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The Review in Nanomedicine in Nanotechnology

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ABSTRACT:

Everall scientific areas have benefited significantly from the introduction of nanotechnology and the respective evolution. This is especially noteworthy in the development of new drug substances and products. This review focuses on the introduction of nanomedicines in the pharmaceutical market, and all the controversy associated to basic concepts related to these nano systems, and the numerous methodologies applied for enhanced knowledge.

Due to the properties conferred by the nanoscale, the challenges for nanotechnology implementation, specifically in the pharmaceutical development of new drug products and respective regulatory issues are critically discussed, mainly focused on the European Union context. Finally, issues pertaining to the current applications and future developments are presented.

INTRODUCTION

Nanomedicine has been defined by the European Science Foundation's. "Nanomedicine uses nano-sized tools for the diagnosis, prevention and treatment of disease and to gain increased understanding of the complex underlying pathophysiology of disease. The ultimate goal is to improve quality of life." Nanomedicine offers the prospect of powerful new tools for the treatment of human diseases and the improvement of human biological systems using molecular Nanotechnology. The term 'Nanotechnology' Generally refers to engineering and manufacturing at the molecular or nanometer length scale (A nanometer is one-billionth of a meter, about the width of 6 bonded carbon atoms [1]

Many researchers believed that in future, scientific devices that are dwarfed by dust mites may one day be capable of grand biomedical miracles.,The vision of nanotechnology introduced in 1959 by late Nobel Physicist Richard P Faynman in dinner talk said, "There is plenty of room at the bottom,"[2]

The beneficial use of nanomaterials can be found in sunscreens, cosmetics, sporting goods, tyres, electronics and several other everyday items (6). Additionally, nanotechnologies have revolutionized advances in medicine, specifically in diagnostic methods, imaging and drug delivery[3]

It is a fact that the available information is dispersed in the current literature, and a single review taking into consideration novel nanomaterial development is missing. The objective of this work is to review currently available techniques for a complete characterization of nanomaterial interaction with biological components, which must be addressed when designing nanomedicines before starting clinical and preclinical studies. For each parameter studied, different techniques are described, highlighting their advantages and disadvantages, indicating which nanomaterials can be properly studied by each technique.

Hereafter, the terms nanosystems, nanomedicines, and colloidal nanomaterials will be used as general synonyms to name nanostructures with nanometric dimensions, independently of the specific entity they represent (e.g., nanorods or nanoparticles), their composition (e.g., polymer or metal), and their use (e.g., drug delivery systems or non-viral gene delivery systems)(figure 1)[4]

TYPES OF NANAOMEDICINE

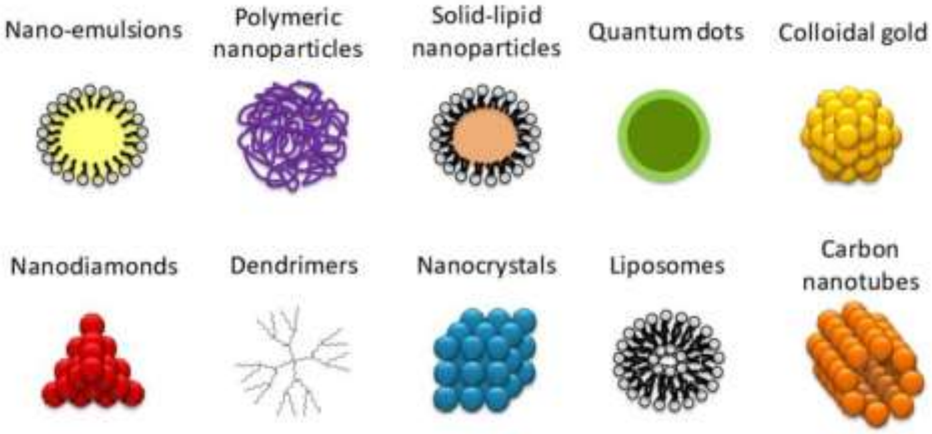


Figure 1

Nanocrystals

Nanocrystals are defined as crystals having at least one dimension less than 100 nm. Nanocrystalline pharmaceuticals that are currently available in the market are discussed here. Each product is described with its history of commercialization and mechanism of action [5]

Drugs under Nanocrystal:[6]

Drug	**Treatment**
Emend	Anti - emetic
Ostim	Ca+ supplement
Repamune	immunosuppressant
vitoss	Canfil the voids ro gap in the skeletal system.
Retalin	ADHA
triCor	Prevent the development of atherosclerosis

Liposome & lipid-based nanopharmaceutical

Liposomal nano formulated drugs are recognized to be some of the most successful commercial DDSs that have been developed to overcome the side effects of many conventional drugs. For example, the liposomal formulation of doxorubicin (known by the commercial name of Doxil®) has made a great impact on the treatment of cancer, and huge benefits for pharmaceutical companies. In this section, liposome and lipid based nanopharmaceuticals as described in regard to their formula and mechanism of action [7]

Drug	**Treatment**
Doxil (Liposomal Doxorubicin	Chemotherapy dru
DaunoXome	Chemotherapy drug
Onivyde (irinotecan liposome injection)	Metastatic Pancreatic cancer
DepoCyt (liposoma l cytarabine)	Lymphomatous meningitis
Marqibo	Anti-cancer alkaloid
AmBisome	Anti-fungal agent
Vyxeos	acute myeloid leukemi
Abelcet	Serious fungal infectio
visudyne	choroidal neovascularizatio

Polymer-based Nanopharmaceuticals

Polymeric NPs have made great strides forward in applications for drug and gene delivery. Functional polymers can be used for encapsulation of therapeutic agents. In the area of commercial nanopharmaceuticals, pegylated drug and protein conjugates have shown major improvements over their nonpegylated counterparts. 'Pegylation' refers to conjugation of any biomolecule to one or more chains of polyethylene glycol (PEG) [8]

Drug	**Treatment**
Cimzia	Rheumetatoid Arthritis, Crohn's Disease, Psoriatic Arthritis, Ankylosing Spondylisis.
Adagen	Immunodeficiency Disease
Neulasta	Febrile Neutropenia
Oncaspar	Acute Lymphoblastic, Leukaemia, Myelogenous Leukemia.
Pegasys	Hepatitis C & HBeAg +ve Chronic Hepatitis B.
Somavert	Protein similar to human Growth Hormon.
Macugen	Mucular Degeneratin
Mircera	Anaemia.
PEGINTRON	Chronic Hepatitis C.
Krystexxa	Refractory Chronic Gout.
Plegridy	RRMS
Adynovate	Hemophilia

Other types of polymer-based Nano pharmaceuticals

As shown below polymer-based nano pharmaceuticals (other than pegylated formulations) either themselves composed of polymer chains such as Copaxone®and Renagel, or where polymers are used to disperse drug molecules such as Ellegard and Estrasorb.[9]

Drug	**Treatment**
Copaxone	Multiple Sclerosis
Eligard®	Prostate Cancer
Renagel	End stage renal disease.
Estrasorb	Moderate Vasomotor.
Zilretta	Knee Osteoarthritis.

Protein Based NanoPharmaceutic [10]

Drugs	**Treatment**
Abraxane®	Metastatic Breast Cancer, Lung Cancer, Metastatic Pancreatic Adenocarcinomas.
Ontak®	T-Cell Lymphoma
Ontak®	Haemophilia

Metal-based nano pharmaceuticals

Today magnetic-based NP have vast arrays of application in drug and gene delivery and diagnosis. Feridex was a commercial product of iron oxide-based NPs used as a contrast agent for MRI. In response to observed side effects its production was discontinued in 2008.[11]

Drug	Treatment
Feraheme	Anemia

DRUG DELIVERY

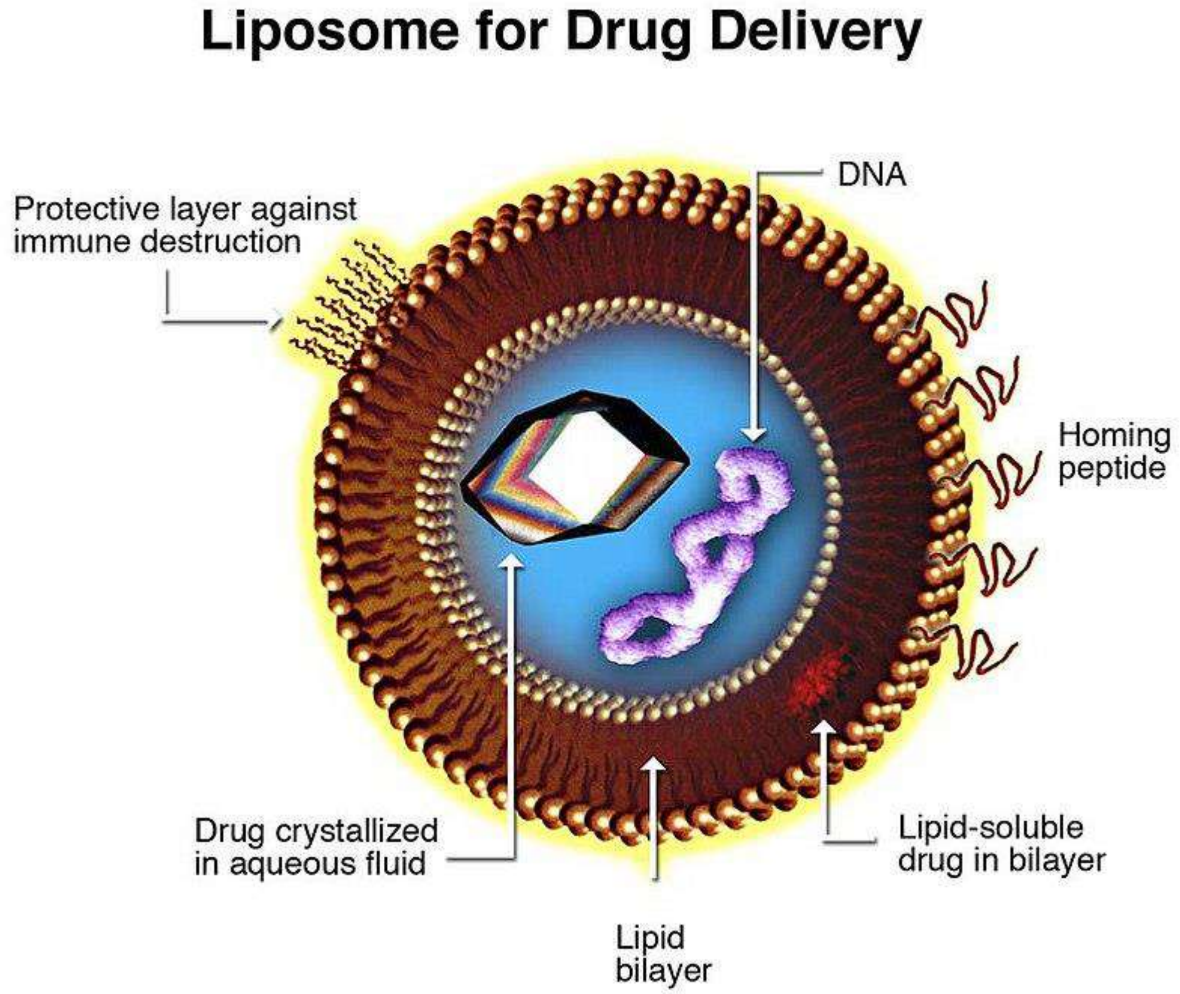
• The efficacy of drug delivery through nanomedicine is largely based upon:

a) efficient encapsulation of the drugs,

b) successful delivery of drug to the targeted region of the body, and

c) successful release of the drug.

•Drug delivery systems, lipid or polymer-based nanoparticles, can be designed to improve the pharmacokinetics and biodistribution of the drug. However, the pharmacokinetics and pharmacodynamics of nanomedicine is highly variable among different patients. When designed to avoid the body's defence mechanisms, nanoparticles have beneficial properties that can be used to improve drug delivery.



• Complex drug delivery mechanisms are being developed, including the ability to get drugs through cell membranes and into cell cytoplasm. Triggered response is one way for drug molecules to be used more efficiently.

•Drugs are placed in the body and only activate on encountering a particular signal. For example, a drug with poor solubility will be replaced by a drug delivery system where both hydrophilic and hydrophobic environments exist, improving the solubility [12]

Potential Therapies

• Cancer

Nano particles have a special property of high surface area to volume ratio, which allows various functional groups to get attached to a nano particle and thus bind to certain tumor cells. Furthermore, the 10 to 100 nm small size of nanoparticles, allows them to preferentially accumulate at tumor sites as tumors lack an elective lymphatic drainage system. Multifunctional nano particles can be manufactured that would detect, image, and then treat a tumor in future cancer treatment . Kanzius RF therapy attaches microscopic nano particles to cancer cells and then "cooks" tumors inside the body with radio waves that heat only the nanoparticles and the adjacent (cancerous) cells[13].

• HIV

HAART therapy for the treatment of HIV-infected individuals using a combination of three antiviral drugs approved by the FDA has been extremely effective in controlling the infection and further preventing the progression of infection to AIDS. This has attributed to decline in the AIDS-related deaths globally. Though HAART can bring the viral load to negligible (and undetectable) levels, the patients still carry the virus throughout their lifetime. This arises because of the emerged drug resistance or due to the presence of the virus in hidden reservoirs in the individuals' body where drugs cannot be delivered.4 The dosage includes frequent administration (once or twice daily) of antiviral drugs, which leads to other associated toxicities and also the emergence of drug resistance due to non-compliance of patients to the required doses.[14]

Imagin

• The small size of nanoparticles endows them with properties that can be very useful in oncology, particularly in imaging. Quantum dots (nanoparticles with quantum confinement properties, such as size unable light emission), when used in conjunction with MRI (magnetic resonance imaging), can produce exceptional images of tumour sites. Nanoparticles of cadmium selenide (quantum dots) glow when exposed to ultraviolet light

. • As a result, sizes are selected so that the frequency of light used to make a group of quantum dots fluoresce is an even multiple of the frequency required to make another group incandesce. Then both groups can be lit with a single light source.

• They have also found a way to insert nanoparticles into the affected parts of the body so that those parts of the body will glow showing the tumour growth or shrinkage or also organ trouble.[15]

Sensing

•Nanotechnology-on-a-chip is one more dimension of lab-ona-chip technology. Magnetic nanoparticles, bound to a suitable antibody, are used to label specific molecules, structures or microorganisms. In particular silica nanoparticles are inert from the photophysical point of view and might accumulate a large number of dye(s) within the nanoparticle shell. Gold nanoparticles (AuNPs) show unique properties for biodetection, namely, optical, electrochemical, and spectral propertie .Gold nanoparticles tagged with short segments of DNA can be used for detection of genetic sequence in a sample.

•Sensor test chips containing thousands of nanowires, able to detect proteins and other biomarkers left behind by cancer cells, could enable the detection and diagnosis of cancer in the early stages from a few drops of a patient's blood.[16]

Tissue engineering

•Nanotechnology may be used as part of tissue engineering to help reproduce or repair or reshape damaged tissue using suitable nanomaterial-based scaffolds and growth factors. Tissue engineering if successful may replace conventional treatments like organ transplants or artificial implants. •Nanoparticles such as graphene, carbon nanotubes, molybdenum disulphide and tungsten disulfide are being used as reinforcing agents to fabricate mechanically strong biodegradable polymeric nanocomposites for bone tissue engineering applications. •The addition of these nanoparticles in the polymer matrix at low concentrations (~0.2 weight %) leads to significant improvements in the compressive and flexural mechanical properties of polymeric nanocomposites Potentially, these nanocomposites may be used as a novel, mechanically strong, light weight composite as bone implants.[17]

Medical Device

•Neuro-electronic interfacing is a visionary goal dealing with the construction of nanodevices that will permit computers to be joined and linked to the nervous system. This idea requires the building of a molecular structure that will permit control and detection of nerve impulses by an external computer.

•A refuellable strategy implies energy is refilled continuously or periodically with external sonic, chemical, tethered, magnetic, or biological electrical sources, while a nonrefuellable strategy implies that all power is drawn from internal energy storage which would stop when all energy is drained. [18]

Cell repair machines

•Molecular nanotechnology is a speculative subfield of nanotechnology regarding the possibility of engineering molecular assemblers, machines which could re-order matter at a molecular or atomic scale.

•Nanomedicine would make use of these nanorobots, introduced into the body, to repair or detect damages and infections. Molecular nanotechnology is highly theoretical, seeking to anticipate what inventions nanotechnology might yield and to propose an agenda for future inquiry. The proposed elements of molecular nanotechnology, such as molecular assemblers and nanorobots are far beyond current capabilities.[19]

Future Prospective

Important factor which has attracted the attention of researchers and companies is the growing role that cancer plays in mortality and morbidity figures worldwide. For instance, in September of 2016, five out of 17 FDA-approved drugs were cancer-related. This and the high number of other cancer related pharmaceuticals approved during past years demonstrates not only the urgent requirement for better cancer treatments by the patients, but also the enormous market for cancer treatment.

The combination of chemotherapy and photothermal or photodynamic therapy also holds great promise. These applications may involve stimulating the immune system to fight infections and cancer, but also down-regulating the immune system to fight against auto-immune diseases and allergies. All in all, we believe that the increasing rate of cancer-related deaths are driving forces behind the expected increase in global nanomedicine market size in coming years.[20]

Conclusions

•Although realization of the full potential of nanomedicine may be years or decades away. recent advances in nanotechnology related to drug delivery, diagnosis & drug development awe beginning to change the landscape medicine.

•The possibilities are endless but will take time to develop.

•Nano therapies could in the long term be much more economic, effective & safe &could greatly reduce the cost of current medical procedures.

•So NANPMEDICINE is future of medicine

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