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Review on Nanotechnology: Advancement in the Formulation and Evaluation of The Nanoparticles and Its Application

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Abstract: *This abstract explores recent advancements in the formulation and evaluation of nanoparticles, delving into their diverse applications. The review encompasses innovative methodologies and techniques contributing to the development of efficient nanoparticle systems, while also highlighting key findings in the realm of their practical applications across various fields. This comprehensive overview aims to provide insights into the evolving landscape of nanoparticle research and its impactful role in advancing diverse technological and biomedical applications.*

Keywords: Nanoparticle; Formulation of nanoparticle; Evaluation of nanoparticle; Application of nanoparticle

I. INTRODUCTION

Nanotechnology is a nanometer-scale scientific technology of about 1 to 100 nanometers and can be used in all fields of science, including life science and healthcare [1]. The concepts and ideas of nanoscience and nanotechnology were proposed by physicist Richard Feynman, known as the father of nanotechnology. In his lecture 'There is a Place Below', delivered at the American Physical Society's annual meeting held in Pasadena, California on December 29, 1959, he explained his idea of creating small objects through the method of making small objects. [2]. Nanomedicine is one of the most studied fields of nanotechnology and is widely used in the prevention, diagnosis, and treatment of diseases. It is used in drug research to reduce drug toxicity and reduce side effects through targeting drugs to specific sites of action, reducing drug dosage by improving bioavailability, and administering drugs in the human body to reduce the frequency of drug use; and extend shelf life by increasing stability. This ultimately helps improve safety, effectiveness, patient compliance, extend the shelf life of the drug, and ultimately reduce healthcare costs [3-5]. Nanotechnology can be used in many fields, focusing on the development of drug delivery systems such as long-acting models, cancer-specific transdermal drug delivery systems (TDDS), and improving bioavailability through improved distribution and absorption. This article focuses on the use of nanotechnology to improve drug delivery in biphasic liquid drugs such as suspensions, emulsions and micelles. Drug nanosuspensions are two-phase liquid systems in which insoluble substances in the submicron range are evenly dispersed in an aqueous carrier. This form is colloidal in nature, often stabilized with surfactants and polymers, and can be used orally, parenterally, topically, nasally, and ophthalmically. It is designed to be used in a variety of ways, including: [6] Nanosuspensions are tools. It is used to solve the problem of low solubility and bioavailability of drugs and sometimes improve the safety and effectiveness of drugs by modifying their properties. their pharmacokinetics. It is used as an alternative approach to lipid systems, when the drug is insoluble in both, aqueous and organic media. The reduced particle size of poorly water-soluble drug to nano range, enormously increases surface area leading to increased rate of dissolution or an increase in saturation solubility due to an increased dissolution pressure. For example, the solubility and dissolution rate and consequently the bioavailability of crystalline simvastatin was increased significantly by preparation of nanosuspension employing nanoprecipitation technique at laboratory scale [7].

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Similarly, oral bioavailability of olmesartan medoxomil was enhanced by improving its solubility and dissolution rate by preparing nanosuspensions [8].

Nanosuspension may also be used to improve the pharmacokinetic and pharmacodynamic profile of the drug and thus therapeutic efficacy of drug, following oral administration. This has been illustrated in case of atovaquone nanosuspension for improved oral delivery in the treatment of malaria [9] and in case of 1,3-dicyclohexylurea, by subcutaneous route in the treatment of hypertension [10].

Nanoemulsions are heterogeneous but clear and transparent dispersions of two or more immiscible liquids, stabilized by an interfacial film of surfactant molecule in which internal phase is present in nano size range. These are isotropic in nature and thermodynamically stable. "Nanoemulsions are alsoreferred to as miniemulsions, ultrafine emulsions and submicron emulsions" [11].

The above mentioned traits of nanoemulsions, such as, increased surface area, optical clarity and transparency and thermodynamic stability makes them important as a tool for solving some of key concerns in drug delivery systems. The clarity and transparency of nanoemulsions is exploited for delivering products that can offer good aesthetic appeal, skin feel and patient compliance [12]. The resulting large surface area of nanoemulsions is applied to enhance the dermal, transdermal and mucosal transport or permeation of various drugs [13]. Ropinirole, an antiparkinson drug was formulated as nanoemulsion for percutaneous delivery [14]. The resulting increased surface area is also utilized in improving oral bioavailability of hydrophilic as well as hydrophobic drugs. A hydrophobic drug, paclitaxel was formulated into nanoemulsion for enhancing its oral bioavailability [15]. The longterm colloidal stability of nanoemulsions is used to impart long shelf-life to many pharmaceutical products. Nanomicelles are nanosized aggregates of amphiphilic monomer units. Ampiphiles are the molecules having polar or hydrophilic as well as nonpolar or hydrophobic groups, having ability to orient themselves as clusters when added above critical micelle concentration in a solvent. They form regular micelles in a hydrophilic solvent and reverse micelles in hydrophobic solvent.

Nano micelles, like other nano liquid systems, enhance solubility profiles of poorly soluble drugs. Normal or regular micelles, where the micellar core is made up of non polar group are suited chiefly for hydrophobic drugs, while, reverse micelles where the micellar core is made up of polar groups are primarily suited for the encapsulation and delivery of hydrophilic drugs. The amphiphilic nature of these micelles can be exploited for targeting drugs to specified sites by affixing ligands to them

History of Nanotechnology uses as Drug Delivery

First Generation-

During this time, simple methods to control drug release were developed and most drug delivery systems were administered orally and transdermally. This chemical process is inert and unstable (16). More than 150 years ago, Michael Faraday proposed nanoscale gold particles. Colloidal gold particles combine with antibodies to achieve a specific target staining called immunogold staining. The application of this gold material is considered a precursor to the recent use of gold material in nanotechnology. In 1960s, Liposomes and polymer micelles were first prepared, however it was never referred as nano-particles until 2000.

In 1970s, NPs and dendrimers were first prepared without the knowledge of nanotechnological application. In 1980s, the period reported to be the successful development of micelles as drug delivery system. And in 1990s, block co-polymers of polyethylene glycol (PEG), PEG-Polylysine have been invented by Kataoka (17). Prior to nanotechnology revolution, in past liposomes, polymeric micelles, nanoparticles, dendrimers, and nano-crystals used for drug delivery, but in the era nanotechnology, the terms were unknown.

Second Generation:The modern nanotechnology uses as drug delivery began when United States launched the national nanotechnology initiatives, the world first program in the field of nanotechnology. Many new methods of drug delivery have emerged in which nanotechnological methods are more efficient and reduce the shortcomings of ordinary DDS (16).

Currently immature nanotechnology uses microchips, carbon nanomaterials, microneedle-based transdermal technology, layer-by-layer assembly and previous nanocarriers, as well as many products created by injection technology.) and ligands. (17).

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II. NANOPARTICLES

Nanoparticles are dispersed or solid particles with lengths of billionths of a meter and billionths of a meter. Simpler structures such as capsules, tablets and pills can be obtained by using simple nanoparticle preparation techniques.

They are nano sized and therefore can be used as parenteral formulations and are 100% bioavailable. The nanoparticles are designed for BCS Class II and IV drugs with poor solubility. BCS class II drug have law solubility and have good permeability but they give law bioavailability because it have law solubility so it give law absorption of drug and thus it give law bioavailability. Same problem is occurring with BCS IV class drug which have law solubility with law permeability so by converting this type of molecules into nanoparticle we can remove this problem [18].

Nanoparticle has different chemical characterization than metal and their oxides, organic material, carbon material and other polymers. It also has different shape like sphere shape, tube shape, disk or hollow shape etc. it can be synthesis from solid, gas or liquid and nanoparticle have different surface properties than pure drug. Nanoparticle are chemically react fast compare other drug. So we can said that nanoparticle have different biological, physical, chemical character than starting material [19].

Surface modification is applied on nanoparticle and which can use for many different action like for onset action, for sustained release, for controlled release, for targeted formulation, for improvement of dissolution of drug, for changing of chemical and biological characteristics. Surface modification can apply by different methods such as by using the polymer, by using the surfactant, by join with ligand, by applying coating on surface, by attached the particle with DNA or protein or any other bimolecular, by applying adsorbent like surfactant or polymer which adsorbed the particle and give action [20].

Nanoparticle is sometime surrounded by stabilizer or other exicipients. Metallic nanoparticles are also available in market which has different physical or chemical character from metal bulk. The example of this is nanoparticle of Au which has different color in different size formulation. Nanoparticles are used in medicine as well as other industries also like in rubber industry they use carbon black particle for fabrication of rubber.

Nanoparticle has different type like carbon-based nanoparticle which contains carbon nanotubes and fullerenes which are better compare to steel. Other type is ceramic nanoparticle which is inorganic solid made by carbides or carbonate or phosphate or oxides and use in drug delivery and photo imaging. other one type is metal nanoparticle which is made by using metal and use in formulation which need high surface energy and they also adsorbed little size molecules. Another type is semiconductor nanoparticle, particles use are like GaN, GaP, lnAs, Zns, Zno,Cdte etc. and they are used in electronic devices, water splitting etc. One type is polymeric nanoparticles which are also known as nanosphere in which active component is layered by polymer and use in pharmaceutical formulation for newer approaches like targeting controlled release. Lipid based nanoparticle is also available which have core in which nanoparticle is stabilize by using surfactant or emulsifier and it is used in cancer like disease condition [21].

Nanoparticle are small in size so they have special characteristics and the size of particle can be controlled by using surfactant and polymer and by controlling the size we can also controlled the absorption wavelength and emission wavelength. Transparency in nanoformulation can be attained if particleare below the light critical wavelength of light. In metal nanoparticle the melting point of metal is decrease and also gives better paramagnetic properties. Nanoparticle has different chemical nature so it gives different affinity to electron and which give different properties of electron transport.

Nanoparticle has more surface area so it cans high affinity to polymer matrix in which particle is incorporated. Surface modification in nanoparticle is used to give better stability to nanoparticle and it also use for improving the reaction and applications. Nano particles are used as smart drug for onset and fast result for disease like cancer, diabetes, artery blockage etc. Nanobots use for artery blockage and nanoparticles are also use in genetic problem and it also help in targeting the cell and it is also use for long lasting effect.Nanoparticle is used in broad area. Most of nanoparticle is used in health and fitness maintenance. They are also used in food and nutrition, for electrical use, for home use etc. Examples include nano toothpaste, nano filters for air filtration, vitamin B-12 nano spray, nano cream as an antibiotic [19].

Nano chips and nano biosensors on the market are medical devices wrapped in nano particles. Nowadays, nanoliposomes are called nanoparticles, which are coated with phospholipids and contain nanoparticles that are approximately 25 to 1 billionth of a billionth of their size. Commonly used liposomes range is size from 500 parts per

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billion to 200 parts per billion. Ambisome is a nanoliposome product that contains amphotericin B particles in liposomes with a size of approximately 65 nanometers and is used for fungal infections. Daunorubicin is also encapsulated in liposomes and can be used for targeted delivery to cancer cells. Some nanometer particles are coated with proteins, which works well. Like PEGylated proteins, which have a longer effect in the blood. Some drugs also bind to proteins, such as paclitaxel, which binds to albumin and has a size of 131 nm. Some nanoparticles have been converted into metal products; for example, Feridex is an approved product of metal oxide nanoparticles that can be used for MRI of the liver and spleen after surface modification. The advantage of this sample is that its particle size is less than 1 micron, so it has greater solubility and dissolution ability than other bulk materials, and we can also produce 100% pure drug without the need to use carriers [22]< br >. It has some disadvantages, for example, nanoparticles are difficult to produce on a large scale, which requires high production costs, and sometimes it requires a lot of technology to produce, so it takes a long time.

Advantages

- It is easy to change the surface properties and size of nanoparticles to achieve high anti-inflammatory and active effects after parenteral administration.
- They change the body's material and then remove the drug, control and promote the release of the drug in the body, improving treatment and reducing side effects, transportation and on-site focus.
- Control output and related features can be easily adjusted by selecting the matrix material.
- The ability to integrate drugs into the body without chemical reactions is an important factor in the management of substance addiction. Drug transport is also higher.
- Targeting ligands can be attached to the particle surface for a specific location or using magnetic guidance.
- This technique can be used for oral, nasal, parenteral, intraocular, etc. It can be used for a variety of applications including.[23]It is biodegradable, non-toxic and can be stored for a long time.
- Also used to control delivery.
- Reduce dose more frequently [24].

Disadvantages

- Less drug carrying capacity.
- Toxic metabolites may be produced during the biotransformation of polymeric materials during recycling.
- Biodegradation is slow and may cause toxicity [24].

Properties of Nanoparticles

Nanoparticles come in many sizes, shapes and patterns. Their shapes include spherical, cylindrical, tubular, conical, hollow, spiral, flat, etc. or special shapes ranging in length from 1 nanometer to 100 nanometers. The edges can be the same or different in different sizes [25]. A few nanoparticles are crystalline or amorphous, with self-aggregating monocrystalline or polycrystalline solids. Materials are based on form and composition and can often be created or modified according to the relative properties of sizes or changes in size or the material level of the space, and primarily by all macroscopic properties. This approach has been around for hundreds of years in metal alloys and has been so successful that many engineering materials today are composites with micro- to nanoscale sizes.

According to the physical or chemical properties of each area, there is an interaction between the structure and composition of the material, resulting in all the problems with the parent material and the surface and the growth of new products at the interface. Chemical selection is present in nanocomposites and has the ability to separate the material into one type or another. Complex systems control this behavior, which involves the release of nanoparticles into the environment [26]

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Types of Nanoparticles

Inorganic Nanoparticles:

In today's materials research, inorganic nanoparticles play an important role, especially in the biotechnology industry, due to their unique properties. As two types of inorganic nanoparticles, they have some physical properties, especially size-dependent optical, magnetic, electrical and catalytic properties. Bio-relevant applications include metal oxide, gold, silver, silica, quantum dots, etc. It involves the preparation of interesting nanoparticles such as New physical objects are related in size down to nanoscale dimensions. [27, 28]

Polymer Nanoparticles

Polymer nanoparticles are also a type of nanoparticles. In recent years, the research field of polymer nanoparticles has made great progress. Dispersion of preformed polymers and polymerization of monomers are two main concepts frequently involved in preparation. 10 is the size associated with 1000nm material. [29]

Lipid Nanoparticles

Lipid nanoparticles played an important role in controlled drug delivery in the 1990s. There are other carrier methods for emulsion, liposomes and polymeric nanoparticles as colloidal carrier systems. [30, 31]

Liposomes

Liposomes are a way of different types of nanoparticles. The structure of liposomes includes one or more phospholipid bilayers, which are spherical vesicles containing the content of interest. Today, liposomes play an important role in the field of reagents and tools in many disciplines.

Liposomes are unique in the market because they are involved in many functions. Many molecules in the cosmetic and pharmaceutical industries serve as carriers, while in the food and agricultural industries liposomes participate in encapsulation to grow delivery systems to capture unstable compounds. [32, 33]

Nanocrystals

Nanocrystals are a type of material with at least one length less than 100 nanometers and most of the atoms arranged in a single or polycrystalline arrangement.

Nanocrystals are aggregates of approximately hundreds or thousands of molecules brought together in crystal form and consist of a pure substance with a thin layer containing only one surfactant or a combination of surfactants. [34,35]

Nanotubes

Nanotubes are nanoscale tubular structures. Nanotubes are members of the fully functional family. They get their name from their long, hollow structures whose walls consist of a single-atom-thick layer of carbon called graphene. The sheets are rolled at a specific and non-uniform (“chiral”) angle, and the combination of the rolling angle and radius determines the properties of the nanotube; for example, whether a nanotube shell is metal or semiconductor. Nanotubes are divided into single-wall nanotubes (SWNTs) and multi-wall nanotubes. [36, 37]

Dendrimers

Dendrimers are derived from two Greek words: Dendron meaning "tree" and Meros meaning "piece". The structure of dendrimers varies in size, shape and molecular weight, and dendrimers are hyperbranched, spherical, monodisperse, three-dimensional nanoscale synthetic polymers. Both molecular and polymer chemistry clearly show dendritic features. [38, 39]

Formulation of Nanoparticles

Precipitation System

This system was discovered in 1980 and used in the production of nanoparticles. This is a simple method in which the API is dissolved in the native solvent and the excipients (such as polymeric surfactants) are dissolved in a miscible inorganic solvent, the organic solvent is added to the inorganic solvent by self-stirring, and the waste is weighed. rain or snow. This generation is simple and costs need to be fixed, so control it with different methods, simple methods and takes less time to complete. To make this formula we want the API to have minimal solubility in an organic solvent and natural solvents have poor properties with inorganic solvents so that is the limit of the technology here [40].

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Crushing Method

This machine was developed in 1990. In this equipment, API and surfactants are packed together with ground pearls in a collision chamber and then shattered using a high-speed motor. Nanoparticles are produced in suspension.

This process should take longer because there are factors such as chemical harshness and many will affect the process. The process requires high energy and sometimes erosion of the pearls can lead to product degradation and the risk of bacterial and microbial contamination. Media grinding chambers are made of zirconia, glass or polystyrene resin. The milling process is used with both aqueous and organic media. It can be used to create both dilute and concentrated suspension formulations. The disadvantages of this method are that it takes a long time and collisions can weaken the body [41].

Homogenization Method

This method was developed in the 1990s for the production of nanoparticles and nanosuspensions. In this device, nanosuspension API and excipients are passed through a homogenizer under different pressures, causing cavitation and nanoparticles are produced using high energy. In a high-pressure homogenizer, both pressure and mechanical force can be used to produce certain products.

There are also different power and pressure options so that the homogenizer can be adjusted to produce the same size. There is also the option to change the temperature. During thermal homogenization, high temperature is used to dissolve the lipid phase and form an aqueous phase. This method is not suitable for chemicals that can be graded at high temperatures. We can use cold homogenization for this solution.

The technology is also used in parenteral formulations and food and cosmetic products.

For these machines, homogenization cycles with applied temperature and pressure must be observed. A pressure between 100 and 1500 bar was used to perform testing in the laboratory. Due to the pressure, the resulting particles are small, have better bioavailability and have a larger surface area, so a better separation can be achieved. Albendazole, ibuprofen, spironolactone, nifedipine and omeprazole have been developed using this strategy [42]. Fenofibrate nanoparticles are used as tablets in the treatment of hypercholesterolemia and its trade name is Triglide, produced by the homogenization method.

Spray Drying Method

This method is used for tablets and powder production. First the macro suspension is produce which contained API and exicipients with proper solvent and then this suspension is passed from homonizer and it give nanosuspension. The second step is removing solvent. For solvent removing two methods are used like freeze drying and spray drying. The freeze-drying method is costly so spray drying method is first choice for industries and it give dry powder form nano powders and crystals [43. The loading capacity of nanoparticle powder can be varied by changing the amount of material and surfactant in the suspension. For the first time spray drying has limitations, they are not used for production, in the past they gave a minimum size of 2 µm, but now this method can be used to produce sizes of 300 nm and smaller, there is a 90% efficiency. The principle of the dryer is simple. First, dry oil enters the system with laminar flow through the heater. The nozzle sprays fine droplets of suspension that turn into particles after drying. Such powders can be used for inhalation, encapsulation, suspension, etc. Can be used as drug carriers for

Dialysis

The technology is similar to nanoprecipitation. It is suitable for the preparation of small and narrowly dispersed nanoparticles. Here the filter tube is filled with a polymer containing an organic solvent. Due to loss of solubility, the polymer comes together to form a homogeneous suspension of nanoparticles. Semi-permeable membranes allow solvent transport, reducing polymer entrainment [44]

Non-aqueous production of nanoparticles

Granulation Method

In general, nanosuspensions are stable; However, we need a design especially for issues such as verbal management and security, so this tool can be used to solve this problem. Nanosuspensions can be formed into thin materials using

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techniques such as freeze-drying, spray-drying, extrusion and spheroidization, or by layering sugar pellets. Using extrusion technology, the final product is produced through a process that involves mixing suspensions with matrix excipients. The product is produced as small free-flowing spheres in the shape of the product [45].

Hot Melt Production Process

This process involves homogenizing the molten material at a certain temperature. The temperature is determined by the melting point of the matrix material. A Micro Lab 40 homogenizer is usually used in this method because the container is covered with a heat shield. The process continues with solidification and when the desired grain size is reached 46 solidifications can be done by cooling at room temperature.

Direct compression method

Using spray drying and other methods to prepare nanoparticle powder from nanosuspension that can be used orally after being placed in capsules. In the case of acid-sensitive drugs, the nanoparticles are packaged in hard gelatin capsules. Another method for oral administration of nanoparticles is to convert them into tablet formulations. Nanosuspensions are mixed with micron-sized polymer powder or matrix-forming materials such as lipids and lactose powder and then spray dried. By this process the liquid phase is go into API-matrix compound and convert into free-flowing powder than direct compression is apply and which give long release tablet formulation [45]

III. ANOTHER SYNTHESIS OF NANOPARTICLES

Various methods have been employed to synthesize nanoparticles (NPs) with controlled `, size, dimensions and structure. There are two main approaches for the synthesis of NPs viz., Top- down and Bottom- up approach These mechanisms are divided into various groups based on activity and reaction (Schemes 1 and 2).

A. Top-Down Method

The Top-Down method involves breaking bulk materials into nanoscale particles. This is a destructive process. Top-down processes are simpler and rely on the extraction or fractionation of bulk materials or small-scale manufacturing processes to create the desired model with the required components. Mechanical milling, nanolithography, laser ablation, sputtering and thermal decomposition are some of the most commonly used nanoparticle synthesis methods.

B. Bottom-up approach

Bottom-up or constructive approach is another method that uses a construction method in which nanoparticles are formed in groups and the groups are derived from atoms.

Characterization of Nanoparticles-

Nanoparticle size

Nanoparticle size determination, It is important for separation analysis, saturated solubility, physical and biological stability are important. The average mass of the particles was determined using photon correlation spectroscopy (PCS). Coulter countermiltisizer and laser diffraction (LD) were also used to analyze these products. The PCS method can also be used for particle size measurement. Dynamic light scattering (DLS) is also used in industry to measure the size of nanoparticles and can also measure the size of particles below 10 nm. In this process, the colloidal liquid sample is subjected to Brownian motion and the scattering of light is used to provide information about the diffusion coefficient. This method measures wavelengths from 2 nm to 2000 nm and provides results in 1 to 10 minutes. A small sample size is required for this method, results are fast, and particle size measurement and polydispersity measurement are easy [47].

Shape and Morphology

Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) can be used to examine this material. TEM requires a liquid or wet sample and SEM requires a solid sample. SEM is sometimes used to examine the size of nanosuspensions, so the solvent must be removed from the suspension, hence the use of freezing or drying methods. This method has clumping and adhesion problems, so cryoprotectants or other excipients are added before the

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method is applied. Like mannitol used in freeze-drying, it works by coating nanoparticles so they don't clump. Sometimes X-ray diffraction (XRD) also use for detection of polymorphic change due to pressure and homogenization [48].

This method is used for tablets and powder production. First the macro suspension is produce which contains API and excipients with proper solvent and then this suspension is passed from homonizer and it give nanosuspension. The second step is removing solvent. For solvent removing two methods are used like freeze drying and spray drying. The freeze-drying method is costly so spray drying method is first choice for industries and it give dry powder form nano powders and crystals [43]. The loading capacity of nanoparticle powder can be varied by changing the amount of material and surfactant in the suspension. For the first time spray drying has limitations, they are not used for production, in the past they gave a minimum size of 2 µm, but now this method can be used to produce sizes of 300 nm and smaller, there is a 90% efficiency. The principle of the dryer is simple. First, dry oil enters the system with laminar flow through the heater. The nozzle sprays fine droplets of suspension that turn into particles after drying. Such powders can be used for inhalation, encapsulation, suspension, etc. Can be used as drug carriers for

Zeta Potential

This measurement is useful to detect the stability of colloidal dispersion after storage. As per literature zeta potecial between ± 20 mv to ±30 mv is give desirably stable nanoparticle into suspension [49].

Differential Scanning Calorimetry (DSC)

The natural drug's physical state with the help of a DSC study (DSC-60, Shimadzu, Japan), nanoparticles were identified. About 2 mg of native drug, polymer, and nanoparticles were inserted separately into various sealed standard aluminum pans and heated at a rate of10°C/min under nitrogen environment before being heated to various temperatures between 25 and 300 °C. The standard was an aluminum pan that was empty [50].

X-ray Diffraction Analysis

An XRD-6000 diffractometer was used to carry out the X-ray diffraction analysis. Diffraction of X-rays formulation and the pure drug's crystallinity were determined through analysis. In a sample holder made of aluminum, the powder was placed. 30 mA and 40 kV were used to create Cu radiation. As previously mentioned, samples were scanned between 10° and 90° at a speed of 10° min-1 [51].

Scanning electron microscopy (SEM)

It can be used to measure the surface phenomenon by visual investigation. Following technique have advantages in sizing analysis and morphology. Here first convert the nanoparticle solution into dry powder and place the sample in sample holder and it coated with metals as such gold by using sputter coater.

Then the sample, focused, scanned with fine beam of electron. Characteristics of sample surface are obtained from emitted secondary electron from sample. In vacuum condition nanoparticles were withstand but polymer can damage by electron beam. Then the obtained mean size from SEM is comparable with DSC. Disadvantages of SEM are time consuming, high cost, need for complementary information about size distribution [52]

Drug release

Drug loading means the amount of drug bound per mass of polymer also it gives percentage relative to the polymer. Analytical technique such as HPLC, UV spectroscopy, ultracentrifugation, gel filtration, ultra filtration, and centrifugal ultrafiltration techniques are used [53,54]

Therapeutic Application

Dermal

Dermal use means drug is apply on skin and absorption of drug is occur from skin by intercellular route of lipid, by transcellular route and by using the follicular penetration. Fluconazole nanoparticle into NLCs and SLNs are used into fungal disease which gives better penetration compare to simple drug. The transdermal penetration is increase by

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nanoparticle by increasing the gradient of concentration between skin and nanoformulation. Like hesperidin and lutein anti-ageing nanoformulation is use to increase the solubilizing power of hesperidin. Another example is the drug diclofenac, which causes serious gastrointestinal problems when taken orally, but this problem can be overcome by converting diclofenac into a nanosuspension (substance in oil) that increases the flow of diclofenac into the pig skin by 3.8 times.Since nanoparticles have larger sizes than micron particles, their solubility and penetration are better and they have a greater effect on the skin. While nanosprays can be used on the mucosal layer, local effects can also be benefited by converting nanoformulations into ointments or creams [55].

Novavax produces liposomal nanoparticle cosmetic products from micellar estradiol under the brand name Estrasorb for menopause treatment. Diclofenac diethylamine drug lipid nanoparticles were placed in a transmucosal patch to release diclofenac into the tooth after surgery. Gold nanoparticle ointment with ribonucleic acid adduct is used to treat skin cancer,where ribonucleic acid.

Eyes

Insoluble drugs are made into nanoparticle ointments or suspensions for intraocular use. The advantage is a long working time and good performance, but the disadvantage is that most drugs have limited solubility in tears, thus limiting the concentration of the drug at the desired location. Nanoparticle can convert into slaw release formulation so it can use for long period and it also reduces the drug loss in lachrymal fluid. Like ibuprofen nanosuspension nanoparticles are use as safe drug formulation for 24 hr. usage [56].

Hydrogel, Dendrimers and polymeric nanoparticle are also used in eye for various diseases. Mucoadhesive nanoparticle loaded with drug is used into contact lenses which can improve patient compliance and increase the bioavailability. Example of this is lenses loaded with timolol drug nanoparticle are given better bioavailability compare to simple eye drops in glaucoma disease and it also need law dose compare to eye drop. In cornea the eye drop is also used but they have disadvantage of drainage and have law enetrationaffinity so nanoparticles are developed which have Mucoadhesive force so give higher effect than eye drops.

PLGA nanoparticle coated by eudragit surfactant gives good effect into eye of mice compare to non-coated particle of PLGA. Liposome is one of nanomedicine which can be used. Samolin ‘et al’ developed the idoxuridine liposome which improve the penetration of drug into cornea with compare to simple solution and used into herpes simplex keratitisdisease. Aclon Pharma alsonanoparticle of Brinzolamide which is use as suspension for Glaucoma disease and have Trade name is Azopt.

Parenteral

0.1µm to 0.3 µm size nanoparticle are used to increase the retention and penetration of drug into tumor. Some drugs which are use into cancer like mycoepoxydine are available in market as IV formulation. For reduce the opsonin attack nanoparticle are coated with other exicipients soitcan give long time effect into tumor. Example is PEG coated nanocrystal; it gives long time circulation into blood compare to other coated nanoparticles. By altering the surface of nanoparticle, it can be used in severe disease like HIV and tuberculosis by altering the protein of plasma. 1, 3-dicyclohexylurea is use to control blood pressure and available as infusion apply as IV.The Enzon company producing drug for fungal nfection with trade name abelcet is containing liposomal nanoparticle of drug amphotericin B given as IV. The Another example is the liposomal IRIV vaccine produced by Berner Biotech as an IM formulation for hepatitis A under the trade name Epaxal. Aprepitant drug granules, trade name Sustenna, manufactured by Johnson & Johnson, are used as intramuscular injections and have an appetite stimulating effect. br Samyang Company produces IV polymer nanoparticle formulations of Methoxy-PEG-poly (D, L-lactide), a drug used to treat metastatic breast cancer, under the trade name Genexol-PM. Another example is the albumin-bound paclitaxel nanoparticle formulation as an IV formulation for metastatic cancer, marketed under the trade name Abraxane and manufactured by Abraxis Bioscience Company. The drug produced by Skyepharma is called cytarabine liposome nanoparticles under the trade name Depocyt and is used in the intrathecal treatment of malignant lymphomatous meningitis [57]. Palmitate is used as an IV preparation to treat eye infections and cataracts and is manufactured by Aclon Pharma under the trade name llevro. Pharmaceutical company Janssen has also developed an intramuscular acetate called Sustenna to treat conditions such as schizophrenia.

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Oral

The first choice of patients is the oral route due to issues such as safety and cost. Nanoparticles are used orally in the form of nanosuspensions, capsules, or direct compression tablets or other tablets. For the drug to work well, we need to focus on the drug's ability to dissolve and then focus on the drug's ability to be absorbed by the intestinal fluid and therefore absorbed into the vessels. medicine is needed. In oral administration, pH of the digestive tract, drug solubility, drug dosage, food interactions, etc. Many important factors such as were observed. [57]. Nanoparticles are intended for oral administration, thus increasing patient compliance with injections. These machines are very useful for patients who take medication every day, hence cholesterol problems, diabetes, etc. Conditions may be better treated without injections. The antiemetic drug is called aprepitant and is manufactured for oral use by the Elan Company under the trade name emend. The company also produces oral preparations of fenofibrate, used as a hypolipidemic drug, under the trade name Tricor. Wyeth Pharmaceuticals produces the anti-viral drug sirolimus, called Rapamune, as an oral formulation of nanoparticles. Some studies have also shown that oral administration of insulin in nanoparticle form is as effective as parenteral administration. Some nanoparticles are used as carriers to carry proteins, hormones, and peptides throughout the body. For example, Apollo has developed nanoparticles called TNF blockers, which belong to a class of protein-based drugs and vaccines that can be used as oral insulin and anti-inflammatory drugs.

There are some nanoparticles on the market for various purposes, such as griseofulvin tablets made from griseofulvin and PEG and used to treat fungal infections under the trade name Gris-PEG. Schwarz Pharma also produce nanoparticle of verapamil HCL which is given as capsule under Trade name of Verelan PM and use to treat arrhythmia. Several research are also in pipeline which is based on subject of chemotherapy and for deliver the medicine which is use in cancer to directly in targeted part.

Subcutaneous

Subcutation means administered drug under the layer of skin. This process is use when intravein usage of drug is not possible or costly. Drug is given in fatty tissue which is located under the skin. The common sites are thing, arm and abdomen. Amgen Company producing nanoparticle use as SC formulation by using PEG with Granulocyte Colony Stimulating Factor under trade name of Neulasta used in chemotherapy of neutropenic cancer. TEVA Pharmaceutics Company also produce SC polymeric nanoparticle for multiple sclerosis disease under trade name of Copaxone which contained L-Glitamic acid, L-tyrosine copolymer, L-alanine, L-lysine. PEG-Hepatocyte Growth Factor combination also in market for disease acromegaly produced by Pfizer Company under trade name of Somavert which is use SC polymeric nanoparticle form [58]. Bioengineering and Nanotechnology institute developed the Nanohydro gel of drug herceptin which is injected under skin layer and give release of drug till a week and decrease the size of tumor into mice.Nanoparticles are also use as adjuvant to increase the immune response into vaccine preparation. Subcutaneous route is preferred for lymphatic drug delivery also so particle which have size less than 1 micrometer are use directly.

The example of this is PMMA nanoparticle which is used as adjuvant in HIV 2 [59]

Nanoparticles for gene delivery:

Polynucleotide vaccines work by delivering genes encoding relevant antigens to host cells where they are expressed, producing the antigenic protein within the vicinity of professional antigen presenting cells to initiate immune response. Such vaccines produce both humoral and cellmediated immunity because intracellular production of protein, as opposed to extracellular deposition, stimulatesboth arms of the immune system.[60] The key ingredient of polynucleotide vaccines, DNA, can be produced cheaply and has much better storage and handling properties than the ingredients of the majority of proteinbased vaccines. Nanoparticles loaded with plasmid DNA could also serve as an efficient sustained release gene delivery system due to their rapid escape from the degradative endo-lysosomal compartment to the cytoplasmic compartment. This gene delivery strategy could be applied to facilitate bone healing by using PLGA nanoparticles containing therapeutic genes such as bone morphogenic proteins.

Nanoparticles for drug delivery into the brain:

The blood-brain barrier (BBB) is the most important factor limiting the development of new drugs for the central nervous system. The BBB is characterized by relatively impermeable endothelial cells with tight junctions, enzymatic

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activity and active efflux transport systems. It effectively prevents the passage of water-soluble molecules from the blood circulation into the CNS, and can also reduce the brain concentration of lipid-soluble molecules by the function of enzymes or efflux pumps.[61] Consequently, the BBB only permits selective transport of molecules that are essential for brain function.

Nanoparticles in Food:

Amorphous silica nanoparticles are used as anti-bacterial agents to preserve the properties of powdered products such as instant soups and thickening pastes. The approved form of amorphous silica is called food additive E551. It is also used in cosmetics, especially sunscreens. Sunscreens contain titanium dioxide and zinc oxide nanoparticles because they are colorless and reflect/emit UV rays better than bulk products. The small size of nanoparticles gives them the effect of making them transparent, thus increasing consumer satisfaction and thus improving the protection of human skin from UV damage. Improving the appearance of materials is still an important application of nanoparticles, as it was in the past. An important example is automotive paint, which has many layers. The time from detection to product is often long. For example, more than 20 years passed from the first report on the use of titanium dioxide nanoparticles in dye-sensitized solar cells to the production of commercial products.

IV. CONCLUSION

In summary, continuing to develop and evaluate nanoparticles represents a promising frontier in many fields, from medicine to information science. These microstructures provide unprecedented opportunities for drug delivery, analysis and more. As scientists continue to advance their understanding and technology, nanoparticle applications are expected to transform the industry by providing better solutions and adaptations. The combination of innovation and rigorous analysis paves the way for a future in which nanoparticles will play a key role in increasing efficiency and accuracy in a variety of applications.

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