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Review Article

A Review on Nanotechnology in Drug Delivery System

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ABSTRACT

Nano delivery systems are a relatively new but rapidly developing science where materials in the nanoscale range are employed to serve as means of diagnostic tools or to deliver therapeutic agents to specific targeted sites in a controlled manner. Nanotechnology offers multiple benefits in treating chronic human diseases by site-specific, and target-oriented delivery of precise medicines. Recently, there are a number of outstanding applications of the Nanomedicine (chemotherapeutic agents, biological agents, immunotherapeutic agents etc.) in the treatment of various diseases. Nanotechnology is the exploitation of the unique properties of materials at the nanoscale. Nanotechnology has gained popularity in several industries, as it offers better built and smarter products.

INTRODUCTION

Nanotechnology can simply be defined as the technology at the scale of one-billionth of a metre. It is the design, characterization, synthesis and application of materials, structures, devices and systems by controlling shape and size at nanometre scale(1,2). It is the ability to work at the atomic, molecular and supramolecular levels to create and employ materials, structures, devices and systems with basically new properties(3). Scientifically, nanotechnology is employed to describe materials, devices and systems with structures and components exhibiting new and significantly improved physical, chemical and biological properties as well as the phenomena and processes enabled by the ability to control properties at nanoscale.(4)

Materials exhibit unique properties at nanoscale of 1 to 100 nanometre (nm). The changes in properties are due to increase in surface area and dominance of quantum effects which is associated with very small sizes and large surface area to volume ratio(5)

Nanotechnologies have had a significant impact in nearly all industries and areas of society as it offers i) better erected, ii) safer and cleaner, iii) longer-lasting and iv) smarter products for drug, dispatches, everyday life, husbandry and other diligence(6) . The use of nanomaterials in everyday products can be generally divided into

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two types. First, nanomaterials can be merged or added to a pre-existing product and improve the composite objects overall performance by lending some of its unique proper- ties. Otherwise, nanomaterials such as nanocrystals and nanoparticles can be used directly to create advanced and powerful devices attributed to their distinctive properties. The benefits of nanomaterials could potentially affect the future of nearly all industrial sectors (7).

Nanotechnology in nature

Nature has enough substantiation of nanotechnology, grounded on its capability to work at the infinitesimal, molecular and supramolecular situations. The mechanisms of the natural and physical world operate substantially at the range of 1 to100 nm. The periphery of a hydrogen snippet is about 0.1 nm which is too small to be seen with mortal eyes. A patch(similar as water patch) may be made up of 20 to 30 tittles and has a periphery of about 1nm. The range of a DNA patch is about 2.5 nm, a typical protein is between 1 to 20nm and ATP biochemical motor is 10 nm in periphery'".(8) The mortal hair is about 10, 000nm thick while mortal cells range from 5,000 to 200, 000 nm in size. Although this is larger than nanoscale, the contagions that attack mortal cells fall within 10 to 200nm, which is within the nanometre region(9). Nature is the ultimate in nanotechnology, producing nanostructures that offer functional proteins and numerous other composites at cellular position of great significance to life on earth. It's allowed that one of the functions of proteins and composites that live at cellular position is that of nanotechnological separations. Biological systems are allowed by some scientists to have come about through a process of dynamic tone-assembly comprising separation and compartmentalization of numerous substances into the asked pattern or device. Some natural systems contain Nano systems that are devoted to specific functions similar as locomotion, where actin moves along myosin and kinesin moves along microtubules" (10) therefore a DNA patch can be seen as a tone-assembly machine which replicates itself and also produces complex organisms under the right conditions. Ribosomes construct protein motes with perfection following instructions from DNA.(11)

Nanotechnology in medicine and health care

Nanomedicine is the term used to refer to the applications of nanotechnologies in medicine and healthcare. Specifically, nanomedicine uses technologies at the nanoscale and nano enabled techniques to prevent, diagnose, monitor and treat diseases (12)Nanotechnologies exhibit sig- nificant potential in the field of medicine, including in imaging techniques and diagnostic tools, drug delivery systems, tissue-engineered constructs, implants and pharmaceutical therapeutics (13), and has advanced treatments of several diseases, including card vascular diseases, cancer, muscle skeletal conditions, psychiatri Back and neurodegenerative diseases to Top bacterial and viral infections, diabetes (14).

NANOTECHNOLOGY IN DRUG DELIVERY

Some of the challenges of utmost medicine delivery systems include poor bioavailability, in vivo stability, solubility, intestinal immersion, sustained and targeted delivery to point of action, remedial effectiveness, side goods, and tube oscillations of medicines which either fall below the minimum effective attention or exceed the safe remedial attention. still, nanotechnology in medicine delivery is an approach designed to overcome these challenges due to the development and fabrication of nanostructures at submicron scale and nanoscale which are substantially polymeric and have multiple advantages. Generally, nanostructures have the capability to cover medicines reprised within them from hydrolytic and enzymatic declination in the gastrointestinal tract; target the delivery of a wide range of medicines to colorful areas of the body for sustained release and therefore are suitable to deliver medicines, proteins and genes through the peroral route of administration(15,16)

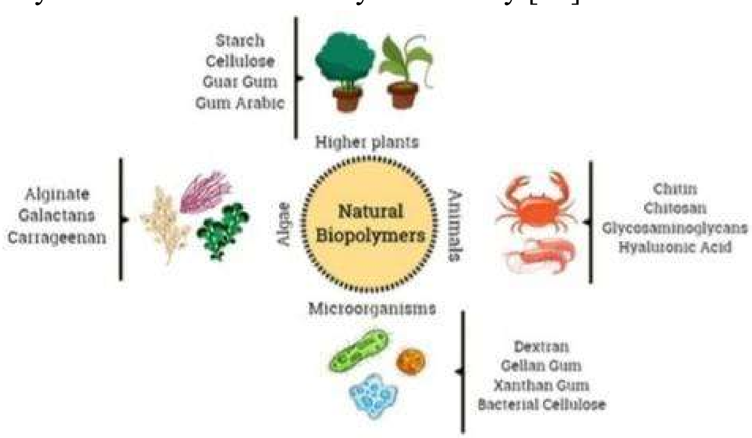
They deliver Medicines that are largely water undoable; can bypass the liver, thereby precluding the first pass metabolism of the incorporated medicine They increase oral bioavailability of medicines due to their technical uptake mechanisms similar as absorptive endocytosis and are suitable to remain in the blood rotation for a longer time, releasing the incorporated medicine in a sustained and nonstop manner leading to lower tube oscillations thereby minimizing side- goods caused by medicines.(17,18) Due to the size of nanostructures, they're suitable to access into apkins and are taken up by celis, allowing effective delivery of medicines to spots of action. The uptake of nanostructures was set up to be 15- 250 times lesser than that of microparticles in the 1-10µm range Through the manipulation of the characteristics of polymers, release of medicine from nanostructures can be controlled to achieve the asked remedial attention for the asked duration(19). For targeted delivery, nanostructures can be conjugated with targeting halves similar that the relation. between the polymer and the active substance can be manipulated to control the point and duration at which the medicine is released. The relation may be achieved by objectification of amino acids, lipids, peptides or small chains as spacer motes(20) medicine targeting is pivotal in chemotherapy, where a medicine delivery system can target only the tumors while shielding the healthy cells from invariant distribution of chemotherapeutics in the body and their dangerous goods. The use of nanostructures similar as polymeric nanoparticles is anon-invasive approach of piercing the blood brain hedge for operation of neurodegenerative diseases, environmental, ethical and safety issues should indicate how to maximize the benefits and reduce the pitfalls. Macro- and micro-technologies had their pitfalls, yet the benefits were accepted. (21)

They Trop J Pharm Res, June 2009 8(3) 271 and seditious cerebrovascular conditions exploration and development of new medicines are capital and time- ferocious which requires that pharmaceutical companies, in addition, hunt for other means of meeting up with request demands. New medicine delivery styles enable pharmaceutical companies reformulate being medicines in the request. Nanotechnology is strategic in developing medicine delivery systems which can expand medicine requests. Nanotechnology can be applied to reformulate being medicines thereby extending products' lives, enhance their performance, ameliorate their adequacy by adding . effectiveness, as well as increase safety and case adherence, and eventually reduce health care costs Nanotechnology may also enhance the performance of medicines that are unfit to pass clinical trial phases. It provides medicine delivery carriers, as well as treatment and operation of habitual conditions which include cancer, HIV/ AIDS and diabetes(18,22)

Natural product-based nanotechnology and drug delivery

As per the World Health Organization (WHO) report, in developing countries, the basic health needs of approximately 80% of the population are met and/or complemented by traditional medicine [23]. Currently, the Staich Cellulose Guar Gum Cum Arabic Alginate Galactans Carrageenan Higher plants Natural Biopolymers Microorganisms Chita Chitpen Decan Xanthan Gum Bacterial Cellulose Plans. animals, micrograms and algae Patre, et al Nangtechner (207801671 Scientific community is focusing on the studies related to the bioactive compounds, its chemical composition and pharmacological potential of various plant species, produce innovative active ingredients that present relatively minor side effects than existing molecules [. 24] Plants are documented as a huge sources of natural cons pounds of medicinal importance since long time and still it holds ample of resources for the discovery of new and highly effective drugs. However, the discovery of active compounds through natural sources is associated with several issues because they originate from living beings whose metabolite composition changes in the presence of stress. In this sense, the pharmaceutical industries have chosen to combine their efforts in the development of synthetic compounds [24,25]. Nevertheless, the number of synthetic molecules that are actually marketed are going on decreasing day y by day and thus research on the natural product based active compounds are again coming to the limelight in spite of its hurdles [25,26))Most of the natural compounds of economic importance with medicinal potential that are already being marketed have been discovered in higher planta (24,27). Sexeral drugs that also possess natural therapeutic agents in their composition are already available commercially their applications and names are as follows: malaria treatment (Artenotil derived from Artemisia annua, 1. A traditional Chinese medicine plant). Alzheimer's disease treatment (Reminy, an acetylcholinesterase inhalator isolated from the Galanthus woranosvli Lusinsk), cancer treatment (Paclitaxel and its analogues destyed from the Taxus brexifolia plant; vinblastine and vincris tine extracted from. Catharanthus roseus camptothecin and its analogs derived from Camptotheca acuminata Decne). liver disease treatment marianum) [24] (silymacin, from Silybum.

The composition and activity of many natural com pounds have already been studied and established. The alkaloids. flavonoids, tannins, terpenes, saponins, ster, compounds, among others, are the bio Qids, phenolic active molecules found in plants. However in most of the cases, these compounds have low absorption capacity due to the absence of the ability to cross the lipid membranes because of its high molecular sizes, and thus resulting in reduced bioavailability and efficacy [28].



Potential risk of nanotechnology

Implicit pitfalls of nanotechnologies Although the arising field of nanotechnology has piqued the public's interest at large, nan- otechnologies have also redounded in expansive conversations regarding their safety and any health pitfalls associated with their use. New challenges arise with the use of nanomaterials, specifically in pre dicting, understanding and gov- erning the implicit health pitfalls. Research has demonstrated that low- solubility nanoparticles are more dangerous and poisonous on a mass by mass base than larger patches(29)

Other potential risks posed by nanoparticles include explosions and catalytic effects. It is important to note that only specific nanomaterials are consider risky, particularly those with high reactivity and mobility. Until more thorough studies can con- firm the hazardous effects of nanomaterials, the mere presence of them in a laboratory setting will not in itself impose a threat ↑ humanity and the environment Back (30)

AREA	RISKS
Health	Nanoparticles can infiltrate the body via several routes: Inhalation, ingestion, absorption through the skin or injection during medical procedures.
	Once nanoparticles have entered the body, their high mobility may allow them to traverse the blood-brain barrier.
	Nanoparticles may affect the body's immune system by overloading the phagocytes. Inflammation and stress reactions may be triggered, leading to a weakened of defence against other harmful challenges.
	They could interrupt with the physiological and biological processes in the body such as enzyme regulatory mechanisms by adsorbing onto the surface of the cells or fluids they encounter in attribute to their large surface area.(31,32)
Environment	High energy demands for synthesising nanoparticles
	May cause environmental harm by disseminating toxic and persistent nanoparticles into the environment.
	Low recycling potential and low and recovery rates.
	Unclear indications of other environmental impacts(32,33)
Society	Possible military applications such as nanosensors to strengthen surveillance and implants for soldier enhancement.
	Nanotechnologies may result in corporate control of these novel technologies. Large corporations are monopolising the market by claiming patents on nanoscale inventions and discoveries. To date, >3,500 nano-related patents were granted in 2016 alone, and the numbers are increasing each year.(34).

Impact of nanotechnology

Nanotechnology a wide technological platform for a varying range of potential applications. The basic level of organization of atoms and molecules at which functions for man-made products and living things are defined can be manipulated by nanotechnology. Nanotechnology is interdisciplinary and SO reverses the trend of specialization in specific disciplines. Thus it integrates all disciplines especially biomedicine, engineering and technology. It has broadened and changed manufacturing capabilities, which were more of bulk manufacturing, toiinclude self-assembling approach. and top-down The speed and scope of research and development have been influenced by nanotechnology such that regulators cannot meet up in assessment and environmental impact. Due to the vast areas of applications of nanotechnology, a number of governments such as U.S., Japan, China and Europe have deemed it fit to invest in nanotechnology. Nanotechnology is currently one of the main propellant for technological, economical change and industrial competitions (35)

Action Mechanism of Nano Drug Delivery Systems:

When designed to avoid the body's defense mechanisms nanoparticles have beneficial properties that can be used to improve drug delivery. Various nanoparticle formulations have been disseminated in drug development in an attempt to increase efficacy, safety and tolerability of incorporated drugs. Nanoparticle based formulations have shown high solubility, control release. improved pharmacokinetic and pharmacodynamic properties. Particle size, surface charge and shape play important roles in creating effective nanoparticle delivery systems that function through a variety of mechanisms (36).

1. Particle size

Particle size and size distribution are the most important characteristics became these determine the chemical and physical properties of nanomaterials. The hydrodynamic size and size distribution determine the in vive distribution, biological fate, toxicity, and targeting ability of these nanomaterials for drug delivery system. They can manipulate drug loading, its release and stability. It has been reported that nanomaterials are advantageous over micro scale particles and due to small size and high Mobility that make them capable of higher cellular uptake suitable for wider range of cellular and intracellular targets [37,38].

2. Surface Charge

Surface charge is usually Expressed and measured in terms of the nanomaterials zeta potential which reflects the electrical potential of particles that is influenced by its composition and the medium in which it is ịs dispersed Zeta potential having a value of 30 mV have been reported to be stable in suspension leads to preventing aggregation of particles (39) Surface charge of nanomaterials is crucial to drug loading. Drugs can be loaded via a number of processes such as covalent conjugation, hydrophobic interaction, charge-charge interaction or encapsulation. Loading of molecules depends upon nature of the drug as well as nature of target molecule, also alters the surface charge. By changing zeta potential attachment or adsorption of charged molecule can be determined on the surface of nanoparticle (40)

3. Drug Loading

Incorporation of a drug on or in nanomaterials is referred to as drug loading. An ideal nanoparticles drug delivery system should have a high drug-loading capacity without aggregation. High drug loading capacity can minimize administration or the number of doses [41]. Dispettihility, is needed for smooth and efficient delivery of the drugs. Drug loading can be accomplished in several ways; however, drug loading and entrapment efficiency depend on drag solubility in the nanoparticles, dispersion medium. nanomaterials size and composition, drug molecular weight (MW) and solubility, drug-nanomaterials interaction, and/or the presence of surface functional groups (eg. Carboxyl, amine, ester, etc.) on either the drugs or on the nanomaterials [42].

4. Drug Targeting

Targeting of tumor leads to improving chemotherapy by Nanomaterials provide a highly specific and versatile Platform for cancer treatment. Enhanced permeability and retention enable selective. localization in tumor spontaneously due to fenestrated blood vessels as in case of drug loaded liposome (doxorubicin-liposome complex). It has been shown to effectively improve selective localization in human tumors in vivo of small-molecule drugs such as doxorubicin as demonstrated by pang size liposomes target tumors spontaneously because of the fenestrated blood vessels. This is due to enhanced permeability and subsequent drug retention [43]. Targeting Of nanomaterials as drug delivery vehicles or panggatziers for site-specific delivery has a number of advantages over targeting ligand-drug conjugates. Efficient drug loading of high concentrations of drug within the nanocarriers can be delivered specifically to the target cell or tissue when a ligand interacts with its receptor which results in the delivery of large payloads of therapeutic agent relative to number of ligand-binding sites. This is very advantageous in imaging tumor through the increase in tumor signal to background ratio[44]. The Dangcartiers, are attached to the ligand and the drug is loaded independent of the coupling Of ligands. This also bypasses drug activity that may be due to formation of ligand-drug complex conjugate or inactivated by potentially aggressive coupling reaction. A Large number of ligand molecules can be attached to the gang carriers, depending upon the size of the nanomaterials and the size of the drug to increase the probability of binding to target cells especially for those with low binding affinities [45,46]. Active targeting enables efficient distribution of the carriers in the tumor, thereby reducing the return of drug back to the circulation that may be caused by high intratuuneral pressure and, when ligand is only attached to the carrier due to the small size of the conjugate, it can only extravagate at the disease site but not in normal vasculature, and such, the ligand ax cannot interact with the target epitopes of normal tissues avoiding side effects [47].

Applications of nanoscale pharmaceuticals in drug delivery.

First author, year	Nanomaterial	Properties	Applications
Serp *et al*, 2003	Nanoparticles in the range of 50-100 nm	Move into tumour more readily.	Treatment of cancer.(48)
Serp *et al*, 2003	Polymers	High accuracy.	Nanobiological drug-carrying devices.(48)
Ghosh *et al*, 2003	Ligands on a nanoparticle surface	High accuracy.	Ligands can recognise markers on damaged tissues and deliver drugs to them.(49)
Ghosh *et al*, 2003	Nanocapsules	Evasion of the body's immune system and allows targeting of drugs to a specific site.	A buckyball-based treatment for AIDS has just entered clinical testing.(49)
Ghosh *et al*, 2003	Improved particle adhesion	Increased localised drug retention.	Controlled drug release(49)

CONCLUSION

There is no doubt that nanotechnologies have helped to improve the quality of life of patients by providing a platform for advances in biotechnological, medicinal and pharmaceutical industries. They have also facilitated healthcare procedures, from diagnosis to therapeutic interventions and follow-up monitoring. There is a constant push to create and develop novel nanomaterials to improve diagnosis and cures for diseases in a targeted, accurate, potent and long-lasting manner, with the ultimate aim of making medical practices more personalised, cheaper and safer.The prospect of nanotechnology lies within using the right nanomaterials and reducing any possible harmful effects. It is important to note that, risk evaluations are required before new nano-based products are approved for clinical and commercial use, as with any other product, to minimise any potential hazards to human health and the environment. A full life cycle evaluation is required to more accurately ascertain the sustainability and safety of their use long term.

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