A PERSPECTIVE REVIEW ON THE INFLUENCE OF NANOPARTICLES AS TOPICAL FORMULATION IN SKIN ALLERGY

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Abstract

Food allergies are becoming increasingly prevalent, leading to potentially fatal reactions. Allergic Rhinitis is a significant atopic disorder affecting all age groups, compromising quality of life. Treatment options include conventional methods, advanced technologies like immunotherapy, surgical methods, and nanoparticles. Current allergy immunotherapy has limitations due to potential anaphylaxis and local side effects.

The nanoparticle approach is a promising and safe option. Nanoparticle-based therapies can address food allergy by disrupting disease-driving immune mechanisms and promoting sustained tolerogenic immune pathways. These therapies involve regulatory T cells, TH1 responses, and suppression of allergic effector cells, leading to beneficial outcomes.

Nanotechnology-based approaches show potential for improving transdermal penetration and enhancing the effectiveness in penetration. Nanoparticles are designed to control particle size, surface properties, and release pharmacologically active agents for site-specific drug action.

Liposomes offer advantages like protection, targeting, and reducing toxicity, but have limitations like low encapsulation efficiency and rapid drug leakage. Polymeric nanoparticles offer specific advantages.

In this review, the ideal properties of polymeric nanoparticles for topical drug delivery is discussed in brief. Special mentions about the recent trends and applications of nanoparticles are also discussed. Further conclusive work needs to be done in treatment of allergic condition using polymeric nanoparticles as it makes its way into the mainstream clinical practice.

Keywords: *Allergy, Nanoparticles (Nps), Therapy. Topical delivery.*

1. INTRODUCTION

Systemic disorders induced by a weakened immune system include allergic rhinitis (AR), allergic asthma (AAS), atopic dermatitis (AD), food allergy (FA), and eczema. Their pathogenesis is complex and involves factors like maternal-fetal environment, living environment, genetics, epigenetics, and immune status. With advancements in immunology, molecular biology, and biotechnology, new drugs have been developed to treat these diseases[1].

The constantly rising incidence rates of these disorders, accompanied by high recurrence rates, are gaining increasing attention.[1] Patients suffer greatly as a result of the increased prevalence of allergic illnesses. AR and AAS are believed to affect about 500 million and 300 million people worldwide, respectively.[2] as the number of cases grows. The mortality rates for AAS in women and men are 90 and 170 per million people, respectively. Low- and middle-income nations account for around 96% of asthma deaths.[3] FA presently affects 1-10% of the overall population, according to current estimates.[4]

The review focuses on NMs designed for topical administration to the skin for skin protection and healing. It examines the penetration of NPs through the skin as well as the factors that influence this process. Furthermore, the current review highlights the experimental models employed for *in vivo* and *in vitro* skin penetration research, as well as the potential environmental risks connected with NM synthesis.

2. THE STRUCTURE OF THE SKIN.

The epidermis and dermis of the skin are separated by a layer of subcutaneous fat. Basale to superficial stratum corneum (SC) via the stratum spinosum and stratum granulosum (SG). The SC is depicted as a "brick and mortar" construction. The epidermis has four histologically different layers, beginning with the deepest stratum.[5]

Corneocytes are immersed in an intercellular lipid matrix. Corneocytes are made up of insoluble keratins that are encased in cross-linked proteins and are stacked in parallel, overlapping multicellular stacks perpendicular to the skin surface.[6] The inter-corneocyte gap is filled with lipids, which are typically in the crystalline phase.[7] During differentiation, the majority of SC lipids are synthesized in the viable epidermis.[8]

Lamellar bodies discharge them into the intercellular gaps at the SG-SC interface. Ceramides, fatty acids, and cholesterol are the most important SC lipids. Ceramides are classified into eight groups. Multiple bilayers of lipids with a periodicity of around 13 nm are formed. Unlike practically all other membranes in the body, the SC lacks phospholipids[9] This "brick and mortar" structure is now recognized as the site of the skin's superior permeability barrier, and the SC is the rate-limiting barrier to the transcutaneous penetration and absorption of most substances after topical treatment.[10]

There are three probable molecular penetration mechanisms across the SC: (i) intercellular via lipids between corneocytes; (ii) transcellular via corneocytes and surrounding lipids; and (iii) appendageal via follicles and sweat ducts.[11]

The primary pathway is widely assumed to be intercellular. The main route is thought to be intercellular, although the appendageal pathway, particularly that enclosing the hair follicle and related sebaceous gland, is also crucial in some cases.[12] Some permeation enhancers (e.g., oleic acid) and vesicular carriers are hypothesized to disrupt the SC lipids and allow for easier transit over the skin.[13] The viable epidermis lies beneath the SC and has a thickness of 100 m, 4 differing from as little as 50 m to roughly 800 m on the load-bearing palms and soles of the feet.[6]

Keratinocytes are the primary cells of the viable epidermis, although there are also melanocytes, Langerhans cells, migratory macrophages, and lymphocytes.[14] The epidermis, on the other hand, lacks blood vessels.

The dermis, a 3-5mm thick layer of human skin, is rich in blood vessels, lymphatic vessels, and nerve endings. It serves as a minimal barrier to drug transport, with hair follicles and sebaceous glands playing a role. The subcutaneous fat layer bridges the dermis to underlying tissue.

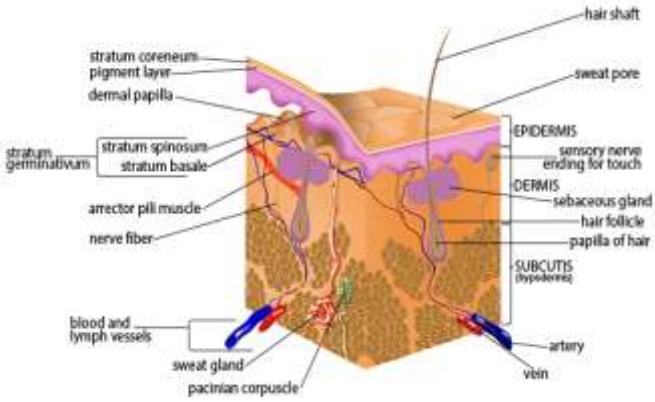

Fig no 1: Structure of skin.

3. NANOPARTICLES

Nanoparticles (NPs) are materials with dimensions smaller than 100 nm and diverse shapes, such as spheres, rods, dendritic shapes, and so on. The European Union (EU) Commission has agreed to this definition.[14,15] The Environmental Protection Agency (EPA) emphasizes, in its judgement, the unique features of NPs that distinguish them from identical chemical substances.[16] In turn, the US Food and Drug Administration (USFDA) specifies definitely that NPs must show dimension-dependent behaviours.[17]

The International Organization for Standardization (ISO) regards the nanoscale size of both the exterior dimension and the inside surface structure as the primary requirement.[18] There are several nanostructures in the human body that are required for regular body function, including as enzymes, proteins, antibodies, or DNA. Human bone, a multidimensional composite of hierarchical inorganic nanohydroxyapatite and organic collagen, is likewise a nanomaterial.[19,20] One of the first synthetic NMs was probably lead(II) sulphide NPs (5 nm) (PbS-NPs), which were used for colouring or the so-called "Egyptian blue," which was a mixture of cuprorivite CaCuSi4O10 and silicon dioxide (SiO2). Michael Faraday published the first scientific article reporting the synthesis of gold NPs (Au-NPs) in 1857.

Carbon nanomaterials, inorganic, organic, and composite-based nanomaterials are the four broad groups of NMs. Nanotubes, fullerenes, quantum dots (QD), metals (silver Ag, gold Au), metal oxides (titanium dioxide TiO2, zinc oxide ZnO, iron (III) oxide Fe2O3, SiO2), and lipophilic NPs are finding increasing use in cosmetics. This is owing to the fact that NPs have a high surface-to-volume ratio.[21]

In addition to their usage as MRI contrast agents, Fe2O3-NPs, like other magnetic nanoparticles (MNPs), can be employed as vehicles in magnetic drug delivery systems (MDDS) when paired with superconductors. MDDS has shown promise in cancer therapy because to the ability to precisely guide MNPs to the necessary region using an external magnetic field. MNPs can not only carry and deliver medications in high concentrations in diseased tissues, but they can also generate heat via the oscillation of their magnetic pulse (44-47 C), allowing for the thermoablation of cancer cells (magnetic hyperthermia).[22]

This review explores nanoparticles (NPs) in dermatological and cosmetic products, their use in treating skin diseases like acne, vitiligo, alopecia, and skin cancer, and their use in cosmetology as anti-aging and UV-protecting agents. It discusses skin penetration, experimental models, and potential environmental threats associated with NP production.

3.1. Compositions of nanoparticles.

3.1.1. Nano capsules

Polymeric nano capsules are submicron colloidal particles with a polymeric shell surrounding a center. The core of nano capsules is often an organic (oil) solvent. Poly-(-caprolactone) (PCL) is one of the most commonly utilized polymers for the nanocapsule shell[35]. Polymers include poly-L-lactide, poly-(glycolic acid), poly-(lactide-co-glycolide), poly-(butylcyanoacrylates), poly-(ethylcyanoacrylates), poly-(alkylene adipate), polyvinyl acetate, cellulose acetate phthalate, poly-(ε-caprolactone)-block-poly-(ethylene glycol), poly-(methyl methacrylate), and polystyrene are also used[23].

3.1.2. Nanosphere.

Nanospheres are made up of a homogeneous polymer matrix with the medicine or active component scattered throughout. In general, processes used to prepare nanospheres can also be employed to create nanospheres, such as interfacial polymerization and emulsion formation.Solvent evaporation and polymerization.[24]

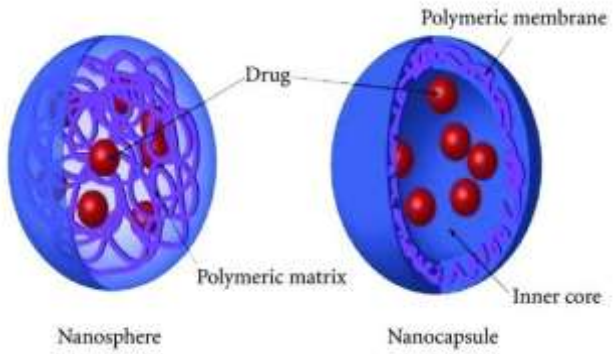

Fig no 2: Major types of Nanoparticles.

4. METHODS FOR IMPROVING NP PENETRATION THROUGH THE SKIN.

NPs must pass through the superficial layer (SC) barrier for effective therapeutic effects, but the lipid layer hinders this. Technologies like microneedles, cavitation ultrasound, and electroporation are used.

4.1. Microneedles

Therapeutic advancements in molecular biology and biotechnology have led to the development of nanoparticle carrier systems to improve targeting, stability, and toxicity profiles. Effective delivery of nanoparticles across the skin barrier is crucial for their therapeutic benefits and health risks. Recent developments, such as the microneedle array, have the potential to enhance transdermal delivery of therapeutics. Surface charge and pore size significantly impact nanoparticle formulation permeation, but maximum dimensions must be limited for pain and safety reasons. Further research is needed to characterize physicochemical and biological barriers influencing permeation properties and distribution of nanoparticle therapeutics.[25]

4.2. Electroporation

Electroporation, a technique extensively used to assist cell transfection, uses applied electric fields to break down the dielectric layer over cell membranes and create many temporary pores through which biomolecules and nanoparticles can enter. Electroporation is a popular method for transporting foreign or endogenous molecules across permeable cell membranes in a matter of microseconds to milliseconds. By producing persistent cell disruption in both prokaryotic and eukaryotic cells, irreversible electroporation has been utilised to extract cellular components such as lipids and genetic materials. The study involved electroporation of a mixture of media and target sample, with the Bio-Rad Gene Pulser II apparatus delivering 6 electric pulses. The most effective media was determined by mixing with Microcystis culture and subjecting to varying voltages. The impact of field strength on cell lysis was investigated using medium #5, with tests performed in duplicate.[26]

5. METHOD OF PREPARATION

5.1. Solvent evaporation method

Using this procedure, an oil-in-water (o/w) emulsion must first be prepared[27]. leading to nanoospheres production[28,29] First, an organic phase is made up of the active ingredient (such as a medication) dissolved or dispersed in a polar organic solvent in which the polymer is dissolved. Chloroform and dichloromethane have been employed extensively, but more frequently in the past.[30] They have been replaced by ethyl acetate because of their toxicity; as a result, it has a superior toxicological profile and is more appropriate for use in biological applications. It has also been common practice to prepare an aqueous phase that contains a surfactant (such as polyvinyl acetate, or PVA).[31,32]After a surfactant is used to emulsify the organic solution in the aqueous phase, it is usually treated using ultrasonication or high-speed homogenization to produce a dispersion of nanodroplets.[33] The polymer solvent evaporates and diffuses through the continuous phase of the emulsion to generate a suspension of nanoparticles. The solvent is evaporated either slowly at low pressure (as occurs when employing, for example, dichloromethane and chloroform) or continuously by magnetic stirring at normal temperature (in the case of more polar solvents). The

formed nanoparticles can be collected and cleaned by centrifugation once the solvent has evaporated. For long-term preservation, freeze-drying can then be done. It is possible to create nanospheres with this technique.

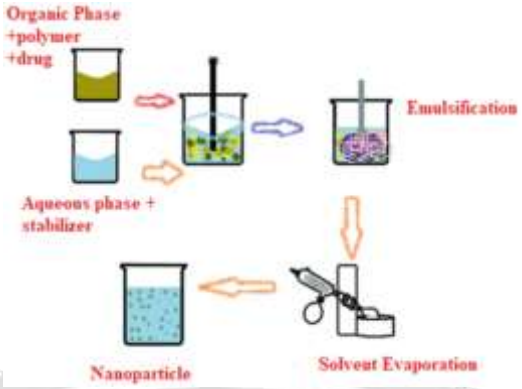

Fig no 3: Solvent evaporation method

5.2. Nanoprecipitation method

Two miscible solvents are needed for this technique, which is also known as the solvent displacement method. An organic solvent that is miscible, like acetone or acetonitrile, dissolves a polymer to form the internal phase.[34] Evaporation is an easy way to get rid of them because they are immiscible in water. This method's basic idea is the interfacial deposition of a polymer following the organic solvent's displacement from a lipophilic solution into the aqueous phase. After dissolving the polymer in an intermediately polar water-miscible solvent, the solution is gradually added—dropwise or at a regulated addition rate—to an aqueous solution while being stirred. The polymer solution diffuses quickly into the aqueous phase, causing the nanoparticles to form instantly in an effort to evade the water molecules.[35] The polymer precipitates as nanocapsules or nanospheres as the solvent diffuses out of the nanodroplets. The aqueous phase is usually supplemented with the organic phase; however, the procedure can be changed without affecting the creation of nanoparticles.[36] While their presence is not necessary to assure the creation of nanoparticles, surfactants can typically be added to the process to maintain the stability of the colloidal suspension. The resulting nanoparticles are usually better than those made by the emulsification solvent evaporation process because they have a well-defined size and a restricted size distribution.[37] A common technique for creating polymeric NPs with diameters of about 170 nm is nanoprecipitation.[38] However, it also makes it possible to obtain nanospheres or nanocapsules. When the active ingredient is dissolved or distributed throughout the polymeric solution, nanospheres are produced. Before the internal phase of the emulsion is dispersed in the exterior phase, the medication is first dissolved in an oil and then the oil is emulsified in the organic polymeric selation to create nanocapsules.[35]

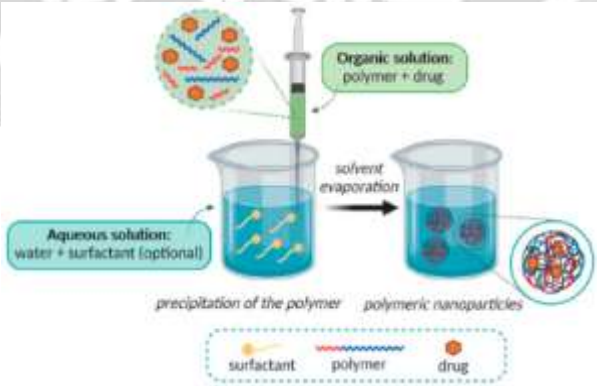

Fig no 4: Nanoprecipitation method

5.3. Solvent diffusion method

With this technique, an aqueous solution containing a surfactant and a somewhat water-miscible solvent containing a polymer and drug combine to generate an o/w emulsion.[39] To guarantee an initial thermodynamic equilibrium of both phases at room temperature, the internal phase of this emulsion is composed of a somewhat hydro-miscible

organic solvent, such as benzyl alcohol or ethyl acetate, which has been previously saturated with water.[40] The process involves dilution with water, causing solvent diffusion, resulting in the formation of colloidal particles. This method is commonly used to produce nanospheres or nanocapsules, with the latter stage eliminated by evaporation or filtration. This method is commonly used for polymeric NPs production, despite the risk of hydrophilic drug diffusion.[41]

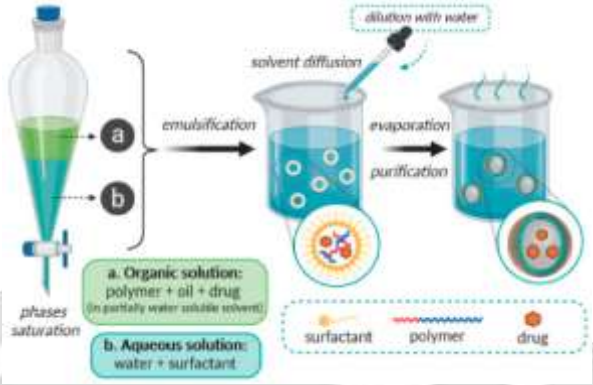

Fig no 5: Solvent diffusion method

5.4. Reverse salting out method

One way to think about the emulsification/solvent diffusion method as a variant of the emulsification/reverse salting-out method is as follows. The salting-out process, which may lead to the production of nanospheres, is the basis for separating a hydro-miscible solvent from an aqueous solution.[42] The primary distinction is in the makeup of the o/w emulsion, which is made from a water-miscible polymer solvent like ethanol or acetone. The aqueous phase comprises a gel, a colloidal stabilizer, and a salting-out agent.[43] Electrolytes, such as magnesium chloride (MgCl2), calcium chloride ($CaCl_2$), or magnesium acetate [Mg(CH,COO)2), as well as non-electrolytes, include examples of appropriate salting-out agents. Sucrose[40] Saturating the aqueous phase reduces the miscibility of acetone and water and permits the creation of a flow emulsion between the other miscible phases.[44] At room temperature, the o/w emulsion is formed while vigorously stirring. The emulsion is then diluted with a suitable volume of aqueous solution or deionized water to enable the precipitation of the polymer, the diffusion of the organic solvent to the exterior phase, and ultimately the creation of nanospheres. Cross-flow filtering removes the leftover solvent and salting-out agent. Although it makes things easier to do, total miscibility of the organic solvent with water is not necessary.[45] The nanospheres produced with this technique range in size from 170-900 nm. By altering the polymer content of the internal phase volume of the external phase, the average size can be changed to values between 200 and 500 nm.[46]

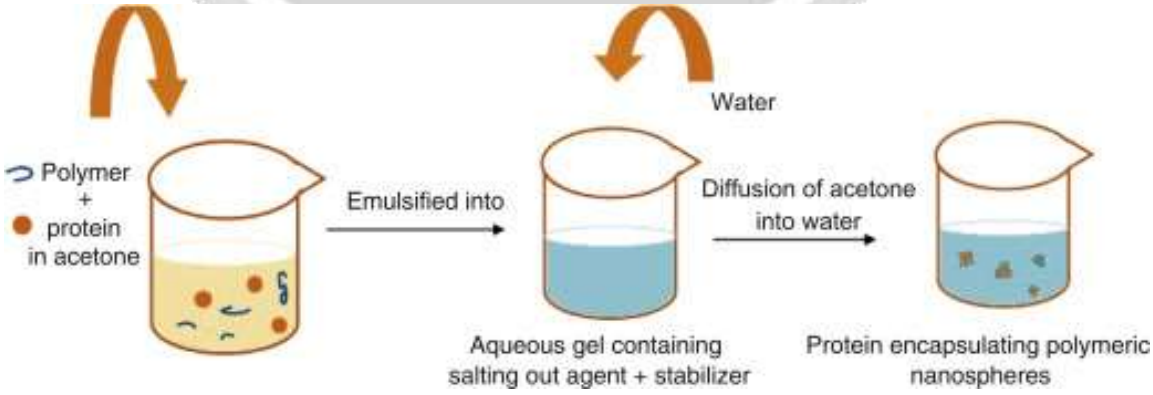

Fig no 6: Reverse salting out method

5.5. Ionotropic gelation method

The foundation of ionotropic gelation is the polyelectrolyte's capacity to cross link to form beads when counterions are present. The ionotropic gelation technique has been widely employed for the encapsulation of drugs and even cells since the usage of alginates, gellan gum, chitosan, and carboxymethyl cellulose. Despite their ability to coat the drug core and act as release rate retardants, natural poly electrolytes contain some anions in their chemical composition. These anions combine with the polyvalent cations to form a meshwork structure, and they mostly bind to the anion blocks to cause gelation. Dropping a drug-loaded polymeric solution into an aqueous solution comprising polyvalent cations yields hydrogel beads.[47]

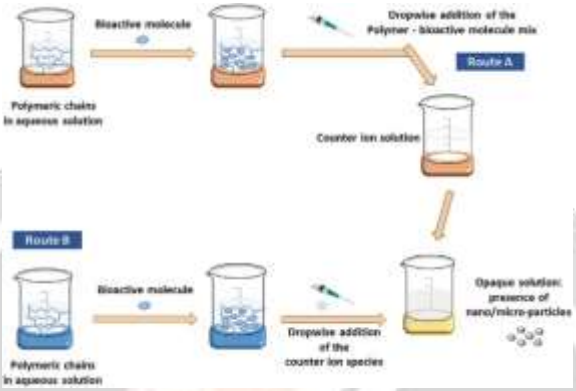

Fig no 7: Ionotropic gelation method

5.6. Interfacial polymerization

This technique includes dispersing a semi polar solvent that is water miscible from a lipophilic solution, and then depositing biodegradable polymers at the o/w interface. Nanocapsules are prepared using this technique. The Marangoni effect explains how the characteristics of polymers can change the physicochemical properties at the interface.[48]

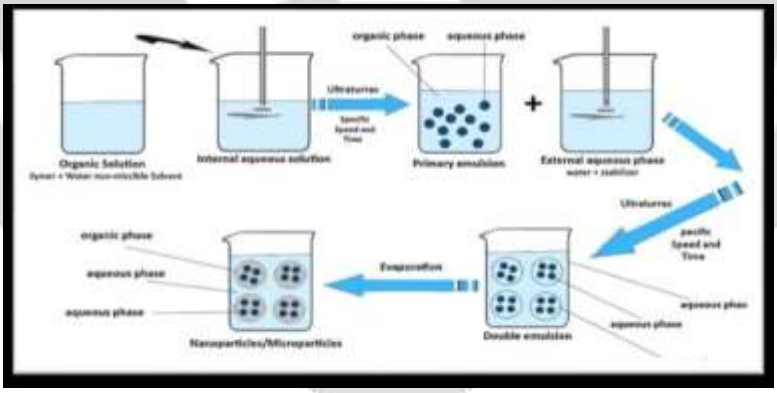

Fig no 8: Interfacial polymerization

5.7. Emulsion Polymerization

This process disperses the monomer in a liquid under agitation into a continuous phase that is immiscible. The reaction of the initiators with the monomer molecules dissolved in the emulsion's continuous phase often starts the polymerization process. Phase separation results from the developing polymer chain becoming insoluble at a given molecular weight. Until then, the chain is soluble.[49]

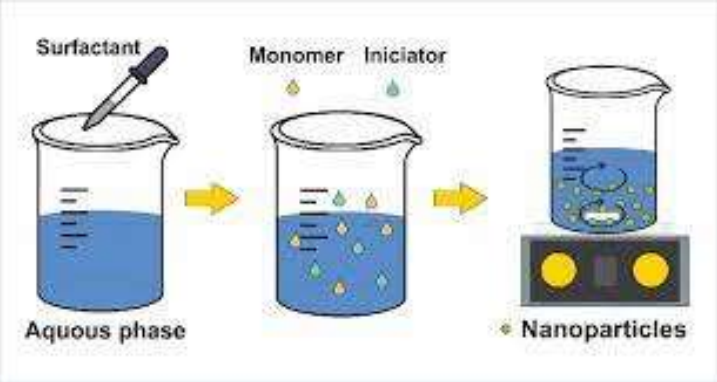

Fig no 9: Emulsion polymerization.

5.8. Desolvation method

A solution of the natural macromolecule and an accompanying active component is made in order to prepare nanoparticles. After that, this system is desolvated by adding a solute that competes with the solvent, like alcohol or sodium sulfate. It is possible to produce colloidal size particles by managing the desolvation process. Pharmaceutically speaking, desolvation-prepared nanoparticles ought to be devoid of potentially harmful contaminants, simple to store and use, and sterile if parenteral administration is recommended. As a result, prior to releasing them for clinical trials, three crucial process parameters are completed. They've been cleaned, dehydrated, and sanitized.[50]

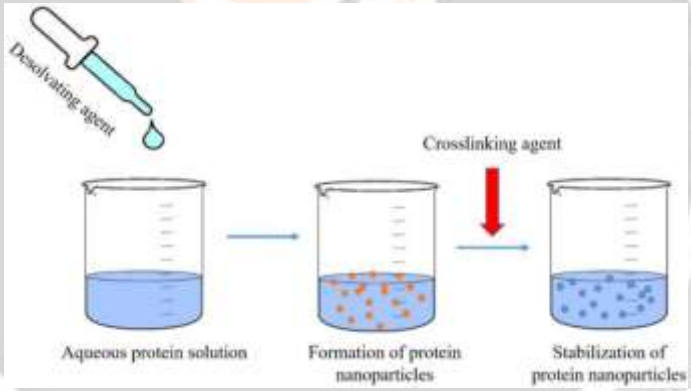

Fig no 10: Desolvation method.

6. SPECIFIC APPLICATION AREAS OF NANOPARTICLES

6.1. Tumor targeting

Nano-carrier systems are colloidal, which makes them more effective than other drug carriers High drug loading capacity Capability of controlling the size and penetration of the carrier Prevention of encapsulated drug's metabolism Long circulating "stealth" nanoparticles, such as PEG-NP, increase the drug's therapeutic index Long circulating nanoparticles can accumulate in tumors due to their long circulation time However, having a long circulating time is not sufficient for nanoparticles Active tumor targeting There are two main methods for active tumor targeting: Direct targeting Covalently coupled nanoparticles are administered together with the drug molecule Pre-targeting In the direct targeting method, drug molecules are not coupled to the ligand The ligand is first administered The therapeutic molecule is then administered After a time lag, the ligand molecules are localized in the tumor[51]

6.2. Nanoparticles for Gene and Vaccine Delivery

There are two types of nucleic acid delivery systems in gene therapy: viral and nonviral. The use of viral vectors is limited due to safety issues. However, nonviral vectors are better than viral vectors. Non-viral nanoparticles are

made from biodegradable and biocompatible polymers that are suitable for gene delivery. Nonviral nanoparticles can rapidly escape the degradative, lysosomal compartment and have a long intracellular retention time. The therapeutic effectiveness of the nanoparticles comes from their ability to protect the therapeutic molecule from lysosomal enzyme degradation. Once the nanoparticles enter the intracellular compartment and escape endo-lyososomal escape, the encapsulated DNA is released at a sustained rate, resulting in sustained gene expression. Nanoparticles containing embedded or adsorbed antigen are effective vaccine antigens and offer sustained release of antigen. They are suitable carriers for oral immunizations to induce systemic or mucosal immunity.[52]

6.3. Oral Delivery of Nanoparticles

The oral bioavailability of therapeutic peptides and proteins is a major concern, and several approaches have been proposed to enhance the oral bioavailability of certain molecules, such as drugs or vaccines. One of these strategies is the delivery of these molecules by polymeric nano-structures. These nano-structures have special properties, such as their stability in the gastrointestinal tract, their ability to encapsulate drugs, their ability to modulate drug release properties, and their behavior under physiological conditions, making them suitable for the oral delivery of a variety of molecules. Due to their submicron sizes and large surface area, these nano-structures are better suited for oral delivery than larger carriers. By encapsulating these proteins and peptides, they can be protected from harsh conditions in the digestive tract.[53]

6.4. Nanoparticles for Brain Targeting

The human brain is separated from blood circulation by the efficient blood brain barrier (BBB), which hinders the transport of water-soluble and lipid-soluble molecules. This poses a major problem for drug delivery to the central nervous system. Nanoparticles are used as drug delivery vehicles to infiltrate the BBB, protecting the drug molecule's original characteristics and reducing leaching. Interaction with specific receptor-mediated transport systems in the BBB is a strategy for targeting nanoparticles to the brain. These nanoparticle-based drug delivery systems are safe, effective, and cost-effective for treating brain diseases.[53]

7. EVALUATION PARAMETERS FOR NANOPARTICLES.

7.1. Percentage Yield Determination

To determine the % yield of Nanoparticles, the weight of drug and polymers utilized and the weight of nanoparticles after drying was determined. The% yield of nanoparticles was calculated using the formula:
% Yield = Weight of nanoparticles obtained / Total expected weight of drug +polymers*100

7.2.Drug entrapment efficiency and Drug content

The entrapment efficiency and drug content of Drug loaded nanoparticles were determined by centrifugation at 1500 rpm for 2 hour using "Ultracentrifuge". Then, the sample supernatant was pipetted, appropriately diluted with 0.IN HCl, and then analyzed using a "UV spectrophotometer" at 277nm. All the experimental units were analyzed in triplicates",
The entrapment efficiency was calculated using following equations:
Entrapment efficiency (EE) %= (Amount of total drug-Amount of free drug)/Amount of total drug x 100
Drug content (%) = (Amount of total drug - Amount of free drug)/Amount of dry nanoparticles × 100

7.3. Scanning electron microscopy

The powders were imaged by a scanning electron microscope (SEM) run at an accelerating voltage of 10kV using Hitachi SU 3500. The powder in few µg were fixed on to stub by a double-sided sticky carbon tape and kept inside the SEM chamber and analyzed at different magnification such as 60X, 200X, 500X, 1.10X and 2.50X respectively to obtain better clarity on the particle morphology/ topology.

7.4. FTIR (Fourier transform infrared Spectroscopy)

Infrared spectra of samples were recorded in Bruker ATR alpha kept at an ambient temperature of 25.0 ± 0.5°C. The analytical procedure was simple and did not need any special sample preparation. The spectra were recorded by placing the samples on a zine solenoid crystal plate and screwing the anvel over the sample carefully and scanning the samples in region of 4000- 400 cm to determine various functional groups. The IR spectra of the samples was checked for any possible drug excipients interaction and confirm chemical integrity of given sample

7.5. DSC (Differential Scanning Calorimetry)

DSC (PerkinElmer-4000 series) experiments were carried out in order to characterize the physical state of the drugs. Sample were placed in aluminum pans and thermally sealed. The heating rate was 20°C per minute using nitrogen as the purge gas. The DSC instrument was calibrated for temperature using Indium. In addition, for enthalpy calibration Indium was sealed in aluminum pans with sealed empty pans as the reference

7.6. Zeta potential

Zeta potential was measured by photon correlation spectroscopy using Zeta sizer (Malvern Zeta sizer Nano ZS, UK; Malvern Instruments, Worcestershire, UK), which measures the potential range from 120 to +120 V. Zeta potential results of nanoparticle Optimized formulation 10 was taken after diluting 20 times with buffer pH 1.

7.7. *In-vitro* diffusion study

ln-vitro diffusion study was carried out by Franz diffusion cell using phosphate buffer pH 7.4 as diffusion media. The biological membrane was mounted on the Franz diffusion cell in between the donor and receptor compartment. The required quantity of nanoparticles was placed over the membrane and samples were withdrawn at different intervals and analyzed for the drug. Iml of the sample was withdrawn from the receptor compartment of the diffusion cell and an equal amount of fresh buffer solution was replaced to maintain the sink condition. Franz diffusion cell was continuously stirred using a magnetic stirrer to avoid the diffusion layer effect. The withdrawn sample was analyzed by UV spectrophotometer and the cumulative percentage of drug release was calculated.

Apparatus	Franz Diffusion cell
Diffusion medium	Buffer
Temperature	37±0.5ºC
Volume withdrawn and replaced	1ml
RPM	100
Duration of study	6 hours
The volume of diffusion medium	200ml

Table no 1: *Invitro* diffusion study table

8. KINETIC ANALYSIS OF IN-VITRO RELEASE RATES OF NANOPARTICLES.

The results of in-vitro release profile obtained for all the nanoparticles were plotted in modes of data treatment as follows:

8.1. Zero-order equation

It describes the systems where the drug release rate is independent of the concentration of the dissolved substance.

$$Qt=Q0+K0t$$

where, Q0: initial amount of drug

Qt: cummulative amount of drug release at time t
K0: zero order release constant
t: time in hour.

8.2. First order release equation

It describes that drug release rate depends on its concentration

Log Qt-Log Q0+Kt/2.303

where, Q0: initial amount of drug
Qi: cumulative amount of drug release at time t
Kt: first order release constant
t: time in hour

8.3. Higuchi release equation

The Higuchi equation suggests that the drug releases by a diffusion mechanism

$Q=KHt^{1/2}$ or Mt=Mo¼ $Kt^{1/2}$

where, Q: cumulative amount of drug release at time t initial amount of drug
KH: Higuchi constant
t: time in hour

8.4. Korsmeyer/Peppas equation

It describes the drug release from a polymeric system.

F= (Mt/M∞) =Kmt"

Where, F: fraction of drug released at time t
Mt: amount of drug released at time t
M∞: total amount of drug in dosage form
Km: kinetic constant
n: diffusion or release exponent
t: time in hour.

8.5. Hixson-Crowell Cube Root model

Hixson and Crowell recognized that the particles regular area is proportional to the cube root of its volume. The equation describes the release from systems where there is a change in surface area and diameter of particles. They derived the equation:

$Wo^{l/}3-Wt^{l/3} = Kι$

where, Wo: initial amount of drug in pharmaceutical dosage form
Wt: remaining amount of drug in pharmaceutical dosage form at time
1K (kappa): constant incorporating the surface volume relation.[54]

9. CONCLUSION

Nanotechnology has significantly advanced dermatology and cosmetology, benefiting both as standalone therapy and enhancing pharmacological effectiveness. The interaction of nanoparticles with human skin and their potential penetration are being studied from a toxicological standpoint, as well as a medication delivery route that minimizes systemic negative effects.

There are numerous advantages to employing NP-enhanced dermal and transdermal medication delivery systems. Advantages include superior skin penetration and regulated medication release (depot effect) to skin and skin appendages. The Nanoparticles have been observed in many physiological and pathological conditions such as

wound healing, Anti-inflammatory action in humans and animals such as eyes, lungs, and liver inflammations, insulin resistance, and anticancer action

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