



“NANOCRYSTALS IN COSMETICS AND IN COSMECEUTICALS BY TOPICAL DELIVERY: REVIEW”

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ABSTRACT:

The main issues with local delivery of cosmetics are their high sensitivity and limited drug loading of active pharmaceutical ingredient [1]. Today, cosmetic formulations incorporating Nanocrystals are a relatively new yet very promising and highly researched area. The application of nanotechnology in cosmetics has been shown to overcome the drawbacks associated with traditional cosmetics and also to add more useful features to a formulation. Nano cosmetics and Nano cosmeceuticals have been extensively explored for skin, hair, nails, lips, and teeth, and the inclusion of nanomaterials has been found to improve product efficacy and consumer satisfaction. Provided are cosmetic preparations for topical application containing Nanocrystals of cosmetic actives leading to an increased bioactivity of the molecules in the skin and methods of making the cosmetic preparations. The Nanocrystals can be added to any cosmetic topical formulation, e.g. creams, lotion, gels and liposomal dispersion, etc. Nanocrystals as nanomaterials are being used in cosmetic products for various effects. However, their use also raises potential safety concerns. Some of these concerns can be addressed by determining the type of nanomaterial used, as well as stability, potential for skin absorption, route of exposure, and how they are formulated in cosmetic products. There has been considerable effort internationally to harmonize approaches in order to address definitional issues and safety concerns related to the use of nanocrystals in cosmetic products [2].

KEYWORDS :- Nanocrystals, Nanomaterial, Cosmetic, Cosmeceuticals, Topical.

INTRODUCTION

Drug Nano crystals (NCs), a type of nanoparticle with a particle size distribution ranging from 1 to 1000 nm, consisting of pure drug without a carrier or any additional polymers, and requiring only a minimal surfactant for stabilization. **“Drug Nano crystals are essentially nanoscopic crystals of the parent compound. A Nano crystal is a crystalline particle with at least one dimension measuring less than 1000 nanometers (nm).”**

Nanocrystals are clustered arrangements of molecules, and they wrap the drug molecule with a thin coating of surfactant. Drug Nano crystals are without any doubt one of the most discussed drug delivery technology of the past twenty years. In contrast to other Nano particulate systems, drug Nano crystals consist mainly of pure API. They are often prepared in aqueous media which contain stabilizers for the colloidal state; therefore these systems can also be referred to as Nano suspensions. Often drug Nano crystals are referred to as drug nanoparticles. This leads to confusion with polymeric nanoparticles, which have normally a significantly lower drug load since they consist mainly of a polymer material loaded with API. Nano sizing is one of the most important drug delivery platform approaches for the commercial development of poorly soluble drug molecules. The research efforts of many industrial and academic groups have resulted in various particle size reduction techniques. From an industrial point of view, the two most advanced top-down processes used at the commercial scale are wet ball milling and high pressure homogenization. Initial issues such as abrasion, long milling times and other downstream-processing challenges have been solved with the better understanding of the biopharmaceutical aspects of poorly water-soluble drugs.

Around the 1990s Gary Liversidge and his colleagues from Sterling Drug have applied a wet media-based milling technique (wet ball milling, WBM), adapted from the paint and photographic industry, to reduce the particle size of poorly water-soluble drugs. This process has evolved since and eventually became well known as Nanocrystal technology in the pharmaceutical industry and is to date the most successful Nano sizing approach. By reducing the particle size to the nanometer range, the bioavailability of many poorly soluble compounds could be improved significantly, which eventually led to a broader acceptance.

NANOCRYSTALS are pure drug crystals with sizes in the nanometer range stabilized or surrounded by a thin coating of surfactant. There is no carrier material in nanocrystals and are composed of 100% drug. Dispersion of nanocrystals in a dispersion media leads to formation of Nano suspension. Nanocrystals can be crystalline or amorphous in nature depending on the Method of preparation, namely, bottom-up technology, top-down technology. Apart from oral route of administration, commercially scalable nanocrystal technology offers an attractive and potential approach to deliver poorly soluble drugs via parenteral route as well.

These nanoparticles have unique physicochemical properties, e.g., ultra-small size (less than 100 nm), controllable size, large surface area-to-mass ratio, high reactivity, no solubility, and target-specific actions.

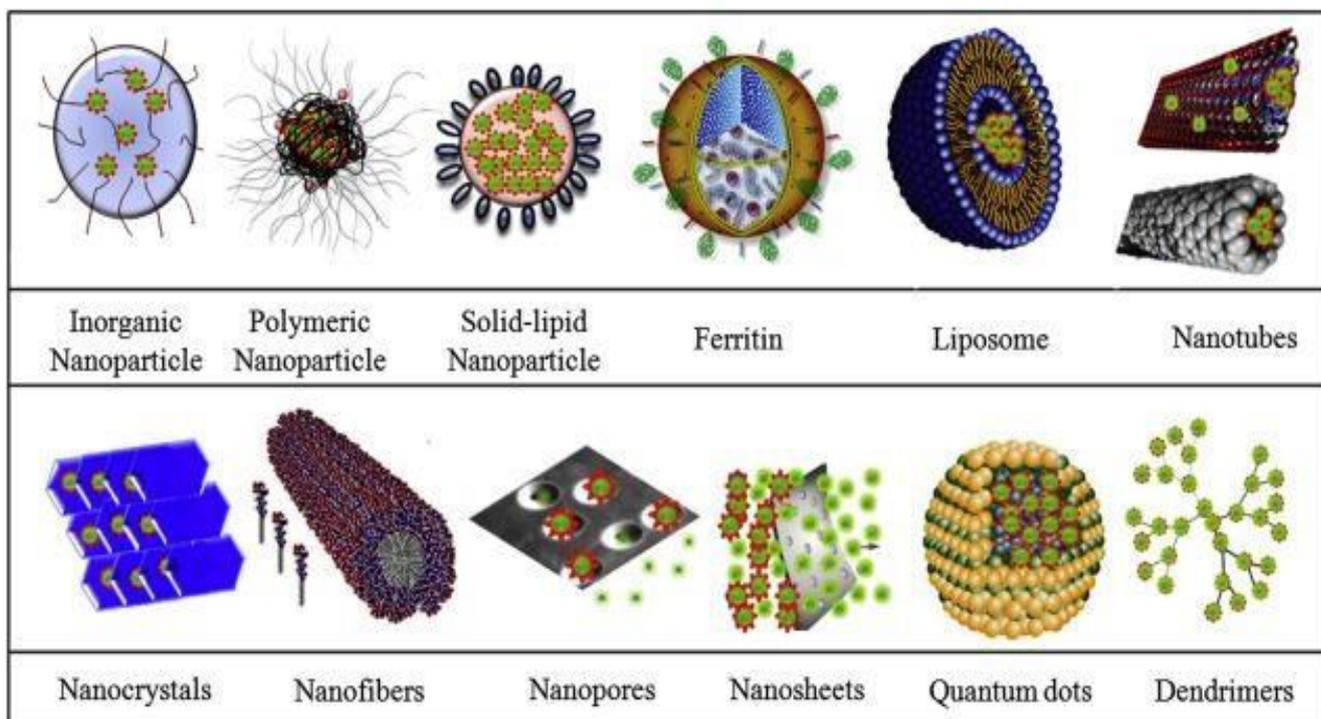


Fig.1:- Structured illustration of various Nanoparticles

NANOCRYSTALS USED IN COSMETICS

A large number of Nano-systems or novel Nano carriers are commonly used in cosmetic formulations to encapsulate active ingredients for their efficient delivery through skin barriers. These Nano-systems can help absorption or penetration of cosmeceuticals active moieties within epidermal layers in a remarkable way of achieving burst or sustained release of actives. Various nanostructured cues used in cosmetics are shown in the figure. This section provides insights into the unique features and role of multiple Nano carriers or nanostructured materials for the delivery of cosmeceuticals in cosmetics.

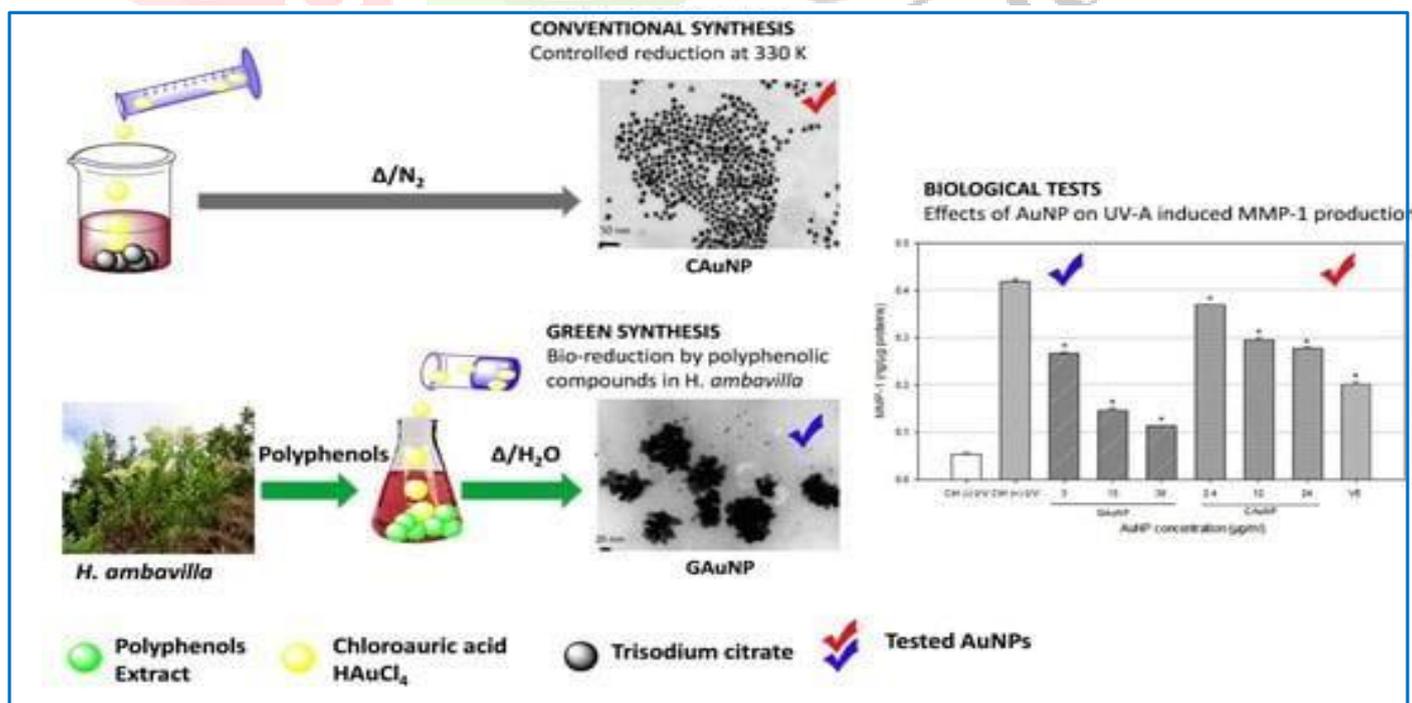


Fig.2:- Synthesis of gold nanoparticles and their antioxidant and dermo-protective activities as a safe cosmetic ingredient.

VARIOUS NANOCRYSTALS USED ARE

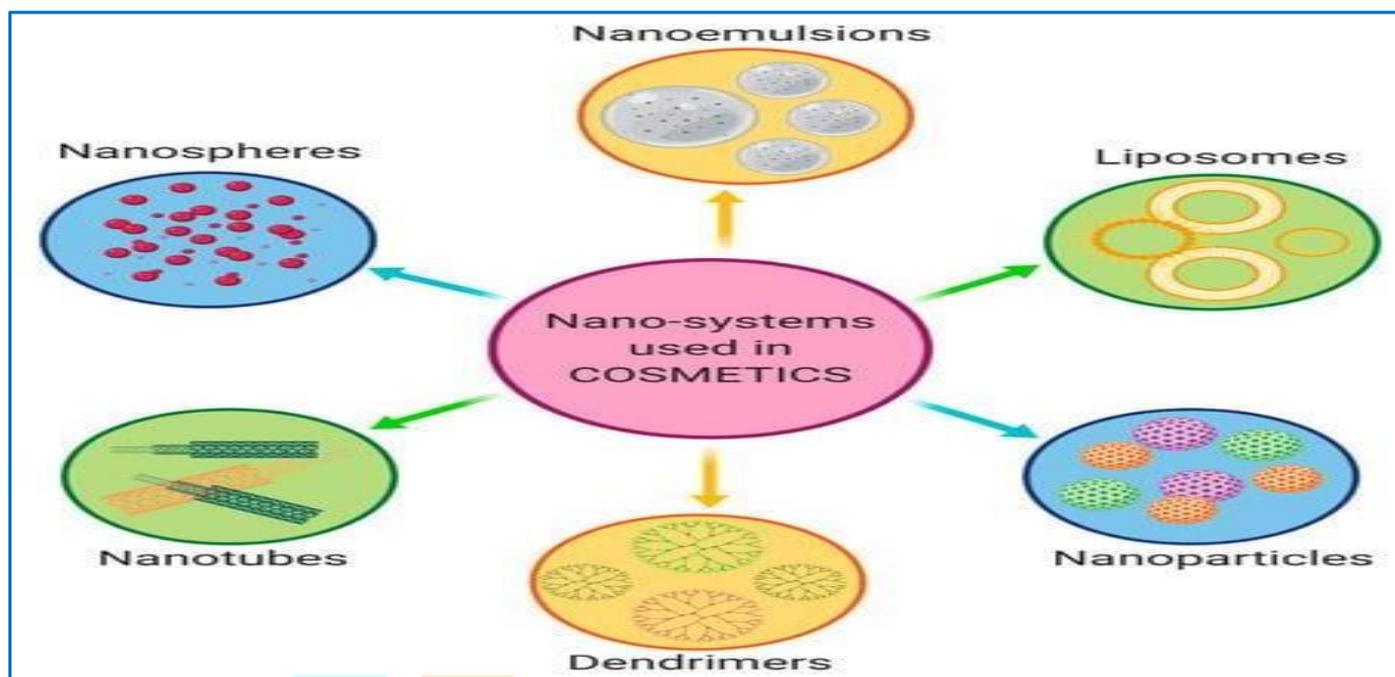


Fig.3:- Various nanostructured cues used in cosmetics

LIPOSOMES

Liposomes are currently among the most widely-known cosmetic delivery system; thus, they are extensively incorporated in the cosmeceutical formulations. The liposome-incorporated cosmeceutical formulations offer better skin penetration and help to protect the skin from harmful radiations. Liposomes are concentric bilayered vesicles in which the aqueous volume is entirely enclosed by a lipid bilayer composed of natural or synthetic phospholipids which are GRAS (generally regarded as safe) products. The lipid bilayer of liposomes can fuse with other bilayers such as the cell membrane, which promotes release of its contents, making them useful for cosmetic delivery applications. Their ease of preparation, enhanced absorption of active ingredients by skin and continuous supply of agents into the cells over a sustained period of time make them suitable for cosmetic applications.

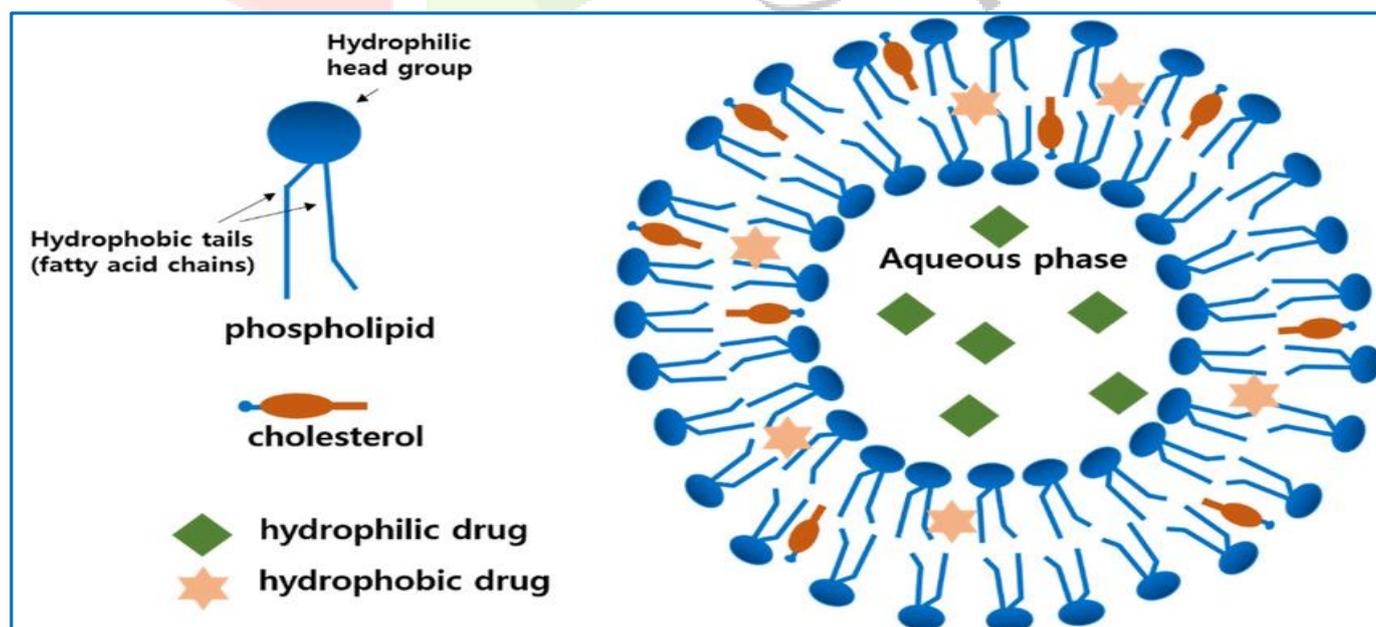


Fig.4:- Structure of Liposome containing hydrophilic and hydrophobic drug molecules

These are suitable to deliver therapeutic molecules with hydrophilic and hydrophobic nature. Their size ranges from 20 nm to several micrometers. Liposomes are used in a wide variety of cosmetics owing to their nontoxicity, biodegradability, biocompatibility, and ability to encapsulate active moieties. Vegetable phospholipids are of particular interest for use in dermatology and cosmetics due to high-esterified essential fatty acid contents.

For instance, owing to the overall surface activity and liposomes forming ability, soya and vegetable-based phospholipids have gained increasing interests. A clinical report demonstrated that the application of flexible liposomes shows beneficial effects such as intensification in skin smoothness, reduction in wrinkles, and decreasing efflorescence in acne treatment additionally, liposomes are potential carrier candidates and extensively utilized in sunscreen, beauty creams, antiaging creams, profoundly conditioning cream, and hair products.



Fig 5:- Liposome-based cosmetic delivery via the skin. The liposome-incorporated cosmeceutical formulations offer better skin penetration and help to protect the skin from harmful radiations

NANOEMULSION:-

They are dispersions of nanoscale droplets of one liquid within another. They are metastable systems whose structure can be manipulated based on the method of preparation. The components used for their preparation are GRAS products and are safe to use. Their smaller particle size provide higher stability and better suitability to carry active ingredients; they also increase the shelf life of the product.

NANOCAPSULE:

Nano capsules are submicroscopic particles that are made of a polymeric capsule surrounding an aqueous or oily core. It has been found that the use of Nano capsules decreases the penetration of UV filter octyl methoxycinnamate in pig skin when compared with conventional emulsions.

NANOSILVER AND NANOGOLD:

Cosmetic manufacturers are harnessing the enhanced antibacterial properties of Nano silver in a range of applications. Some manufacturers are already producing underarm deodorants with claims that the silver in the product will provide up to 24-hour antibacterial protection. Nano-sized gold, like Nano silver, is claimed to be highly effective in disinfecting the bacteria in the mouth and has also been added to toothpaste.

DENDRIMERS:-

Dendrimers are unimolecular, monodisperse, micellar nanostructures, around 20 nm in size, with a well-defined, regularly branched symmetrical structure and a high density of functional end groups at their periphery. They contain large number of external groups suitable for multifunctionalization.

CUBOSOME:-

Cubosomes are discrete, sub-micron, nanostructured particles of bi-continuous cubic liquid crystalline phase. It is formed by the self-assembly of liquid crystalline particles of certain surfactants when mixed with water and a microstructure at a certain ratio. Cubosomes offer a large surface area, low viscosity and can exist at almost any dilution level. They have high heat stability and are capable of carrying hydrophilic and hydrophobic molecules. Combined with the low cost of the raw materials and the potential for controlled release through functionalization, they are an attractive choice for cosmetic applications as well as for drug delivery.

METHOD OF PREPARATION OF NCs

Nanocrystal preparation methods can be divided into top-down and bottom-up. Techniques. The size reduction of relatively large particles into smaller particles are known as top-down technique, whereas bottom-up techniques consist of the growth of small particles from individual molecule. The driving force for the growth of a crystal from individual molecules is super saturation. Bottom up technique is usually a precipitation or crystallization technique and considered as the oldest technique to prepare Nanocrystals.

Top down Approach: Milling & High pressure Homogenization

The top down approach is the most important technique for the production of nanocrystals. Milling and high-pressure homogenization are the two basic top-down techniques for size reduction. Wet milling produces the most nanocrystal products that have reached the market. Wet milling involves mechanical attrition, where particles are wetted by an aqueous solution of surfactants and sheared and grinded by milling balls in a milling container. The particle size is reduced and may reach a few hundred micro-meter, but the conventional milling with modifications can be used for generating nanosized crystals. The preparation process can be carried out in a reproducible manner. The contamination from erosion of metal milling balls or pearls, high energy input, prolonged operation time and decreased crystallinity are the major drawbacks of the technique. The use of polymeric beads may be helpful in minimizing the erosion and contamination.

A new process known as Jet milling to prepare micro-particles without the use of organic solvent was described by Nykamp et al. The important advantages of solvent free jet milling are the prevention from toxicity due to the absence of organic solvents and very short preparation time.

High-pressure homogenization is the process in which two fluid streams of particle suspensions collide under high pressure in a chamber, leading to particle collision and subsequent particle rupture. Nano sized solid particles are produced in Piston-gap homogenizers by forcing a suspension of drug particles with a piston through a thin gap under high pressure. The high shear forces, and turbulent flow fractures the particles and the particle outcome was decided by the power of homogenization, particle hardness, and number of the piston-moving cycle. High- pressure homogenization required high process temperature, high-energy input, required complex equipment and might have possible degradation of the component.

Bottom-Up Technique Control Flow Cavitation:

CFC creates the optimum process condition for Nano crystal production after controlling the size, location, density, and intensity of implosion of bubbles in the cavitation zone. The controlled energy released by the implosion of micro bubbles and the ability to control the energy of cavitation, the particles can be brought to desired particle size distributions, CFC converts destructive force into constructive with high intensity energy force to produce Nano and micro structured materials, CFC technology has been exploited in many industries with multiple CFC chamber designs customized for hydrodynamic, chemical, biomedical and cleaning applications. The CFC is highly scalable and efficient process with excellent process control and outstanding reproducibility.

Spray Drying:

Spray Drying is a single-step process for converting solutions, emulsions, suspensions, slurries, and pastes into powders in a continuous manner. It also allows the production of particles with controlled size and morphological aspects. Due to the limited collection efficiency related to cyclone separators, the traditional spray drying process is limited for producing particles of 2– 5 μm sizes. A spray dryer with a piezoelectric driven vibrating mesh atomizer and a high- efficiency electrostatic powder collector seems to correct these limitations. A new Nano spray dryer technology B-90, has been developed by Büchi®(Switzerland) and has been applied to perform Nano crystallization and drying. The other new technology includes the dissolution of drug and a polymeric dispersant system in a suitable solvent. After spray drying the resulting solution the powder containing the drug are produced as either the molecularly dispersant system in the polymer matrix to form a solid solution or dispersed as submicron particles to form solid suspension. The spray drying process is very rapid; can be designed to any capacity, adaptable to a fully automated control system that allows continuous preparation, and also wide ranges of spray dryer designs are available in the market. The spray dryer can be used for heat resistant and heat sensitive products and the feedstock can be as a solution, slurry, gel, suspension or melt form. The current advantage of nanotechnology has increased the stress on existing spray dryer systems to produce nanoparticles with high yield and controlled size distribution.

Supercritical Fluid:

Supercritical antisolvent (SAS) processes are lately proposed for the production of micro- and Nano sized particles. The solute, solvent, and the supercritical antisolvent are the three important components of SAS. A very high level of super saturation was generated due to the high power of supercritical fluids to dissolve the organic solvents as well as by the low solubility of the solute in the SAS. A very fast diffusion and high super saturation creates precipitation of nanoparticles that are not possible to obtain with antisolvent precipitation or any other techniques. The main advantage is the complete removal of antisolvent by pressure reduction to the gas phase. In case of SAS the solvent power can be obtained by varying pressure and temperature and their diffusivities can be about two orders of magnitude greater than those of liquids. More recently Caputo et al. proposed the use of SAS for the precipitation of sulfathiazole from acetone solution by the use of urea as habit modifier and in the recent past poly (sebacic unhydride) was used by Jarmer et al. as growth inhibitor for griseofulvin using a SAS.

Emulsion Method:

The method of preparation of nanocrystals by micro emulsion is gaining a significant interest in both basic research and in different industrial fields. The organic nanocrystal fabrication using the emulsion method is a three-step process. The first step is the preparation of emulsion by the quick addition of solution of compound in the organic phase to the aqueous phase at high temperatures. High stirring speed and irradiating ultrasound was used to produce the stable emulsion. In the second step the solutes are crystallized by gradually cooling the dispersion to low temperatures. In the third step an antifoaming agent was added to break the emulsion and separate the organic solvent. A nanocrystals were obtained as a stable dispersion in an aqueous phase. Ujiye-Ishii and co-workers described how to prepare perylene nanocrystals using emulsion and Re-precipitation method. Schulman et al. first described the method in 1959 and prepared macro emulsion and micro emulsion of hydrocarbons. A significant feature of this method is its ultralow interfacial tension, large interfacial area, and thermodynamic stability of the resulting nanocrystal dispersions in aqueous media.

Microfluidics Device:

A microfluidic system can be used for the continuous production of nanocrystals mainly due to the improved reaction control and performance of mixing, the particle size distribution becomes sharper and the particle size decreases. The microfluidic devices fall into broad categories: capillary- and chip- based systems. In capillary reactors the simple fluidic components can be joined by appropriate lengths of tubing. Chips are precisely tailored and typically fabricated from a plastic, glass or silicon substrate, wet etching or micromachining techniques. Both types of reactor play an important role in nanocrystal synthesis. Single phase or two-phase reactors are two important microfluidic reactors. The single-phase reactors are commonly used reactors, in which miscible streams of reagents are injected into a channel or capillary where they mix and react, making it easy to conduct multistep reactions and produce more complex structures. The undesirable velocity dispersion and fouling on the reactor wall are the two important limitations and can limit the performance of a single phase reactor. In case of two-phase reactors an additional immiscible fluid was injected (which can be a gas or a liquid) into the channel divides and creates a split plug that passes through the reactor at a common speed, eliminating velocity dispersion. The size of the split plugs was proportional to the relative flow rates in the two outlet channels and can be controlled by varying the relative hydrostatic pressures at the two outlets. The microfluidic reactor is still a long way from displacing the conventional reactor for nanocrystal synthesis, which cannot satisfy industrial demand.

PENETRATION OF NANOPARTICLES VIA SKIN:-

Scientific studies have shown that nanoparticles can penetrate skin, especially if skin is flexed. Broken skin is a direct route for the penetration of particles even up to a size of 7000 nm. The presence of acne, eczema and wounds may enhance the absorption of nanoparticles into the blood stream and may lead to further complications. A preliminary study found that nanoparticle penetration was deeper in skin affected by psoriasis than in unaffected skin. Recently, the base carriers are being modified in order to enhance the skin penetration by incorporating certain penetration enhancers, both physical and chemical, and also by preparing newer vesicular systems with increased skin penetrability like ethosomes and transferosomes. Even flexing and massage can increase the skin penetration of nanoparticles. One study found that even particles up to 1000 nm in size can be taken up through intact skin to reach living cells, when skin is flexed.

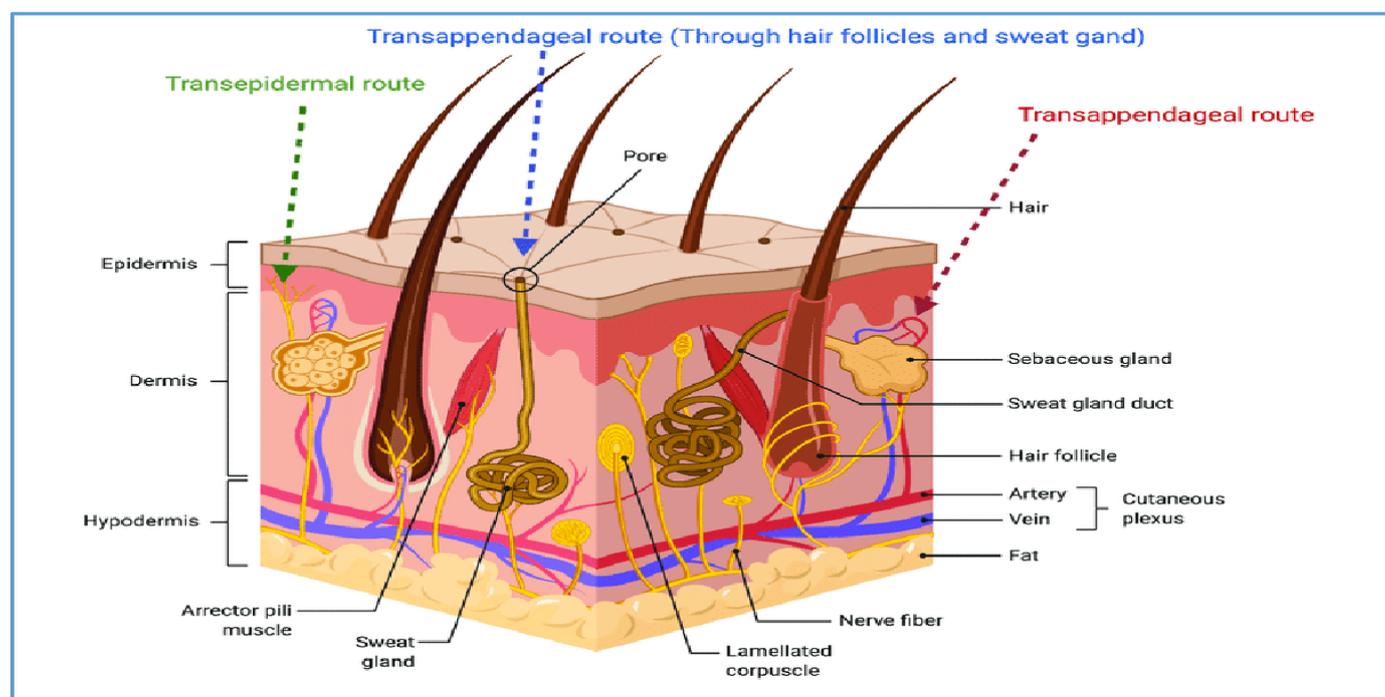


Fig 6: -Schematic illustration of the skin layer and showing penetration routes of the drug administered through the skin.

COSMETICS & COSMECEUTICALS:-

On the average, an adult uses about nine cosmetic products daily. No doubt, cosmetics are probably among the most widely used products in the world. Cosmetics are substances used to enhance the appearance or odour of the human body. Cosmetics include skin-care creams, lotions, powders, perfumes, lipsticks, finger nail and toe nail polish, eye and facial makeup. Towelettes, permanent waves, colored contact lenses, hair colours, hair sprays and gels, deodorants, hand sanitizer, baby products, bath oils, bubble baths, bath salts, butters and many other types of products. A subset of cosmetics is called "make-up" which refers mainly to colored products intended to change the user's appearance. Their appeal is directly linked to their functionality in achieving man's innate desire of looking beautiful and remaining ever young. Plautus, a Roman playwright worded it this way, "A woman without paint (cosmetics) is like food without salt". How those words convey the important role of cosmetics! From imparting confidence to fine-tuning beauty, cosmetics and related materials are applicable and have been employed from time immemorial.

According to the Food and Drugs Act (FDA) of the United States of America (USA), cosmetic is any product/article to be rubbed, poured, sprinkled or sprayed on, introduced to or otherwise Applied to the human body or part of it, except soap, intended for cleansing, beautifying, promoting attractiveness, or altering the appearance. Cosmetics cover a wide range of personal care products. On the basis of body parts they are applied, cosmetics could be classified as 1) skin-care cosmetics e.g. moisturizing agents, cleansing agents 2) hair-care products e.g. hair colorants, styling agents, shampoos 3) face-care products e.g. lipsticks, mascara, powders, face foundations 4) nail-care products e.g. paint removers, nail vanishes, 5) fragrance products e.g. cologne, deodorants, aftershaves, perfumes and 6) ultraviolet (UV) light screening preparations such as sunscreens.

In the light of this definition, it is evident that cosmetics are not medicines! However some cosmetic products could contain ingredients that can elicit a biological effect, mild therapeutic action or drug-like benefit on the skin, hence such ones are described by the term “**Cosmeceutical**”. When the ingredients of cosmeceuticals are of nano sized, then they are fittingly called **Nano cosmeceuticals**.

Cosmeceuticals means combination of cosmetics and pharmaceuticals. Cosmeceuticals are cosmetic products with biologically active ingredients purporting to have medical or drug-like benefits. Cosmeceuticals are used to improve and nourish the skin appearance and known to treat different dermatologic conditions. Like cosmetics, cosmeceuticals are also applied topically having ingredients that influence the skin’s biological function. Cosmeceuticals are meant to improve appearance by delivering nutrients necessary for healthy skin. Cosmeceuticals usually claim to reduce wrinkles and to improve tone, texture and radiance of the skin. Cosmeceuticals are used for a variety of applications, e.g., to improve skin texture by stimulating collagen growth, as anti-aging formulations as their antioxidants neutralize reactive oxygen species and protect the structure of keratin, which results in a healthier skin. Marketed anti-aging Nano cosmeceuticals as hair care products (e.g., shampoos, conditioners, hair growth stimulants, coloring and styling products) may be composed of nanotubes, poly (lactic-co- glycolic acid (PLGA) Nano spheres, fullerenes, gold nanoparticles, niosomes, micro emulsions, Nano emulsions, liposomes, with the purpose of sealing the moisture around the cuticles and optimizing the contact time with the scalp and the follicles, by forming a protective film. Nano cosmeceuticals have also been included in lipsticks, lip balms, lip glosses, and lip volumizers. The use of nanoparticles in lip-care products is aimed to increase the lip softness, to prevent the Trans epidermal water loss, and to keep the desired styling effect (e.g., acolor) for a longer timeframe. Lip volumizers containing Nano cosmeceuticals are based on liposomes to increase the lip volume by filling the wrinkles in the lip contour, keeping the lips hydrated and Well-outlined. Nano cosmeceuticals have also been successful in the field of nail care. Nail polishers enhance the toughness, dry faster than conventional products, have more durability and resistance, and have a higher elasticity which facilitates the application. The use of silver and metal oxide nanoparticles in these formulations provide them with antifungal properties, which is very useful for the treatment of toenails in case of fungal infections.

Cosmetic product can be classified into various categories based on their intended use, ingredients, and regulatory guidelines. Some common cosmetic product classification include:-

- 1. SKINCARE:** - This category includes products like moisturizers, cleansers, serums, and toners design to improve and maintain the health and appearance of the skin.
- 2. MAKEUP:** - Makeup product encompass items like foundation, lipsticks, eyeshadow, mascara, and more, used to enhance or alter person’s appearance.
- 3. HAIRCARE:** -Hair care products include shampoo, conditioners, hair masks, and styling products aimed at cleaning, conditioning, and styling the hairs.

4. PERSONALCARE: - This category includes items like deodorants, antiperspirants, and oral care products like toothpaste and mouthwash.

5. SUN PROTECTION: - Sunscreens and sunblock's are designed to protect the skin from the harmful effects of ultraviolet (UV) radiation.

Micellar nanoparticles technology or nanocrystals are considered as one of the efficient and latest nanotechnology-based cosmeceutical that has been enormously implemented in skin cleanser product segments.

TOPICAL DELIVERY:-

A topical cosmetic drug delivery system refers to a method of delivering active ingredients, such as drugs or beneficial compounds, to the skin's surface or deeper layers. This system enhance the effectiveness of cosmetics by allowing controlled release and targeted application.

It's a promising approach for improving skincare and other cosmetic products. Topical cosmetic type could include creams, lotions, serums, gels, ointments, masks, among others. Each type serves a different purpose and has a unique formulation to deliver various benefits to the skin. A topical delivery system, or vehicle, is defined as the substance that carries a specific drug into contact with and through the skin. The challenge to topical drug delivery is the transport across the skin barrier.

Skin is a major human body component as delivery medium of cosmetic active ingredient, which contain multi-layered structure; (1) stratum corneum that composed with dead keratinized cells, (2) epidermis and dermis, and sub-cutaneous tissue. Stratum corneum (SC) is acting as an excellent barrier properties to the skin. Due to keratinized cells of SC containing lipid matrix composed of fatty acids, ceramides, cholesterol, and cholesterol ester which has a cement-like function characteristic. Through the topical delivery of active ingredient, there are three possible pathway which are intercellular, hair follicles and Tran's cellular pathways. First, the well-known pathway (intercellular) is taking place where substance diffuses through stratum corneum via the lipid layers surrounded by keratinized cells. Second, delivery path which known as the hair follicles path, functions as a reservoir of active compound topically applied onto skin. This is attributable to the hair follicles part containing a dense network of blood capillaries that serve as supporting penetration medium. Third path is Tran's cellular penetration that involve a direct delivery of active compound through the lipid layers and corneocytes to the living cells.

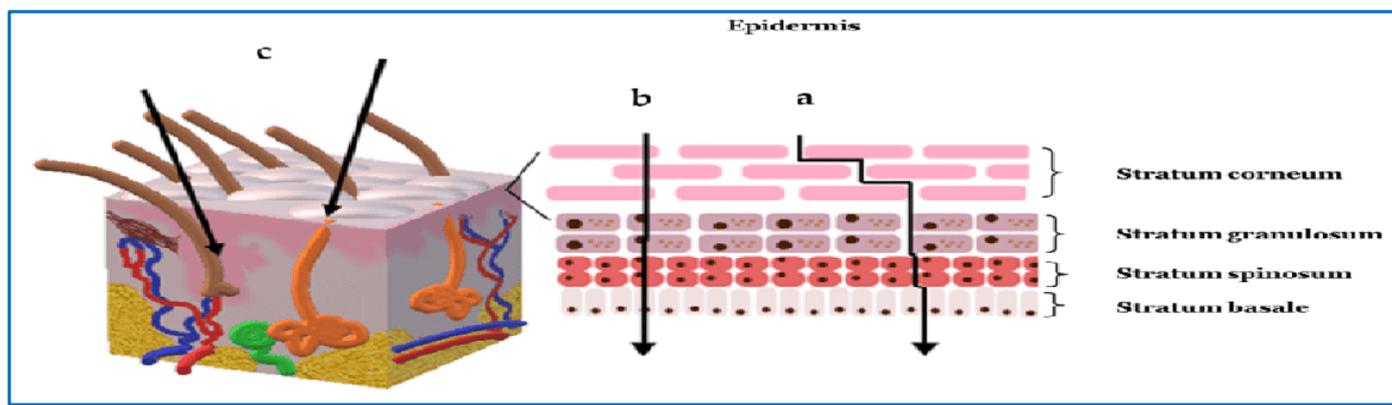


Fig. 7: Skin Layer Structure and Penetration Route: - a) Intercellular b) Transcellular c) Trans Appendageal Pathway

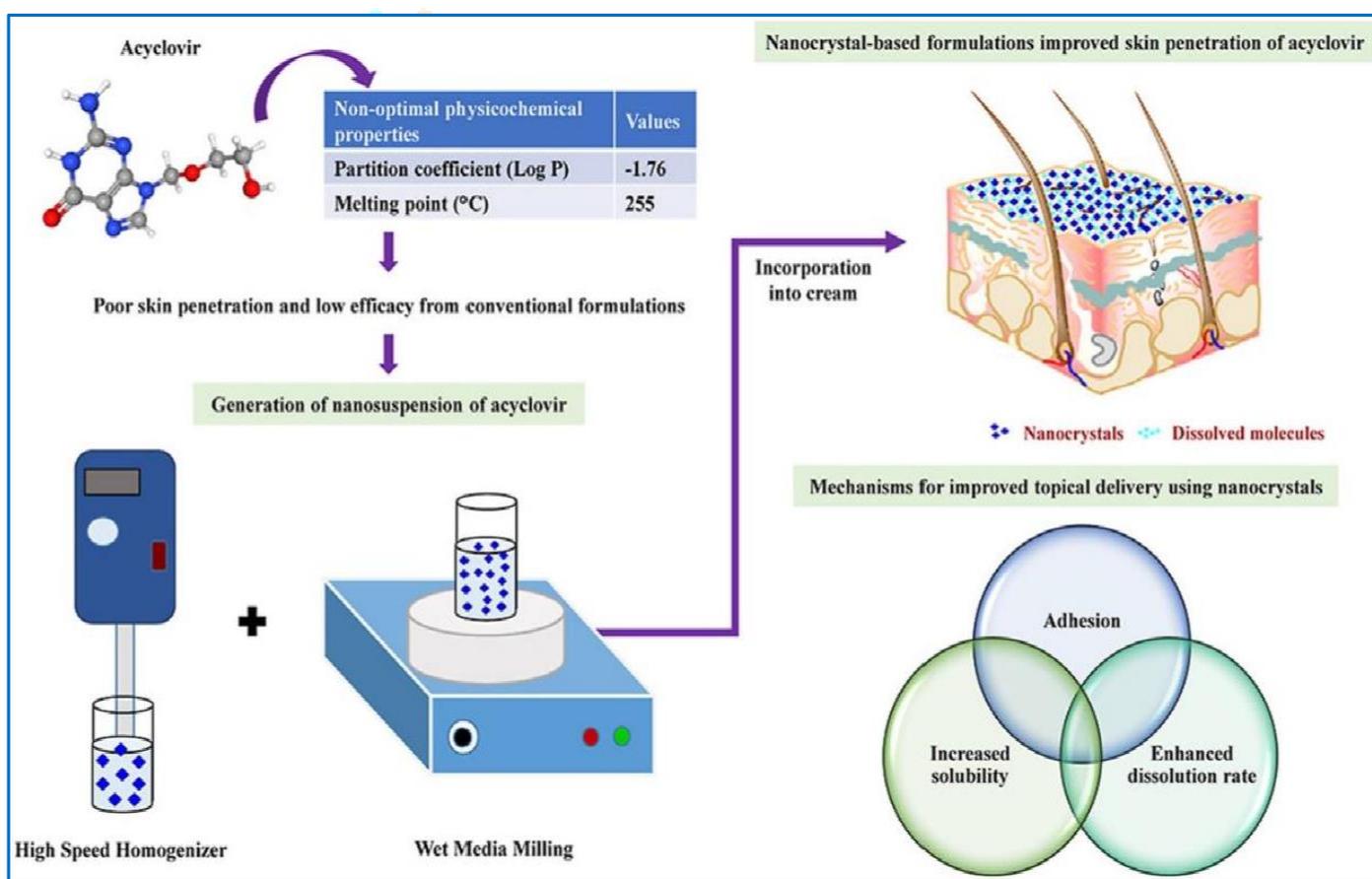


Fig. 8:- Nanocrystals of acyclovir for improved topical delivery

ADVANTAGES:-

- Localized Treatment:** They allow targeted drug delivery to a specific area, minimizing systemic exposure and reducing potential side effects on the rest of the body.
- High Drug Concentration:** Concentrated drug delivery directly to the target area increases the therapeutic effect at the desired site.

3. **Reduced Systemic Side Effects:** By bypassing the systemic circulation, these systems can minimize the risk of systemic side effects and toxicity.
4. **Enhanced Patient Compliance:** Often easier to administer than systemic treatments, leading to better patient adherence to the prescribed regimen.
5. **Potential for Reduced Dosing Frequency:** Controlled release systems can provide sustained drug release, potentially reducing the frequency of application or administration.
6. **Avoidance of First-Pass Metabolism:** For drugs that would undergo significant metabolism if administered systemically, topical delivery bypasses the liver's first-pass effect.
7. **Suitable for Localized Conditions:** Ideal for treating skin conditions, wounds, burns, and certain types of infections at the site of application.
8. **Minimized Drug-Drug Interactions:** Reduced exposure to other medications circulating in the bloodstream can decrease the likelihood of drug interactions.
9. **Direct Access to Target Tissue:** Offers direct contact with target tissues, which can be advantageous for conditions where accessing the site of action is challenging.
10. **Enhanced Cosmetic Effects:** Common in dermatology, where topical treatments can also improve the appearance of skin conditions.
11. **Rapid Onset of Action:** Some topical treatments can provide quicker therapeutic effects compared to systemic administration.
12. **Ease of Application:** Often applied as creams, ointments, gels, patches, or sprays, making them user-friendly and convenient.
13. **Reduced Need for Invasive Procedures:** In certain cases, topical drug delivery can replace or postpone the need for surgical or invasive interventions.

DIS-ADVANTAGES:-

1. **Limited Depth of Penetration:** Topical treatments may not effectively reach deep-seated tissues or organs, limiting their applicability to certain conditions.
2. **Variable Absorption:** Skin characteristics and conditions can affect drug absorption, leading to

inconsistent therapeutic outcomes.

3. **Skin Barrier:** The skin's barrier function can impede drug penetration, requiring the use of penetration enhancers that might cause irritation.

4. **Patient Compliance Challenges:** Application of topical treatments can be time-consuming and require regular reapplication, leading to potential patient non-compliance.

5. **Risk of Allergic Reactions:** Some patients may experience skin allergies or sensitivities to the components of the topical formulation.

CONCLUSION:-

Because of the rising demand for APIs in the creation of cosmetics, which are used for a variety of skin care, including anti-inflammation and acne, anti-bacterial, lightening and speckle removal, anti-aging, and UV protection, cosmetics manufacturers are turning to nanotechnology using NANOCRYSTALS for assistance. These components are used to create NCs, which not only removes the barrier between medicine therapy and cosmetics but also improves the ability of cosmetics to permeate the skin and release active ingredient. The introduction of newer advancement and novel approach of nanocrystals make cosmetics and cosmeceuticals more popular with increased market share. Today, these cosmetics are in indispensable part of daily routine; further, this enhanced acceptance among users all around the world.

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