for the reduction of metal ions furnishes a flexible method to obtain nano particles with control over their size and shape that can be attributed to the flexibility of changing the medium pH and reaction temperature. This review provides an outlook on a range of devices and tools that can make a system for detection of a therapeutic agent and to determine its action on an intended target, facilitating the research in diagnosis and prevention of cancer. The validation of nano particles with these exciting approaches may serve a strong foundation for modified chemotherapies in the next phase of clinical trials which would lead to profound changes in oncological practices by facilitating the realization of personalized medicines through demonstration of safety as well as efficacy in human clinical trials.

Keywords: Green technology; Wonder materials; Personalized medicines; Cancer; Modified chemotherapy.

Introduction

Since the first preparation of the nano-particles that was carried out by Michael Faraday as early as in 1857, nano has become a flavor in the world of science. Nanoparticles, because of their exciting phenomenon of small size and variable shapes as spherical, wiry, tubular or sheet like has gained tremendous importance in the areas of medical diagnostics, drug delivery, chemical industry, textile industry and electronics. The utilization of this technology for the preparation of nano based products in area of research and development is growing at a great pace and is still expected to grow further in the coming years. The revolutionary impact of nanoscience in today's world is associated with the unforeseen hazards of these particles related to its method of synthesis.

The intersection of nanotechnology and biotechnology has led to a fairly new area of technology; Nano biotechnology. This new area of research has been used in the development of nanomedicine that covers health care related areas of nanoscience and technology and serves structured nanodevices to analyze the specific biological system.

Top-down and bottom-up approaches

The synthesis of nanomaterials and effective fabrication of nanostructures follows two basic approaches; the top down approach involves successive cutting of larger parts to get nano sized particles of smaller and smaller dimensions. Bottom up approach follows building of material from atoms or molecules or by clusters. However, the disadvantage associated with the top down approach is the structural damage leading to imperfection of surface structure and patterns. Bottom up approaches provides a better chance to form nano structure with fewer defects although; the process frequently in Nanotechnology is not a newer concept.

Nano synthesis: a green remedy

A remarkable area of nanoresearch is often concern with the global environment. A great deal of effort has been put on that provides a better platform for the biosynthesis of nano particles by using plants [1] that are more innocuous, inexpensive, and environmentally friendly as they do not leave hazardous residues to pollute the atmosphere [2-6]. Although, the chemical method of synthesis requires less time for the fabrication of large quantity of nano particles, but are considered toxic and often lead to products that are non-eco-friendly [7]. In recent years, the in vitro green approaches for the reduction of metal ions provides a flexible, method to obtain nano particles with control over their size and shape that can be attributed to the flexibility of changing the medium pH and reaction temperature [8]. Variety of different plant species in combination with acid and salts of metals can be used to reduce ions of gold, copper, silver, platinum, iron and many others [9].

Current appearance in cancer diagnosis and drug delivery

Facilitating the research in diagnosis and prevention of diseases, Nanotechnology offers a range of devices and tools that can make a system for detection of a therapeutic agent and to determine its action on an intended target. In recent years, nanotechnology has become a boon in cancer research by helping the oncologist to spot the cancer in early stages by detecting biomarkers that are undetectable through conventional detection techniques. Nanotechnology researchers have provided nano medicine based approaches that have been considered safe and effective treatment of cancer. Of the advances driven by National Cancer Institute (NCI), the discrimination of a healthy and cancerous cell by the use of photo luminescent nano particles will enable the clinician to identify the precancerous lesions thereby providing an early signal to reverse the premalignant changes and also allowing a time release of an anticancer drug sequentially at a desired location (www.cancer.gov). Tumors targeting objective has also influenced the role of Gold Nano particles (AuNP's) by their conjugation to Polyethylene Glycol (PEG) and unique biomarker binded antibodies on tumor cells. The fabrication of AuNP's with PEG prevented the unwanted aggregation and lengthened the retention time in blood by preferential accumulation of the particles in the tumor [10]. In another study, researchers at Cornell University have figured out the attachment criteria of gold nano particles by merging with iron oxide into colorectal cancer cell seeking the role of antibodies that can deliver the gold to the cancerous cell which can be heated by passing infrared laser because of the efficient property of the tiny particles of gold alloy which in turn will kill the cancerous cells [11].

Nano particle based drug delivery have also gain considerable potential for effective drug delivery in cancer therapy. The major challenge in the treatment of the disease is to get the drug at a specific place that is needed thereby avoiding side effects to other non-targeted organs. The limitations associated with the chemotherapeutics used against such dreaded disease are their non-restricted cytotoxicity in context to increasing dosage concentration. The nano particle formulation resulted in enabling the strategy of targeted drug delivery and these includes benefits of their small size which allow an easy penetration into the cell membrane, binding and stabilization of protein and lysosomal escape after endocytosis [12] thereby leading to the development of faster and safer medicines. Recently, the emergence of numerous proteinic and other drugs for targeting various cellular process have created a demand for the development of intelligent drug delivery system [13]. To meet the requirements for intelligent release of therapeutic agents to perform various function of detection, isolation and treatment of diseased conditions, a smart delivery system such as stimuli responsive nano materials will be a promising approach [14].

Carbon nano tube with its hollow structure is one of the wonder nano material that have motivated the researchers to explore their potential in the application of drug delivery to transport drug molecules, proteins and nucleotides. The size and shape of these materials allow them to enter living cells by adhering covalently or non-covalently to the surface without causing cell damage [15]. The potential application of carbon nano tubes in biotechnology is of much interest for exhibiting its advantages in biosensors [16], biomedical devices [17] and drug delivery systems [18]. However, the fictionalizations of CNTs is needed to reduce the chances of cytotoxicity and improving their biocompatible properties. The surface properties of the CNTs greatly influence their internalization behavior into the cell that is aided by the hydrophilicity of the tube. Also, the shorter length nano tubes are more effectively transported across the cell than the bundled CNTs [19].

Engineering of polymeric nanostructures for drug delivery inputs the use of a highly branched polymer known as Dendrimers that resemble the architecture of a tree. These multi branched macromolecules have attracted the researchers for various application in many fields due to its low polydispersity and high functionality. Dendrimers have offered escalating attention in scientific research particularly in the area of biomedical and pharmaceutics as a potential drug vehicle. A well-defined globular structure of these materials ensures a reproductive pharmacokinetics besides causing an increased cellular uptake of the drugs conjugated to them [20].

Mesoporous silica nanoparticles have reported exponential increase in research and are one of the hottest areas in the field of nanomedicine and nano biotechnology for its functional application as biocompatible nanocarriers. With a mesoporous structure, MSNs have been explored to treat various kind of disease parameters including tissue engineering [21] diabetes [22] inflammation as well as cancer [23]. The unique tailor able structure of mesoporous silica nano particle with their high surface area to large pore volume endow them to encapsulate variety of therapeutic agent to emphasize the targeted delivery into desired location [24]. Currently, delivery of variety of molecules of pharmaceutical interest has been appeared by employing mesoporous materials [25]. Mesoporous Silica Nanoparticle of size 50 to 300nm is considered facile for endocytosis without cytoxicity. Materials including MCM-41,

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SBA-15, SBA-1, SBA-3, HMS and MSU are groups of mesoporous materials that have been functionalized for improving the biocompatibility and release kinetics of various drugs [13] (Figure 1).

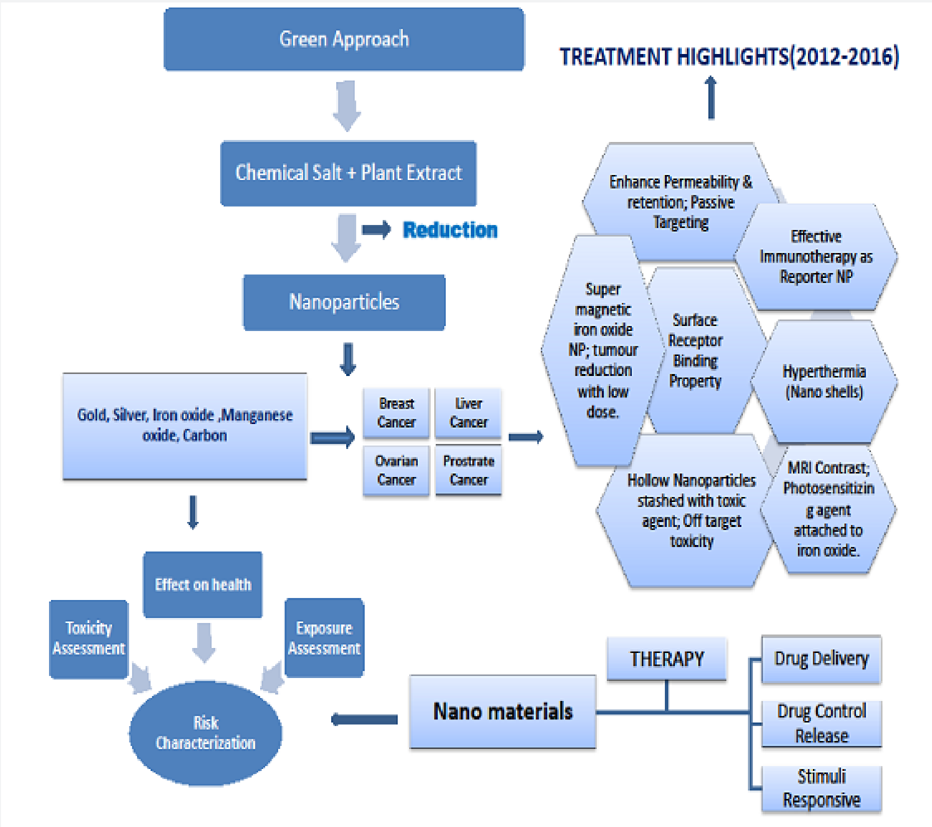

Figure 1: Green synthesis of Nano particles and their application in treating cancer.

Nanotechnology in toxicity outlook; a concern/ lacunae

Although the use of wide variety of nanostructures continued to alter the current scenario of cancer disease and diagnostics as a carrier system due to its biocompatibility and ability to reduce systemic toxicity, a crucial investigation regarding the toxicological effect of nanoparticles and the route of particle administration as a potential source of toxicity has to be emphasized which may arise due to its size, shape, dosage, charge as well as surface chemistry. The effect of these Nano materials results from its interaction particularly with the proteins that may lead to clumping of the protein molecules and linking up of various medical conditions. The large sized particles, once inside will move to circulation and may accumulate in organs including liver, spleen heart and brain. Also, direct cell to cell transfer of these particles is very unlikely as the pores between the cells are even smaller than their size.

The absorption and opsonisation of nanomaterials or nanoparticles by serum protein may alter the effective size of the particles resulting in the change of an in vivo hydrodynamic diameter which is often lager than the size of in vitro Nanoparticles. There may be different trends of bio toxicity of nanomaterials in different ranges. Therefore, with the explosive increase in the research of this robust technology, it is necessary to have a concern outlook to fulfill the biomedical demand by well controlled fabrication of nano materials prior to be implemented in clinical practices.

Nanotechnology; validation in clinics.

The tremendous effort of the scientist towards protective utilization of nano particle based medicines or Nano medicines in fighting against cancer are showing promising outcomes. Concerning the issues associated with the drug circulation time and a localized therapy to the site of the disease, the utilization of Nano based therapeutics have a clear benefits than the unmodified drugs.

The progress route of Nano therapeutics has already been demonstrated in the clinic. Doxorubicin contained in a hollow nanoparticle used to treat ovarian cancer was the first Nano based cancer drug approved by Food and Drug Administration. Likewise, the evidence of nanoparticle delivered clinical RNA interference (RNAi) published in Nature [26], first demonstrated by Calando Pharmaceuticals was approved by FDA in various stages of trials.

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The reduction of lung and toxillar lesion with a nanoparticle based therapeutic whereby the particles were combined with prostrate specific membrane antigen (PSMA) was reported by BIND Biosciences [27]. The outcome of the trial was greater efficacy compared to a lone drug at substantially lower doses. Furthermore, an albumin functionalized paclitaxel formulation of Celgene's Abraxane has got recognition for its necessary effect in the treatment of lung and pancreatic cancer along with breast cancer therapy by FDA (The-Scientist.com).

Drs. Ciaus Radu, Owen Witte and Micheal Phelps have designed a series of positron emission tomography (PET) at the Nano system Biology Cancer Center. The system was used for assigning chemotherapy to the patients such as gemcitabine, cytarabine, fludarabine and others to treat metastatic breast cancer, ovarian, lung as well as leukaemia and lymphomas. A bio distribution study was also conducted in eight healthy volunteers. A nanoparticle magnetic resonance imaging contrast agent found on the surface of newly developing blood vessels associated with early detection of tumor was developed by Dr. Gregory Lanza and his team at Siteman Center of Cancer Nanotechnology Excellence, Washington University. Phase I clinical trial was performed for assessing the utility of the agent in early detection of tumor.

A Nano sphere diagnostic company founded by Dr. Chad Mirkin at Nanomaterial for cancer diagnostic and therapeutic center has received approval by FDA for detecting cancer biomarkers by using Nano sensor. A clinical study using human tissue sample was performed to monitor low level of Prostate Specific Antigen (PSA) successfully.

Nanomaterial using silica, metal, polymers as well as carbon based particles have been demonstrated on preclinical front which shows satisfactory results. Recently, a report on multi drug delivery action and efficacy of nanoparticles to mediate resistance in relapsing cancer and improving triple negative breast cancer was by a team of researchers (The-Scientist.com). Other approaches including layer by layer siRNA delivery for breast cancer, sequential administration of Nanoparticles for pancreatic cancer treatment and tumor penetrating peptides against ovarian cancer are very recent.

Thus, the validation of nanoparticles with these exciting approaches may serve a strong foundation for modified chemotherapies in the next phase of clinical trials which would lead to profound changes in oncological practices by facilitating the realization of personalized medicines through demonstration of safety as well as efficacy in human clinical trials.

Future prospects

Dealing with the most significant issue of cancer cells of Multi Drug Resistance (MDR) the heightened technology has shown inimitable benefits owing to a targeted delivery with its small sized vectors. The clinical prospects of nano materials are tremendously affecting the treatment of malignant cells which are more likely to possess the scene of multi drug resistance. The use of dendrimers as a promising material in nano-oncology has been proved as an ideal candidate for delivering drugs to the tumor region, Besides this, dendrimers have been investigated for its use in killing bacterial cells as well as an agent for gene transfer and trans-membrane transport [12]. The case of synthesis of carbon nanotubes are considered as one of the strongest nano materials for considering the pathobiology of the disease under treatment. The efficient possibility of the nano tubes to target the cell receptors and blocking the cellular pathway of the disease by enabling the drug through the cell membrane is however a preferable system to kill the tumor. The promise of a successful cancer treatment using gold nano particles have led to bio affinity of gold nano particle probes for molecular and cellular imaging for early screening of the cancerous cells [28].

Mesoporous silica nano particles also meet the demand of cancer therapy by reducing the toxicity issues of many chemotherapeutic drugs. Due to the highly dynamic and heterogenous nature of the cancer, they can readily adapt to the stress imposed onto them. MSN-based nanocomposites target different phenotypes of a tumour thus holding a promising way to develop a co-operative therapy. FDA has recently approves a kind of ultrasound multimodal silica nanoparticles(Cornell dots) against advanced melanoma for even more specific diagnosis [24]. Besides that, the green method of synthesizing nanoparticles generated using plant phytochemicals can be also used in the discovery of new biomarkers and thus forming the basis of new drugs to fight cancer with refining diagnosis [29].

Conclusion

Nanotechnology covers a lot of domain today and will cover a lot more in near future. The creation of nanodevices with their changing form and multiple purposes as in cancer research will help in understanding the behavior of physiological markers of a disease and responsiveness of a drug [30-33]. Thus, exploiting the materials at atom and molecular level for the promising production of new materials controlling their shape and size at nano scale level has become a matter of potential concern. Also, it is necessary to envision that green method of synthesis of the base product of these devices has number of substantial benefits in context to several parameters including non-toxicity and cost effectiveness. However, the assessment of nano materials into human body while treating several disparities, the release of particulate materials into the disease environment as well as the extent to which they enter the intended sites of penetration will determine the ultimate risk of exposure particularly for those that cannot be metabolize by our body. Therefore, it is worth considering before formulating them into such scenarios.

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