Nanomedicine And Nanotechnology

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I. INTRODUCTION

Over the last years, nanotechnology has been introduced in our daily routine. This revolutionary Technology has been applied in multiple fields through an integrated approach. An increasing Number of applications and products containing nanomaterials or at least with nano-based claims Have become available. This also happens in pharmaceutical research. The use of nanotechnology In the development of new medicines is now part of our research and in the european union (eu).It has been recognized as a key enabling technology, capable of providing new and innovative Medical solution to address unmet medical needs .The application of nanotechnology for medical purposes has been termed nanomedicine and is Defined as the use of nanomaterials for diagnosis, monitoring, control, prevention and treatment Of diseases. However, the definition of nanomaterial has been controversial Among the various scientific and international regulatory corporations. Some efforts have been Made in order to find a consensual definition due to the fact that nanomaterials possess novel Physicochemical properties, different from those of their conventional bulk chemical equivalents,Due to their small size. These properties greatly increase a set of opportunities in the drug Development; however, some concerns about safety issues have emerged. The physicochemical Properties of the nanoformulation which can lead to the alteration of the pharmacokinetics, namely The absorption, distribution, elimination, and metabolism, the potential for more easily cross Biological barriers, toxic properties and their persistence in the environment and human body Are some examples of the concerns over the application of the nanomaterials (7,11,13).

To avoid any concern, it is necessary establishing an unambiguous definition to identify the presence of nanomaterials. The European Commission (EC) created a definition based on the European Commission Joint Research Center and on the Scientific Committee on Emerging and Newly Identified Health Risks. This definition is only used as a reference to determine whether a material is considered a nanomaterial or not; however, it is not classified as hazardous or safe. The EC claims that it should be used as a reference for additional regulatory and policy frameworks related to quality, safety, efficacy, and risks assessment (7,12).

NANOMATERIAL

Definition

According to the EC recommendation, nanomaterial refers to a natural, incidental, or manufactured material comprising particles, either in an unbound state or as an aggregate wherein one or more external dimensions is in the 100rticles, according to the number size distribution. In cases of environment, health, safety or competitiveness concern, the number size distribution threshold of 50% may be substituted by a threshold between 1 and 50%. Structures with one or more external dimensions below 1 nm, such as fullerenes, graphene flakes, and single wall carbon nanotubes, should be considered as nanomaterials. Materials with surface area by volume in excess of 60 m2/cm3 are also included (Commission Recommendation., 2011). This defines a nanomaterial in terms of legislation and policy in the European Union. Based on this definition, the regulatory bodies have released their own guidances to support drug product development. The EMA working group introduces nanomedicines as purposely designed systems for clinical applications ,with at least one component at the nanoscale, resulting in reproducible properties and characteristics, related to the specific nanotechnology application and characteristics for the intended use (route of administration, dose), associated with the expected clinical advantages of nano-engineering (e.g., preferential organ/tissue distribution; 8).

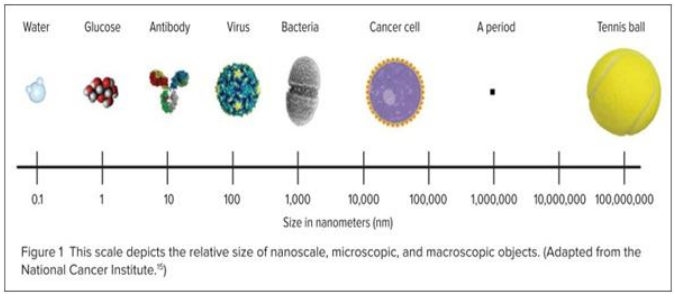

Figure 1 This scale depicts the relative size of nanoscale, microscopic, and macroscopic objects. (Adapted from the National Cancer Institute.[9])

Fig.1 The schematic shows the different objectives at the nanoscale (52).

NANO MEDICINE

INTRODUCTION

The Nanomedicine is a medical application of nanotechnology. The Nanomedicine comes from the medical applications of the nano materials and biological devices, the nano electronic biosensors, and even possible future applications of molecular nanotechnology as biological machines. The Advancement in the field of nanotechnology and its applications to the field of medicines and pharmaceuticals has revolutionized the twentieth century. The Nanotechnology is the study of extremely small structures. The word "nano" means very small. The Nanotechnology is the treatment of individual atoms, molecules, or compounds into structures to produce materials and devices with a special property. The Nanotechnology involves work from the top down i.e. in reducing the size of large structures to the smallest structures. e.g. The photonics applications in nano electronics and nano engineering, top-down or the bottom up, which involves changing individual atoms and molecules into nanostructures and more closely resembles the chemistry biology (1,2,5,6).

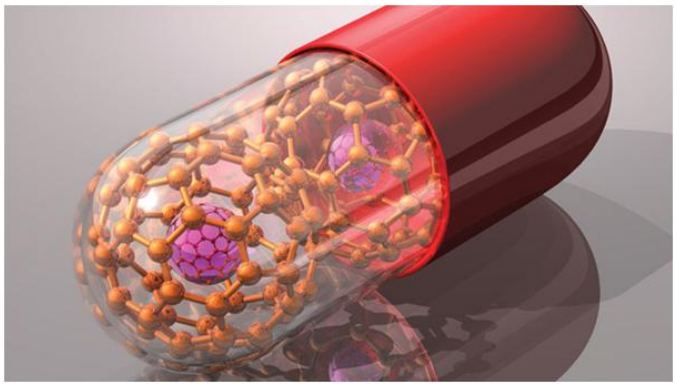

Fig 2. NANOMEDICiNES (51).

Nanomedicine is application of nanotechnology to medicine, is currently at an early stage but it is expected to have a revolutionary impact on health care. Nanomedical research is heavily supported by public policy and investment, and is progressing rapidly. The continued development of nanomedicines has the potential to provide numerous benefits, including improved efficacy, bioavailability, dose–response, targeting ability, personalization, and safety compared to conventional medicines. The most exciting concept in nanomedical research may be the design and development of multifunctional nanoparticle (NP) complexes that can simultaneously deliver diagnostic and therapeutic agents to targeted sites. These capabilities are unprecedented and represent tremendous progress toward improving patient diagnosis, treatment, and follow up. However, despite these potential benefits, essential data regarding the pharmacokinetics, pharmacodynamics, and toxicity of many nanomaterials are currently lacking.(1,2,5,6)

HISTORY Of NANOMEDICINES

The Nanomedicine is a young science. The nanotechnology can be use in medicine, medical technology and pharmacology has only been researched since the 1990s. The Nanotechnology itself has only existed for a few decades. After the invention of high resolution microscopy it evolved simultaneously in the field of biology, physics and chemistry as in the course of the 20th century and spawned new disciplines such as microelectronics, biochemistry and molecular biology. The nanomedicine, nanobiotechnology knowledge which investigates the structure and function of cells as well as intra- and intercellular processes. This research study only became possible at the beginning of the 20th century when the door to the nanocosmos was burst open with the invention of innovative microscopes as needed in all the fields. Nanomedicine is defined as the monitoring, and repairing, construction and controlling of human biological systems at the molecular level, by using engineered nanodevices and nanostructures. The Current problems for nanomedicine involve as understanding the issues in relation to the toxicity and environmental impact of nanoscale materials (materials whose structure is on the scale of nanometers, i.e. billionths of a meter) [3].

The Functionalities can be added to the nanomaterials by interfacing them with in biological molecules or structures. The size of nanomaterials is similar to that of most biological molecules and structures; therefore, nanomaterials can be useful for both in vivo and in vitro biomedical research and applications. The nanomaterials have the development of diagnostic devices as to use contrast agents, analytical tools, physical therapy applications, and drug delivery vehicles or channels. The Nanomedicine seeks to deliver a valuable set of research tools and the clinically useful devices in the near future days. The Nanotechnology Initiative in new applications in the pharmaceuticals that may include advanced drug delivery system, application of new therapies, and in the vivo imaging processes. The Nanotechnology has provided the possibility of delivering of drugs to the specific body cells by using nanoparticles [4]. As the benefit of using nanoscale materials for medical technologies is that smaller devices are less invasive and can possibly be implanted inside the body, plus biochemical reaction times are much shorter. These devices are faster and more sensitive than typical drug delivery system. (7)

The efficiency of drug delivery through nanomedicine is a largely based upon the followings as

- The Efficient encapsulation of the drugs,
- The Successful delivery of the drugs to the targeted region of the body, and
- The Successful release of the drugs in to the body.

What Is Nanomedicine?

The convergence of nanotechnology and medicine has led to the interdisci i8plinary field of nanomedicine.In genetics, proteomics, molecular and cellular biology, material science, and bioengineering have all contributed to this developing field, which deals with physiological processes on the nanoscale level. Many of the inner workings of a cell naturally occur on the nanoscale level, since the dimensions of many biologically significant molecules like water, glucose, antibodies, proteins, enzymes, receptors, and hemoglobin are already within the nanoscale range (see fig.3).Many researchers are currently working on medical treatments, devices, and instruments that use nanotechnology to increase efficacy, safety, sensitivity, and personalization. Potentially beneficial properties of nanotherapeutics include improved bioavailability, reduced toxicity, greater dose response, and enhanced solubility compared with conventional medicines (6,11,28,29)

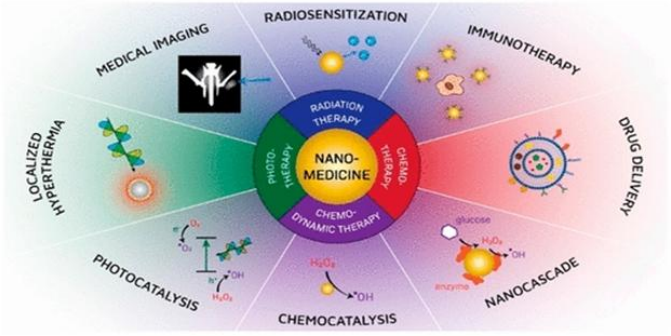

Fig.3 ***VARIOUS THERAPY BY NANOMEDICINE(53).***

Nanomedicine Formulations: Clinical Development and Approved Materials

In recent years, both the broadening in nanocarrier typology and the increase in the complexity of particles and materials employed have inspired explorations for new nanodelivery systems and brought about various products as well as numerous clinical trials for biotechnology and nanomedicine applications. However, before the premarket authorization, nanocarriers are subject to a range of preclinical and clinical validation by regulatory agencies, such as the European Medicines Agency (EMA) and the Food and Drug Administration (FDA) in the USA. Recent review articles provide asummary of the range of approved therapeutic nanomedicines and a description of novel nanoplatforms that are emerging through the clinical trial pipeline (30,31,32).

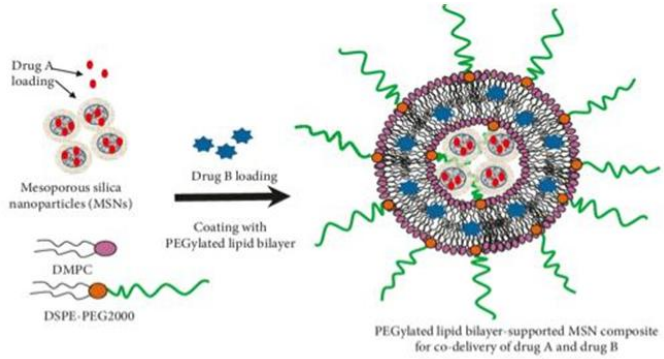

Figure 4 : Design strategies of a PEGylated lipid bilayer-supported mesoporous silica nanoparticle (MSN) composite for dual drug synergistic codelivery (30,31,32).

In Table 1, we report the main organic and inorganic nanomedicines approved by FDA . Among the organic nanomedicines approved for use on the market, it is useful to distinguish between the two main categories of polymer-based and lipid-based nanoparticles. Despite theintensive (preclinical) research involving block copolymer micelle nanocarriers, only a few of them have reached clinical evaluation or have been approved for the employment in the market . The degradable hydrophobic polymers PLA, PLGA, and PDLLA are the most promising polymer systems for the development of nanoformulation, as they slowly decompose into constituent monomeric units over well-defined time courses. For example, Eligard for-mulation, obtained from the incorporation of leuprolide (a testosterone-inhibiting drug) into a polylactide-co-glycolic acid (PLGA) nanoparticle, represents a long-established polymer nanoparticle for the treatment of the prostate cancer symptoms (30,31,32).

As evidenced in previous sections, the employment of PEG ensures the shield action against the recognition and degradation by the immune system and can ameliorate the biodistribution of the drug by increasing the circulation half-life. This effect is exploited in the Adynovate formulation (obtained by the PEGylation of the antihemophilic factorVIII), which is employed for the treatment of hemophilia A, and in the Cimzia formulation (obtained by the PEGylation of the antibody fragment Certolizumab) which is employed for the treatment of Crohn's disease,rheumatoid/psoriatic arthritis, and ankylosing spondylitis (30,31,32) .

Table 1. The list of the organic and inorganic nanomsdicines approved by FDA (31,32 , 33).

Table 1: List of relevant (polymer-based and lipid-based) organic and inorganic (and metallic) nanomedicines approved by the FDA.

Clinical products	Formulation	Indication	Company	Year
Polymer-based nanoparticles				
Renagel	Poly(allylamine hydrochloride)	Chronic kidney disease	Sanofi	2000
Eligard	Leuprolide acetate and polymer PLGA (poly (DL-lactide-co-glycolide))	Prostate cancer	Tolmar	2002
Estrasorb	Micellar estradiol	Menopausal therapy	Novavax	2003
Cimzia/certolizumab pegol	PEGylated antibody fragment (certolizumab)	Crohn's disease Rheumatoid/psoriatic arthritis Ankylosing spondylitis	UCB	2008-2013
Genexol-PM	mPEG-PLA micelle loaded with paclitaxel	Metastatic breast cancer	Samyang Corporation	2007 South Korea
Adynovate	Polymer-protein conjugate (PEGylated factor VIII)	Hemophilia	Baxalta	2015
Lipid-based nanoparticles				
Doxil/Caelyx	Liposomal doxorubicin	Ovarian, breast cancer, Kaposi's sarcoma, and multiple myeloma	Janssen	1995-2008
DaunoXome	Liposomal daunorubicin	AIDS-related Kaposi's sarcoma	Galen	1996
Myocet	Liposomal doxorubicin	Combination therapy with cyclophosphamide in metastatic breast cancer	Elan Pharmaceuticals	2000
Marqibo	Liposomal vincristine	Acute lymphoblastic leukemia	Talon Therapeutics Inc.	2012
AmBisome	Liposomal amphotericin B	Fungal/protozoal infections	Gilead Sciences	
Visudyne	Liposomal verteporfin	Choroidal neovascularisation, macular degeneration, wet age-related, myopia, and ocular histoplasmosis	Bausch and Lomb	2000
Onivyde	Liposomal irinotecan	Pancreatic cancer	Merrimack	2015
Inorganic and metallic nanoparticles				
INFed	Iron dextran (low MW)	Iron deficiency in chronic kidney disease (CKD)	Sanofi Aventis	1957
Feridex/Endorem	SPION coated with dextran	Imaging agent	AMAG Pharmaceuticals	1996-2008
Venofer	Iron sucrose	Iron deficiency in chronic kidney disease (CKD)	Luitpold Pharmaceuticals	2000
GastroMARK; umirem	SPION coated with silicone	Imaging agent	AMAG Pharmaceuticals	2001-2009
NanoTherm	Iron oxide	Glioblastoma	MagForce	2010

Over the last decade, a number of promising block copolymer micelle formulations entered the clinical development, with two receiving regulatory approval: namely, the Cynviloq (paclitaxel-loaded PEG-PDLLA block copolymers) and Nanoxel (docetaxel-loaded PEG-PDLLA block copolymers) . Finally, Genexol-PM is a poly(ethylene glycol)-block-poly(D,L-lactide) (PEG-PDLLA) diblock copolymer micelle loaded with paclitaxel (developed by Samyang Corporation) which was first introduced in the Korean market and is actually approved by FDA in clinical trials for the treatment of metastatic breast cancer. (32)

Advantages of nanomedicine

1. Nanomedicines might someday provide answers to longstanding problems in medical research, ranging from poor drug solubility to a lack of target specificity for therapeutic compounds. [(2)]
2. Nanomedicine also has tremendous promise as a noninvasive tool for diagnostic imaging, tumor detection, and drug delivery because of the unique optical, magnetic, and structural properties of NPs that other tools do not possess.(2)
3. The Drug delivery systems may also be able to prevent tissue damages through proper regulated drug release methods; in reducing drug clearances rates; or lower the volume of distribution and reduce the effect on non-target tissues (3)
4. The Nanoparticles used in combination therapy for decreasing antibiotic resistance or for their antimicrobial properties. The Nanoparticles might also used to the circumvent multidrug resistance (MDR) mechanisms. Some potentially important applications include cancer treatment with iron nanoparticles or gold shells. (3)
5. The Nanotechnology helps in identifying new opportunities in drug delivery systems, this rapid rise may cause difficulties with toxicity, and drug efficacy can diminish as the drug concentration falls below the targeted ranges .(5)
6. The Drug delivery to the exact location.
7. To reduce lesser side effects.
8. The Molecular targeting by nano engineered devices.
9. The disease Detection is relatively easy.
10. No surgery required.

CHALLENGES FOR NANOMEDICINE

Despite the benefits that nanomedicine has to offer, much research is still required to evaluate the safety and toxicity associated with many NPs. Nanomedicine of nanomedical research has concentrated on drug delivery, with relatively few studies focusing on the pharmacokinetics or toxicity of NPs. Investigating NP pharmacokinetics, pharmacodynamics, and potential long-term toxicity *in vivo* is essential to monitoring the effects of NPs on patient populations. Validating every nanotherapeutic agent for safety and efficacy, whether drug, device, biologic, or combination product, presents an enormous challenge for researchers and the FDA, which is currently struggling to formulate testing criteria and accumulate safety data.(5,32,59).

APPLICATION OF NANOMEDICINES

[1] ***Contrast agents for cancer cell imaging :-***The Nanoparticles of cadmium selenide (quantum dots) glow when exposed to ultraviolet lights. These When injected, as they seep into cancer tumors. The surgeon can see the glowing tumor, and use it as a guide for more accurate tumor removal procedures . (35)

[2] ***Therapeutics for treating the cancer diseases :-*** The Gold nano shells can be targeted to bond to the cancerous cells. By causing irradiating the area of the tumor with infrared lasers, as which passes through the flesh without heating it and the gold is heated sufficiently to cause death to the cancer cells (35).

[3] ***The Medical applications of nanomaterials :-*** This could solve the difficulties and blood leaks caused when the surgeon tries to re stitch the arteries that have been cut during a kidney or heart transplantation.(36).

[4] ***The Nano electronic biosensors Diagnostic devices :-***The Nanotechnology is advancement in the use of arthroscopes that are used in surgeries with lights and cameras, so surgeons can do the surgeries with smaller incisions(34).

[5] ***The physical therapy applications :***It is used in photodynamic therapy; a small particle is placed within the body and is identified with light from the outside. The light gets absorbed by the particle and if the particle is

metal, energy from the light will heat the particle and surrounding tissue.(37).

[6] ***The application of Neuro-electronic interfaces*** :- The application of the 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 (35).

[7] ***The application in Tissue repair :-***The Nanotechnology may be able to help reproduce or repair damaged tissue. The "Tissue engineering" makes use of artificially stimulated cell proliferation by using suitable nano material-based on scaffolds and growth factors. For example, bones could be re grown on carbon nano tube scaffolds. The Tissue engineering might replace today's conventional treatments like organ transplants or artificial implants.(39)

[8] ***The Molecular nanotechnology:-***The Nanomedicine would make use of nanorobots, will introduced into the body, to repair or detect damages and infections. The Carbon could be the primary element used to build these nano robots due to the inherent strength and other characteristics of some forms of carbon (diamond/fullerene composites), and nano robots would be fabricated in desktop nano factories specialized for this purpose only. (40).

- The nanomedicine applications as include activity monitors, chemotherapy, pacemakers, biochips, OTC tests, insulin pumps, nebulizers, needleless injectors, hearthing aids, medical flow sensors and blood pressure, glucose monitoring and drug delivery systems.(40).
- The nanomedicine involves the use of nano robots as mini surgeons. Such as machines might repair damaged cells, or get inside cells and replace or assist the damaged intracellular structures.(40).
- The nano machines might replicate themselves, or correct the
- genetic deficiencies by altering or replacing DNA (deoxyribonucleic acid) molecules (40).

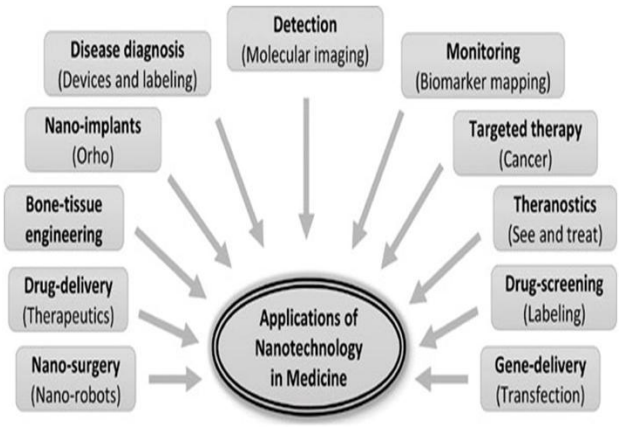

Fig.5. Application of nanotechology in medicine(54).

USES OF NANOMEDICINES

The possible uses of nanotechnology in medicine are based on three basics as:

1. The Nanomaterials and nanoinstruments which can be used as biosensors, as aids in treatment and as transporters of active substances. (37).

2. The knowledge of molecular medicine in the fields of genetics, proteomics and synthetically produced or modified microorganisms.(34).

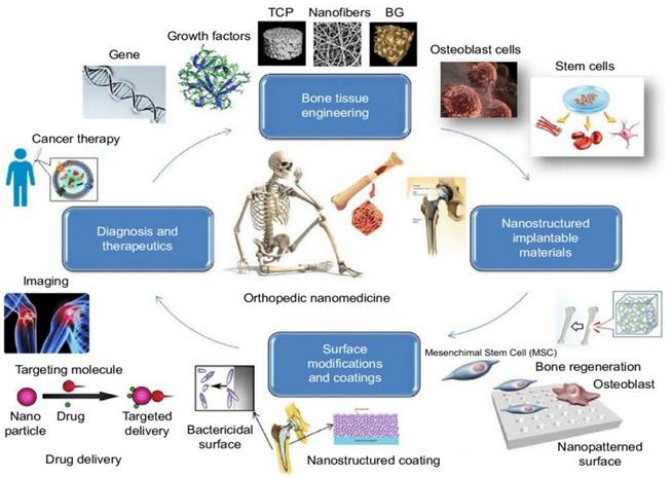

Fig 6 . Potential applications of nanomedicine.(55).

3. The nanotechnologies which can be used for the rapid diagnosis and for therapy, for repair of genetic materials and for the cell surgery, as well as for the improving of natural physiological functions(40).

NANOTECHNOLOGY

INTRODUCTION

Nanotechnology is going to revolutionize the world. For pharmacists, the applications of nanotechnology mean drugs containing nano-sized active ingredients.

1. The smaller drug delivery systems allow deposition of medications in previous inaccessible areas of the body; it also has a great importance in the treatment and diagnosis of certain diseases as cancer. A recent discovery in the drug delivery form is target therapy and improving the diagnostic tests and medical devices.(41)
2. But with the advances comes concern, the science behind nanotechnology is still in its' original state. According to the National Nanotechnology Initiative (NNI), nanotechnology refers to the study of all particles have about 100 nanometers or less. A nanometer is one-billionth of a meter in size(42).
3. One of the most important advantages of the smaller particle size is the ratio of surface atoms or molecules to the total number increases. That means they have large surface areas which lead to increase their surface activity and produce changes in their physical properties, and biological properties. (42).

Definitions of nanotechnology

The National Nanotechnology Initiative (NNI), a federal research and development program, defines nanotechnology as the science of materials and phenomena in the range of 1 to 100 nm in diameter..Manyeral agencies,including the FDA and the Patent and Trademark Office (PTO), continue to use this definition.2 However, some experts say that this size limitation is artificial and misleading, since nanomaterials can have unique properties even in sizes up to several hundred nanometers (2,43).

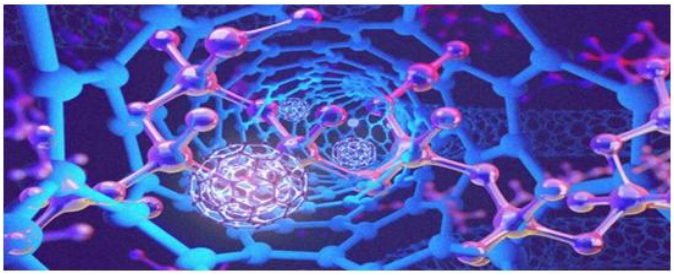

Fig.Nanotechnology nature (57).

The National Institutes of Health (NIH) has presented an alternative definition of nanotechnology that doesn't rely on size; instead, it defines the field as ,1.studies that use nanotechnology tools and concepts to study biology, 2.the engineering of biological molecules to have functions that differ from those that they have in nature, 3.the manipulation of biological systems by methods more precise than standard molecular biological, synthetic, chemical, or biochemical approaches.(2,43,50)

I. What Is Nanotechnology?

Nanotechnology is a rapidly advancing field that is expected to have a revolutionary impact on many industries, including medicine . Nanotechnology has been made possible through the convergence of many scientific fields, including chemistry, biology, physics, mathematics, and engineering.(1,2,28).

A nanometer (nm) is one billionth of a meter, and the prefix "nano-" comes from the Greek word for "dwarf." provides scientists with new tools for the investigation, manipulation, and control of atoms, molecules, and submicroscopic objects, generally ranging from 1 to 100 nm. Nanotechnology allows scientists to take advantage of naturally occurring quantum effects at the nanoscale level that influence biological, physical, chemical, mechanical, and optical properties. unique effects often give nanoscale materials desirable chemical, physical, and biological properties that differ from those of their larger, or "bulk," counterparts.(12,1,6,10,11,43).

CHALLENGES IN PHARMACEUTICAL DEVELOPMENT :-The translation of nanotechnology form the bench tothe market imposed several challenges. General issues to consider during the development of nanomedicine products including physicochemical characterization, biocompatibility, and nanotoxicology evaluation, pharmacokinetics and pharmacodynamics assessment, process control, and scale-reproducibility (Figure 7) are discussed in the sections that follows

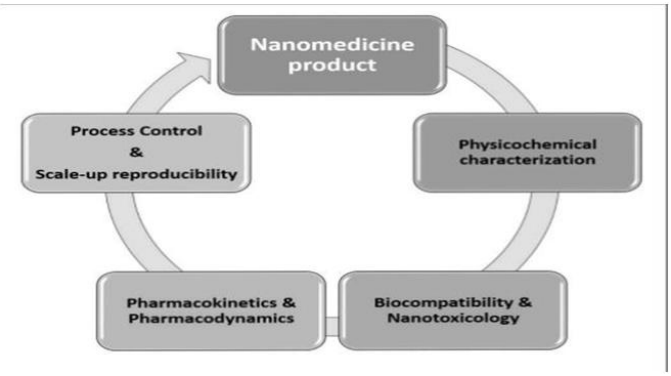

FIGURE 7.| Schematic representation of the several "barriers" found throughout the development of a nanomedicine product(56).

1.Physicochemical Characterization :- The characterization of a nanomedicine is necessary tounderstand its behavior in the human body, and to provide guidance for the process control and safety assessment.This characterization is not consensual in the number of parameters required for a correct and complete characterization(19).

Internationally standardized methodologies and the use of reference nanomaterials are the key to harmonize all the different opinions about this topic . Ideally, the characterization of a nanomaterial should be carried out at different stages throughout its life cycle, from the design to the evaluation of its in vitro and in vivo performance. The interaction with the biological system or even the sample preparation or extraction procedures may modify some properties and interfere with some measurements.In addition, the determination of the in vivo and in vitro physicochemical properties is important for the understanding of the potential risk of nanomaterials .The Organization for Economic Co-operation and Development started a Working Party on Manufactured Nanomaterials with the International Organization for Standardization to provide scientific advice for the safety use of nanomaterials that include the respective physicochemical(19).

characterization and the metrology. However, there is not an effective list of minimum parameters

1. *The following characteristics should be a starting point to the characterization:* - particle size, shape and size distribution, aggregation and agglomeration state, crystal structure, specific surface area,porosity, chemical composition, surface chemistry, charge,photocatalytic activity, zeta potential, water solubility,dissolution rate/kinetics, and dustiness .Concerning the chemical composition, nanomaterials can be classified as organic, inorganic, crystalline or amorphous particles and can be organized as single particles, aggregates, agglomerate powders or dispersed in a matrix which give rise to suspensions,emulsions, nanolayers, or films (14,17,19,).

Regarding dimension, if a nanomaterial has three dimension100nm, it can be for example a particle, a quantum dot or hollow sphere. If it has two dimensions below 100 nm it can be a tube, fiber or wire and if it has one dimension below 100nm it can be a film, a coating or multilayer. Different techniques are available for the analysis of these parameters. They can be grouped in different categories,involving counting, ensemble, separation and integral methods,among others (15,16).

2.Biocompatibility and Nanotoxicology:-Biocompatibility is another essential property in the design of drug delivery systems. One very general and brief definition of a biocompatible surface is that it cannot trigger an undesired' response from the organism. Biocompatibility is alternatively defined as "the ability of a material to perform with an appropriate response in a specific application" .Pre-clinical assessment of nanomaterials involve a thorough biocompatibility testing program, which typically comprises in vivo studies complemented by selected in vitro assays to prove safety. If the biocompatibility of nanomaterials cannot be warranted, potentially advantageous properties of nanosystems may raise toxicological concerns.Regulatory agencies, pharmaceutical industry, government, and academia are making efforts to accomplish specific and appropriate guidelines for risk assessment of nanomaterials (14,17,19).

3.Scale-Up and Reproducibility:- A forthcoming challenge in the pharmaceutical development is the scale-up and reproducibility of the nanomedicines.

A considerable number of nanomedicines fail these requirements and, consequently, they are not introduced on the pharmaceutical market .The traditional manufacturing processes do not create three dimensional medicines in the nanometer scale. Nanomedicine.manufacturing processes, as already mentioned above,compromise top-down and bottom-down approaches, which include multiple steps, like homogenization, sonication, milling, emulsification, and sometimes, the use of organic solvents and further evaporation. In a small-scale, it is easy to control and achieve the optimization of the formulation. However,at a large scale it becomes very challenging, because slight variations during the manufacturing process can originate critical changes in the physicochemical characteristics and compromise the quality and safety of the nanomedicines, or even the therapeutic outcomes. A detailed definition of the acceptable limits for the CQA is very important, and theseparameters must be identified and analyzed at the small-scale,in order to understand how the manufacturing process can change them: this will help the implementation of the larger scale. Thus, a deep process of understanding the critical steps and the analytical tools established for the small-scale will be a greatly help for the introduction of the large scale (24).

Nanotechnology Products on the Market

Nanotechnology has the potential to be used in a wide range of products, including medicines, electronics, cosmetics, and foods.According to the Project for Emerging Nanotechnologies at The Woodrow Wilson International

Center for Scholars, more than 800 nanotechnology-based products are already on the market. Nanotechnology has been used in laptop computers, cell phones, digital cameras, water-filtration systems, and cosmetics. Nanotechnology research is also under way to improve the bioavailability of food nutrients and to develop food packaging that detects and prevents spoilage.(46,47,48).

Nanotechnology has also been applied to improve a number of medical products and processes; these include drugs, medical imaging, antimicrobial materials, medical devices, sunscreens, burn and wound dressings, dental-bonding agents, sunscreens, and protective coatings for eyeglasses. Nanotechnology has improved drug targeting and bioavailability, diagnostic imaging, biomarker detection sensitivity, and drug-delivery efficiency.Some nanomedicines that are currently on the market include doxorubicin HCl liposome injection (Doxil, Ortho Biotech) for ovarian cancer; daunorubicin citrate liposome injection (DaunoXome, Diatos) for advanced AIDS-related Kaposi's sarcoma; and amphotericin B liposome injection (AmBisome, Gilead) for fungal infections. In addition, paints containing silver NPs, which have antimicrobial properties, are being used in indoor medical settings, such as in hospitals.(47,48).

Dynamic Behavior of Nanomaterials and

Applications in Nanomedicine

Nanomaterials can be applied in nanomedicine for medical purposes in three different areas: diagnosis (nanodiagnosis), controlled drug delivery (nanotherapy), and regenerative medicine. A new area which combines diagnostics and therapy termed theranostics is emerging and is a promising approach which holds in the same system both the diagnosis/imaging agent and the medicine. Nanomedicine is holding promising changes in clinical practice by the introduction of novel medicines for both diagnosis and treatment, having enabled to address unmet medical needs, by (i) integrating effective molecules that otherwise could not be used because of their high toxicity (e.g., Mepact), (ii) exploiting multiple mechanisms of action (e.g., Nanomag, multifunctional gels), (iii) maximizing efficacy (e.g., by increasing bioavailability) and reducing dose and toxicity,(iv) providing drug targeting, controlled and site specific release, favoring a preferential distribution within the body (e.g., in areas with cancer lesions) and improved transport across biological barriers .This is a result of intrinsic properties of nanomaterials that have brought many advantages in the pharmaceuticaldevelopment. Due to their small size, nanomaterials have a high specific surface area in relation to the volume. Consequently, the particle surface energy is increased, making the nanomaterials much more reactive. Nanomaterials have a tendency to adsorb biomolecules, e.g., proteins, lipids, among others, when in contact with the biological fluids. One of the most important interactions with the living matter relies on the plasma/serum biomoleculeadsorption layer, known as "corona," that forms on the surface of colloidal nanoparticles. Its composition is dependent on the portal of entry into the body and on the particular fluid that the nanoparticles come across with (e.g., blood, lung fluid, gastro-intestinal fluid, etc.). Additional dynamic changes can influence the "corona" constitution as the nanoparticle crosses from one biological compartment to another one (8,10,18,24).

Conclusion

The Nanomedicine is a new nanotechnology that has a huge impact on the human lives. As with many studies and researchers, the human has used to the nano medicine to operate many various medical functions such as drug delivery system, the cancer therapeutics, in tissue engineering, etc. The opportunities for nano medicine to improve health are limitless. To maximize gains in individual and population health, inclusion of public health expertise is essential. This influence in the development of nano medicine will help to identify the greatest areas of need for technological innovations, to determine how to best allocate funding, and shape polices to protect humans and the environment for better maintenance of health.(58).

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