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A REVIEW ON NANO PARTICLES IN PHARMACY

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Abstract :

In recent years there has been exponential intrest in development of novel drug delivery systems using nanoparticles ,generally nanoparticles dimensions . There are two types of nano particles i.e, nanosphere which is matrix type and nanocapsule which is reservoir type. They show properties which are enhanced such as strength,sensitivity,high reactivity,stability,surface area etc.Current applications and research in to the use of nano catalyst in waste water management,textile,agriculture and medicin has also been reviewed .

Keywords : Nanoparticles, Scope In Health Care Industry, Applications of Inorganic Nanoparticles, Therapeutic applications.

INTRODUCTION

Nanoparticles are solid colloidal structures or drug carrier composed of synthetic or semisynthetic polymers. Nanoparticles size ranges above molecular dimension and below microscopic ones i.e. generally greater than 1 nm to below 100 nm. They consist of macro- molecular materials in which the active ingredients (drug or biological active materials) is dissolved, entrapped or encapsulated or adsorbed. The term nanoparticle is a combined name for both Nano spheres and nanocapules. Nanospheres are solid core spherical particulates which contain drug embedded within matrix or adsorbed onto the surface (matrix type) while nanocapsules are the vesicular system

in which drug is essentially encapsulated within the central core surrounded by a unique polymeric membrane (reservoir type).

It was realized that the nanoparticles loaded bioactives could not only deliver drug(s) to specific organ within the body but delivery rate in addition could be controlled as being bystanders, burst controlled, pulsatile or modulated. The possibilities and potentials further prompted the work and as a result a great deal of related information covering preparation methodologies, characterization, engineering, bio- fate and toxicology has been gathered.

The understanding that relates to the bio distribution in particular has propelled and motivated the development of functionally designed Nano particulates. The first reported nanoparticles were based on non-biodegradable polymeric systems (Polyacrylamide, polymathic methacrylate, polystyrene etc.). The possibilities of chronic toxicity due to tissue and immunological response towards non-degradable polymeric burden, their use for systemic circulation could not be considered. Soon the bio- degradable polymers were taken up and nanoparticles based on poly (cynoacrylate) were extensively studied. The polymeric nanoparticles can carry drug(s) or proteinaceous substances, i.e. antigen(s). These bioactives are entrapped in the polymer matrix as particulates enmesh or solid solution or may be bound to the particle surface by physical adsorption or chemically. The drugs may be added during preparation of nanoparticles or to the previously prepared nanoparticles.

Novel drug delivery systems have several advantages over conventional multi dose therapy. For the past few decades, there has been a considerable research interest in the area of drug delivery using particulate delivery systems using nanoparticles. Nanoparticles can offer significant advantages over the conventional drug delivery in terms of high stability, high specificity, high drug carrying capacity, ability for controlled release, possibility to use in different route of administration and the capability to deliver both hydrophilic and hydrophobic drug molecules. Nanoparticles are the fundamental components of Nano technology. Nano particles size ranges from 1 to 100nm which are made up of metal, metal oxides, organic matter, carbon. Nanoparticles differ from various dimensions, to shapes and sizes apart from their material. Surface can be irregular with surface variations or a uniform. Among nanoparticles some are crystalline or amorphous with single or multi crystal solids either agglomerated or loose. In the process of synthesizing new drugs, most drug candidates are insoluble or poorly soluble in water which causes a huge downfall for the pharmaceutical industry. One of the main reasons for a drug‟s insolubility is its complex and large molecular structure. It has been reported that over 65% of new active pharmaceutical ingredients (APIs) are either poorly soluble in water or insoluble. Due to their low aqueous solubility properties and high permeability, they are categorized as class II of the Biopharmaceutics Classification System (BCS), where the dissolution step is the rate limiting factor in drug absorption. The pharmaceutical industries are now facing a challenge to improve the dissolution characteristic of poorly watersoluble drugs which is the key factor in enhancing drug bioavailability. For instance, they help to increase the stability of drugs/proteins and possess useful controlled release properties. This review predominately focused on synthesis of different types of nanoparticles using chemical, physical and biological methods. However, chemical and physical methods are

expensive and harmful but biological method is simple, non-toxic, rapid and eco- friendly. It also explains about the characteristics of nanoparticles and concluded with various applications.

Pharmaceutical industry

The pharmaceutical industry discovers, develops, produces, and markets pharmaceutical drugs for the use as medications to be administered to patients (or self-administered), with the aim to cure and prevent diseases, or alleviate symptoms. Pharmaceutical companies may deal in generic or brand medications and medical devices. They are subject to a variety of laws and regulations that govern the patenting, testing, safety, efficacy using drug testing and marketing of drugs. The global pharmaceuticals market produced treatments worth $1,228.45 billion in 2020 and showed a compound annual growth rate (CAGR) of 1.8%. A drug manufacturer inspection by the US FDA.

History

The origin of medicines

Medicines of ancient civilizations

The oldest records of medicinal preparations made from plants, animals, or minerals are those of the early Chinese, Hindu, and Mediterranean civilizations. An herbal compendium, said to have been written in the 28th century BC by the legendary emperor Shennong, described the antipyretic capabilities of a substance known as *chang shan* (from the plant species *Dichroa febrifuga*), which has since been shown to contain antimalarial alkaloids (alkaline organic chemicals containing nitrogen). Workers at the school of alchemy that flourished in Alexandria, Egypt, in the 2nd century BC prepared several relatively purified inorganic chemicals, including lead, carbonate, arsenic, and mercu3ry. According to *De materia medica*, written by the Greek physician Pedanius Dioscorides in the 1st century AD, verdigris (basic cupric acetate) and cupric sulfate were prescribed as medicinal agents. While attempts were made to use many of the mineral preparations as drugs, most proved to be too toxic to be used in this manner.

Many plant-derived medications employed by the ancients are still in use today. Egyptians treated constipation with senna pods and castor oil and indigestion with peppermint and caraway. Various plants containing digitalis-like compounds (cardiac stimulants) were employed to treat a number of ailments. Ancient Chinese physicians employed ma huang, a plant containing ephedrine, for a variety of purposes. Today ephedrine is used in many pharmaceutical preparations intended for the treatment of cold and allergy symptoms. The Greek physician Galen (*c.* 130–*c.* 200 AD) included opium and squill among the drugs in his apothecary shop (pharmacy). Today derivatives of opium alkaloids are widely employed for pain relief, and, while squill was used for a time as a cardiac stimulant, it is better known as a rat poison. Although many of the medicinal preparations

used by Galen are obsolete, he made many important conceptual contributions to modern medicine. For example, he was among the first practitioners to insist on purity for drugs. He also recognized the importance of using the right variety and age of botanical specimens to be used in making drugs.

Pharmaceutical science in the 16th and 17th centuries

Pharmaceutical science improved markedly in the 16th and 17th centuries. In 1546 the first pharmacopoeia, or collected list of drugs and medicinal chemicals with directions for making pharmaceutical preparations, appeared in Nürnberg, Ger. Previous to this time, medical preparations had varied in concentration and even in constituents. Other pharmacopoeias followed in Basel (1561), Augsburg (1564), and London (1618). The *London Pharmacopoeia* became mandatory for the whole of England and thus became the first example of a national pharmacopoeia. Another important advance was initiated by Paracelsus, a 16th-century Swiss physician-chemist. He admonished his contemporaries not to use chemistry as it had widely been employed prior to his time in the speculative science of alchemy and the making of gold. Instead, Paracelsus advocated the use of chemistry to study the preparation of medicines.

Isolation and synthesis of compounds

In the 1800s many important compounds were isolated from plants for the first time. About 1804 the active ingredient, morphine, was isolated from opium. In 1820 quinine (malaria treatment) was isolated from cinchona bark and colchicine (gout treatment) from autumn crocus. In 1833 atropine (variety of uses) was purified from *Atropa belladonna*, and in 1860 cocaine (local anesthetic) was isolated from coca leaves. Isolation and purification of these medicinal compounds was of tremendous importance for several reasons. First, accurate doses of the drugs could be administered, something that had not been possible previously because the plants contained unknown and variable amounts of the active drug. Second, toxic effects due to impurities in the plant products could be eliminated if only the pure active ingredients were used. Finally, knowledge of the chemical structure of pure drugs enabled laboratory synthesis of many structurally related compounds and the development of valuable drugs.

Pain relief has been an important goal of medicine development for millennia. Prior to the mid-19th century, surgeons took great pride in the speed with which they could complete a surgical procedure. Faster surgery meant that the patient would undergo the excruciating pain for shorter periods of time. In 1842 ether was first employed as an anesthetic during surgery, and chloroform followed soon after in 1847. These agents revolutionized the practice of surgery. After their introduction, careful attention could be paid to prevention of tissue damage, and longer and more-complex surgical procedures could be carried out more safely. Although both ether and chloroform were employed in anesthesia for more than a century, their current use is severely limited by their side effects; ether is very flammable and explosive and chloroform may cause severe liver toxicity in some patients. However, because pharmaceutical chemists knew the chemical structures of these two

anesthetics, they were able to synthesize newer anesthetics, which have many chemical similarities with ether and chloroform but do not burn or cause liver toxicity.

Scope In Health Care Industry

It is important to differentiate between 'free' and 'fixed' Nano particles. The formers pose a direct health threat because they are more difficult to contain due to airborne and can be inhaled. Nanoparticles can enter the human body in several ways (i) via the lungs where a rapid translocation through the blood stream to vital organ is possible, including crossing the BBB and absorptions by (ii) the intestinal tract (iii) the skin (Hoet et al., 2004).

Lungs: Based on three particle types titanium dioxide (TiO2) carbon black and the diesel particles, hazards studies in rats, demonstrate that ultrafine nanoparticles administration to the lung produce more potent adverse effect in the form of inflammation and subsequent tumors compared with larger sized particles, of identical chemical composition at equivalent mass concentration. Surface properties such as surface chemistry may play a significant role in nanoparticles toxicity (Lee et al., 1998).

Intestinal Tract: The epithelium of the small and large intestinal is in close contact with ingested material so that nutrients can be utilized. A mixture of disaccharides, peptides, fatty acids and monoglycerides generated but digestion in small intestine are further transformed and taken in the villi. Charged particles like carboxylated polystyrene Nano particles or those composed of positively charged polymer exhibit poor oral bioavailability through electrostatic repulsions and means entrapment (Jani et al., 1989). The smaller the particles diameter the faster they could penetrate the mucus to reach the colonic eutrocytes;14nm diameter permeated within 2 mints, 415 nm particles look 30 mints while 1000 nm particles were unable to translocate this barrier (Jani et al., 1990).

Skin: Particles 500-1000 nm in size theoretically beyond the realms of Nano technology can penetrate and reach the lower levels of human skin, 128 and smaller particles are likely to deeper into the skin (Lademann et al., 1989).

General applications of Nanoparticles

As anti-Infective Agents: Metallic nanoparticles have been described as a HIV preventative therapeutic. In a couple of studies, it has been shown that as virucidal agent silver acts directly on the virus by binding to the glycoprotein gp120. This binding in turn prevents the CD4 dependent virion binding which effectively decreases HIV1"s infectivity. and it has also been reported that metallic nanoparticles have been effective antiviral agents against herpes simplex virus, influenza, respiratory syncytial viruses.

As anti-Angiogenic: Angiogenesis is the development of new blood vessels and occurs during normal development and in some disease states. It plays a main role in number of diseases such as cancer, rheumatoid arthritis. In normal conditions, angiogenesis is tightly regulated between various pro-angiogenic growth factors (VEGF, PDGF, and TGF-B) and anti-angiogenic factors (platelet factor 4, TSP-1). Under diseased conditions, angiogenic is turned on. Some reviews have reported that these agents have serious toxicities such as fatal

hemorrhage, thrombosis, and hypertension. It may be overcome if these nanoparticles alone can be efficacious as an anti-angiogenic agent.

In Tumor Therapy: It has been studied that naked gold nanoparticles inhibited the activity of heparin binding proteins such as VEGF165 and bFGF in vitro and VEGF induced angiogenesis in vivo. Further work in this area has been reported that onto the surface of AuNPs heparin binding proteins are absorbed and were subsequently denatured. The researchers also showed that surface size plays a main role in the therapeutic effect of AuNPs. Mukherjee and colleagues also experimented the effect of gold nanoparticles on VEGF mediated angiogenesis using a mouse ear model injected with an adrenoviral vector of VEGF. A week later, the AdVEGF administration, mice treated with AuNPs developed lesser edema than the same treated mice. Eom and Colleagues revealed the anti-tumour effects of 50 nm AgNps In vitro and In vivo.

In Multiple Myeloma: Researchers have designed a nanoparticle based therapy that is effective in treating mice with multiple myeloma. Multiple myeloma is a cancer that affects plasma cells.

In Leukaemia: B-chronic Lymphocytic Leukaemia (CLL) is an incurable disease predominantly characterized by apoptosis resistance, by co-culture with an anti-VEGF antibody, found induction of more apoptosis in CCL B cells. In CLL therapy, gold nanoparticles were used to increase the efficacy of these agents. Gold nanoparticles were chosen based on their biocompatibility, very high surface area, surface functionalization and ease of characterization. To the gold nanoparticles, VEGF antibodies were attached and determined their ability to kill CLL B cells.

In Rheumatoid Arthritis: Scientists from the University of Wollongong (Australia) have built a new class of anti-arthritis drug which could be used by gold nanoparticles and it has fewer side effects. Rheumatoid arthritis is an autoimmune disease that occurs when the immune system does not function properly and attacks a patient‟s joints. New research has shown that gold particles can invade macrophages, and stop them from producing inflammation without killing them. In the Journal of inorganic biochemistry it has been published that by reducing the size of gold into smaller nanoparticles (50 nm), it was able to cause more gold to immune cells with lesser toxicity.

In Photo Thermal Therapy: Gold nanoparticles absorb light strongly as they convert photon energy into heat quickly and efficiently. Photo-thermal therapy (PTT) is an invasive therapy in which photon energy is converted into heat to kill cancer. In Radiotherapy Tumours are loaded with gold, this absorbs more X-rays as gold is an excellent absorber of X-rays. Thus, deposition of more beam energy and resulting in a local dose which increases specifically to tumour cells. Gold nanoparticles have been more useful to treat cancer.

Therapeutic applications of ceramic nanoparticles:

Ceramic nanoparticles like titania have also been added into polymer matrices to adjust composite surface chemistry, topography, and wettability (surface energetics) of the polymer matrix, aiming at the promotion of osteogenic responses on the material surfaces.

- Functionalized magnesium oxide, zirconia, sulfate, and calcium carbonate are added to polymethylmethacrylate (PMMA) bone cement to reduce the exothermic effect of PMMA while increasing its cytocompatibility, X-ray radiopacity, as well as antibacterial potential.

- Antibacterial effects of BaSO4 nanoparticles against Staphylococcus aureus and Pseudomonas aeruginosa have been discovered, suggesting their potential applications as anti-infective additives to bone cement, implant coating, and medical tubing.

- Therefore, these NPs are used by researchers across the globe in wide applications, such as catalysis, photocatalysis, photo degradation of dyes, and imaging applications. Medical technologies use nanoceramics for bone repair.

- Ceramic NPs are also used in energy supply and storage, communication, transportation systems, construction, and medical technology.

- One of the main uses of nanoceramics has been in biomedicine and medical technology, particularly in bone repair. Bioactive ceramics closely match the properties of bone and can act as a nanoscaffold to help support bone regrowth

- It has also been suggested that nanoceramics might find uses in energy supply and storage, communications, transportation systems, aerospace and construction. They have also found use in electronics as insulators, semiconductors, conductors and magnets.

- Nanoceramics might also find a use in armor to replace the stiff, tough layers of woven fiber which absorbs impact. A hard body armor is under development that includes ceramic inserts and steel or titanium panels that could offer greater protection against blunt trauma and high velocity ammunition. The inserts could absorb kinetic energy of the projectile and dissipate it in a localized shattering of the ceramic insert.

Therapeutic applications of Polymeric nanoparticles

- They develop innovative drug delivery system in the treatment of neurodegenerative and brain associated diseases.

- Polymeric NPs provide protection to the drugs via encapsulating, entrapping them inside the core, conjugating, or adsorbing them on to the particle surface.

- Polymeric NPs deliver cargo-loaded molecules across the BBB by following endocytosis and transcytosis pathways.

- This polymeric coating is thought to reduce immunogenicity, and limit the phagocytosis of nanoparticles by the reticulo-endothelial system, resulting in increased blood levels of drug in organs such as the brain, intestines, and kidneys.

- These have been applied in gene therapy to breast cancer cells, resulting in anti-proliferative effects.

Therapeutic applications of lipid based nanoparticles

- These are mainly used to various types of cancer like GIT cancer, lung cancer, breast cancer, pancreatic cancer, prostate cancer

- It significantly enhances transdermal penetration of phytomedicines inside skin.

- SLNs increase the therapeutic potential of eugenol and efficiently inhibited the growth of Candida infection during oral candidiasis.

- It has enhanced antimicrobial activity.

Therapeutic applications of semiconductor nanoparticles: It has significant attention in research and applications in emerging technologies such as nanoelectronics, nanophotonics, energy conversion, nonlinear optics, miniaturized sensors and imaging devices, solar cells, catalysis, detectors, photography biomedicine etc**.**

Therapeutic applications of carbon based nanoparticles Drug and gene delivery: The application as drug delivery is very common in carbon-based nanoparticles, especially, the graphene-based nanoparticles. The πconjugated structure of six-atom rings of carbon can be conceptually considered as a planar aromatic macromolecule. This unique structure offers a large loading capability to a variety of fluorescent probes and drugs. The chemical modification of graphene can allow the conjugation with targeting ligands, therefore, achieve the targeted delivery of the drug. Both in vitro and in vivo studies have provided the evidence of the graphene for delivering anti-cancer drugs to the desired location of tumor cells, rather than the normal and healthy cells.

Bioimaging: Carbon-based materials have long been investigated in many imaging applications. For example, fluorescence imaging (FL), two-photon FL, Raman imaging, magnetic resonance imaging (MRI), tomography (CT), photoacoustic imaging (PAI), computed positron emission tomography/single photon emission computed tomography (PET/SPECT), and multimodal imaging. Recently, a new form of carbonbased nanomaterials, carbon quantum dots, has attracted tremendous interests in its bioimaging applications.

`components of hydrogen storage systems. Due to their intrinsic characteristics, carbon-based materials are a desired material as electrodes in capacitors and batteries. CNTs have shown a high reversible capacity for use in lithiumion batteries and also in a variety of fuel cell components. The high electrical conductivity also allows the

CNT be used in current collectors and gas diffusion layers. The high surface area and thermal conductivity make CNT and graphene very useful as electrode catalyst supports in fuel cells.

Conclusion : A nano particle or ultrafine particle is usually defined as a particle of matter that is between 1 and 100 nm in diameter. The emergence of nano technology likely to have a significance impact on pharmaceutical field. It has several merits over the conventional drug delivery system in terms of high stability, high specificity, high drug carrying capacity, ability for controlled release, possibility to use in different route of administration . Nano particles are now being used in the manufacture of scratchproof eye glasses, transparent sun screens , transparent repellants , and some others include gene theraphy, cancer therapy, AIDS theraphy, and radiation theraphy. The major aims of nano particle design as a delivery system are to control particle size , surface properties, and drug drug delivery and API release so as to ensure site-targeted drug activity at an appropriate therapeutic rate and dosing regimen.

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