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Formulation, Development and Optimization of Polymeric Nanoparticles containing Momentasone Furoate and Hydroquinone for Hyperpigmentation and Psoriasis

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Abstract

This work aimed to create and optimize gel systems and formulations of polymeric nanoparticles (PNP) for the regulated and sustained delivery of mometasone furoate (MTF) and hydroquinone (HYQ). The solvent evaporation process was used to create the nanoparticle formulations, with polyvinyl alcohol (PVA) acting as a stabilizer and Eudragit RS 100 acting as the encapsulating polymer. The polymer content, surfactant concentration, and stirring time were among the formulation parameters that were optimized using Design of Experiment (DOE) software (Design Expert Version 12.0.1.0). Particle size, stability, and entrapment efficiency (EE) were assessed for a total of 12 formulations with different characteristics. When Mometasone furoate and Hydroquinone were combined, the maximum UV absorption (λmax) was detected at 274.0 nm. Because of their same λmax, both medications can be estimated simultaneously using UV spectrophotometry, guaranteeing precise and effective analysis in combination formulations. To assess the linearity of the suggested UV spectrophotometric approach for simultaneous determination of mometasone furoate and hydroquinone, a calibration curve analysis was performed using the least squares linear regression method. The study showed that NG1 nanoparticles and the related gel formulation provide a viable method for transdermal delivery of mometasone furoate and hydroquinone, with favorable drug penetration characteristics, good stability, and prolonged drug release.

Key words : Polymeric Nanoparticles (PNP), Mometasone Furoate–Hydroquinone Combination, Solvent Evaporation Technique, Transdermal Drug Delivery, Entrapment Efficiency and Sustained Release.

Nanoparticles :

Nanoparticles offer better benefits over other carrier systems. Nanoparticles' submicron size, which permits extravasations and occlusion of terminal blood arteries, is benefit that makes them an effective delivery mechanism. Furthermore, these nanoparticles can frequently encapsulate, distribute, or dissolve a significant number of therapeutic agents; the preparation method will ascertain the specific qualities and release features of the entrapped substance. Despite this adaptability, a number of documented technical drawbacks, such as low stability and reproducibility. Moreover mechanisms for delivering drugs designed as liposomes not suitable for regulated drug release because of leakage of drug entrapped inside liposomes. However, polymeric nanoparticles have certain advantages, like enhancing the consistency of medications or proteins and having practical controlled release capabilities[1].

Nanoparticles (NP) are natural, incidental or manufactured material containing particles, where 50% or more of particles fall within the valu of 1–100 nm. Two major categories could apply to describe nanoparticles: (i) inorganic and (ii) organic. Semi-conductor nanoparticles (like ZnO, ZnS, and CdS), magnetic nanoparticles (like Co, Fe, and Ni), and metallic nanoparticles (like Au, Ag, Cu, and Al) are instances of inorganic nanoparticles, whereas carbon nanoparticles or fullerenes, Carbon nanotubes and quantum dots serve as illustrations of organic nanoparticles. Gold and Ag Nanoparticles of noble metals furnish superior characteristics

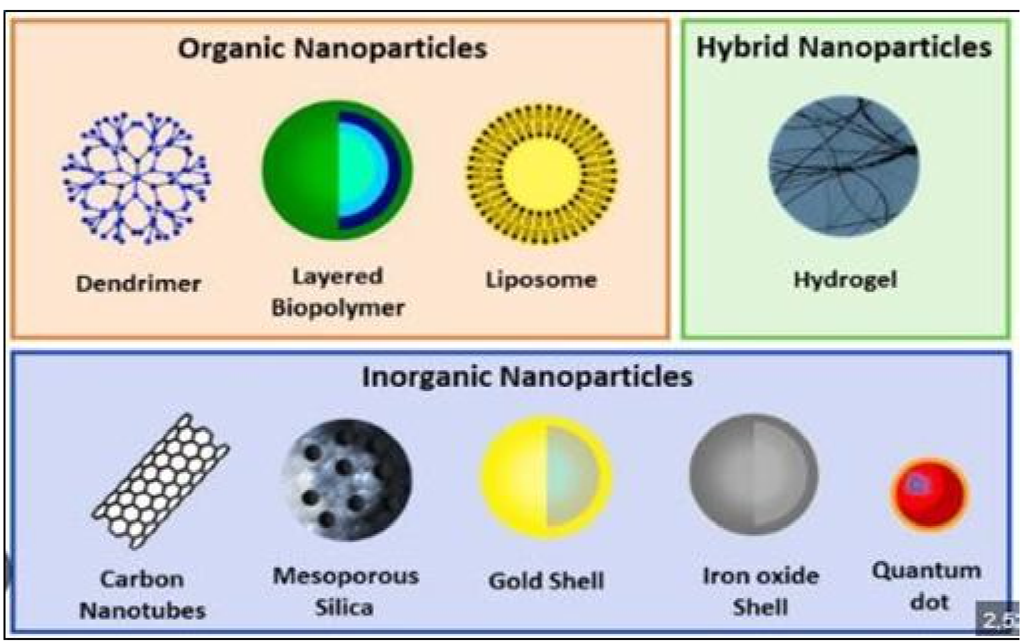

Figure 1. Structure of different Types of Nanoparticle

with useful flexibility[2].

Silver nanoparticle history :

Silver has been utilized for numerous purposes. For ages, drinking water has been fumigated by storing it within silver vessels because of the antibacterial qualities of silver. Ancient Egypt and Rome used nanosilver, according to anecdotal evidence. To help to promote wound healing, the Macedonians employed silver plates, and Hippocrates applied silver to ulcers. Paracelsus utilized silver orally in 1520 and applied a caustic made regarding silver nitrate to wounds; these practices are still use today. In a purgative, a counterirritant, and a remedy for brain illnesses, Angelo Sala used internal silver nitrate in 1614 [3].

Silver Nanoparticles :

Due of their special qualities, both chemical and physical, AgNPs, or silver nanoparticles are being utilized more and more in an assortment of industries, including consumer, industrial, food, medical, and health care. These include biological qualities, thermal, electrical, and optical characteristics, in addition to high electrical conductivity. Their unique characteristics have caused their use in numerous uses, including as antibacterial agents, consumer goods, coatings for medical devices, optical sensors, and cosmetics; in the pharmaceutical and food sector; in diagnostics; in orthopedics; drug delivery; as anti-cancer substances; and, lastly, in augmenting the tumor-killing properties of anticancer drugs[4].

Properties and Structure of Ag NPs :

As Ag NPs possess a multitude of applications, it is essential to research their properties, which are greatly impacted by the dimensions and form of NPs. Researchers have found several antibacterial materials since human infections with Molds, yeast, viruses, and bacteria represent several of the most prevalent microorganisms. Due of their remarkable optical, physicochemical, antibacterial, electronic and magnetic propertiesin along with their huge surface atoms and surface area, MNPs are the subject of in-depth investigation. Ag NPs have incredibly strong antibacterial qualities among MNPs. With NPs affixed to the membrane of the cell and inside the bacterium, silver offers a sizable surface area for bacterial interactions[5].

The production of Ag nanoparticles in glass and ceramic has different electrical conductivities because their sizes range between 4 and 12 nm. An investigation into the Ag NP film's resistance of direct electricity between 80 and 300 K revealed a linear relationship between surface resistivity and temperature from 120–300 K. also looked into the linear relationship between Ag NP size and Debye temperature. Ag NPs melt between 4 and 50 nm, and their thermal characteristics are studied at 3–6 nm diameters[6].

Properties of silver nanoparticles :

Reflecting typical NP traits, silver NPs exhibit distinct chemical and physical characteristics due to their diminutive size and high surface-area-to-volume ratio. Their dimensions, composition, coating, surface chemistry, and aggregation all play a major role in these qualities, which include optical properties, substantial electrical and thermal

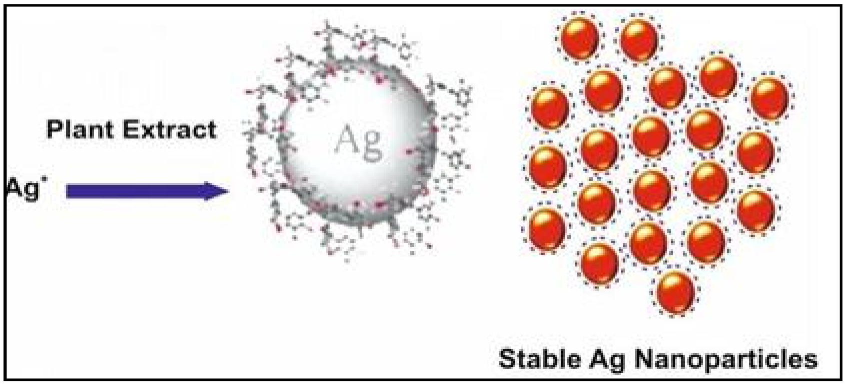

Figure 2. Silver nanoparticles (Selvaraj *et al*., 2019)

conductivity, along with antibacterial activities[7].

Size :

The Silver nanoparticles' traits that are chemical, physical, and biological are largely according to their dimensions. It creates opportunities in several disciplines and possesses a major effect on their conductivity, optical, and surface-area-to-volume ratio. Their 20 size enhances their responsiveness and Capacity to communicate with additional molecules, whether on surfaces or in solutions. Because Silver nanoparticles have size-dependent surface characteristics, their enhanced reactivity is mostly used in detecting and catalysis investigations[8].

Shape :

Star-shaped, wire-like, cubic, triangular, spherical, and rod-shaped Ag nanoparticles have the capacity to all be created. The shape of silver nanoparticles affects different properties, including electrical, both catalytic and optical. As an illustration, the silver nanoparticles' structure and size greatly enhance how they engage in relationships in relation to biological systems. They are therefore appropriate for use within the area of biomedicine, particularly in coatings Key techniques for delivering drugs[9].

Surface Charge :

Among the essential features of nanoparticles that have a substantial impact regarding their steadiness and molecular interactions is surface charge. Consequently, It is thought because in applications related to biomedicine, additionally, the charge at the surface is essential, where altered surface charges enhance treatment efficacy, targeting, and absorption. Additionally, surface functionalization Moreover, pH adjustments is applicable to control surface charges. In general, these charges affect how they interact Having additional surfaces or biomolecules in addition to how they disperse in matrices or solvents[10].

Melting point and electrical conductivity :

When Silver, in contrast possesses a few of the best atomic structures as opposed to metals, including free electrons give it conductivity of electricity at standard temperature. The topmost shell of silver contains a single electron of valence like those of other metals, is loosely attached toward the nucleus. Consequently, it permits a conductive channel by enabling the unrestricted movement of electrons across the metals. To put it another way, A field of electricity will cause these electrons to travel freely limiting the resistance to the electrical current. Zeta potential is an essential measure of stability because it demonstrates strong particle-to-particle electrostatic repulsion that inhibits agglomeration at higher values (both positive and negative values)[11].

Thermal Conductivity :

It is widely recognized that silver has an extraordinary heat conductivity of about 429 W/mK in a room temperature setting. This characteristic makes it easy for silver to transfer heat. Silver nanoparticles' elevated ratio of surface to volume that doesn't change even on a nanoscale, has remarkable heat conductivity. The efficient transport of heat by electrons and phonons, with the help of the particles' small size, is in charge of reason for the increased heat conductivity. This lessens resistance and dispersion at the edges of the grains[12].

Synthesis of Silver Nanoparticle :

Two methods are commonly employed to produce nanoparticles of silver. (i) The "top to bottom" method (ii) the bottom to top method. Using "top-down" approach include grinding bulk metals mechanically and then stabilizing them with colloidal protective agents. In the "bottom-to-top" approach, biological and chemical strategies are used to make nanoparticles methods by atoms self-assembling into fresh nuclei that develop into nanosize particles. Decrease of chemicals and electrochemical techniques, and sono-decomposition represent instances of "bottom-up" approaches. In the top-to-bottom method, appropriate bulk material is reduced in size utilizing variety of methods, including sputtering, grinding, milling, thermal/laser ablation, etc.

Biological Methods :

Conventional methods of NP production are costly, dangerous, and bad for the environment. Green routes—natural source moreover, their by products that are applicable to synthesis NPs—have been investigated by researchers as a way around these problems. Using plants moreover, to their extracts, along with templates like membranes, diatoms, and viruses, is another straegy.

- *Production in bacteria :*

A recent investigation used the supernatants of culture of multiple bacteria to lower water Ag+ ions and produce silver nanoparticles. This approach was demonstrated to be quick; in about five minutes, silver nanoparticles were produced through the interplay between thecell filtrate with ions of silver[13].

- *Fungi based synthesis :*

Numerous fungi are reportedly engaged when creating silver nanoparticles. It's been located that fungi may quickly manufacture silver nanoparticles. The fungus that generates silver nanoparticles has been thoroughly investigated by numerous researchers. One study claims that extracellular biosynthesis produces round silver nanoparticles from Fusarium solani and silver nitrate[14].

➢ *Production in algae :*

This method's low cost and ease of use make it is an excellent substitute for physical and chemical procedures for producing nanoparticles Ecological friendliness. Additionally, the capacity of algae to absorb metals is high. Certain reactions have demonstrated themselves to be set off by biological causes, including sea algae. For practical and contemporary biosynthesis programs, this capability is essential. According to a study using an algae extract, the conversion a shift in color turning turning from yellow to brown indicates the converting silver nanoparticles to silver ions. The silver nanoparticles' rich brown hue after 32 hours was demonstrated to be directly proportional to the duration of the incubation time[15].

Production in yeast :

According to reports, silver particles have potential use. For produced by yeasts. Furthermore, yeast-based techniques in order to produce silver nanoparticles, both economical and environmentally beneficial. A Saccharomyces cerevisiae-based research was conducted in this context. Ag+ ions are added regarding the yeast culture, it was discovered that the colorless sample gradually turned reddish-brown as the incubation period increased. Additionally, the solution's color turned a vibrant reddish-brown.

Chemical methods : Most widely used method to create Ag NPs is a chemical technique because of its great efficacy and affordability. Chemical reduction (P) is the most commonly used of this utilized technique. Ag NPs were initially created using the citrate approach, which was a useful technique for seeing how they behaved. However, because of its superior reducing capacity over the citrate approach, borohydride reduction provides specific control of Ag NPs' dimensions and form

➢ *Chemical reduction :*

Silver nanoparticles are most commonly created through reduction of chemicals, which employs Inorganic and organic reducing agents. The reducing agents that are frequently utilized to lower silver ions (Ag+) in aqueous or non-aqueous solutions include sodium citrate, ascorbate, sodium borohydride (NaBH4), elemental hydrogen, polyol process, Tollens reagent, N, N-dimethylformamide (DMF), and copolymers of poly (ethylene glycol)-block. These agents that reduce generate metallic silver (Ag0) after reducing Ag+, which subsequently clumps together to form oligomeric clusters

Methods of Preparation of Polymeric Nanoparticles :

Nanoparticles can be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers. The selection of matrix materials is dependent on many factors like: Nanoparticles can be prepared by following methods:

Pre-formulation study of Mometasone furoate and Hydroquinone :

Organoleptic evaluation :