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A REVIEW ON NANOEMULGEL

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Abstract:

A Nanoemul gel is a topical gel that contains a nanoemulsion dispersed within a gel matrix. The nanoemulsion is typically prepared using high shear mixing techniques and contains droplets of an oil[8] phase dispersed in an aqueous phase stabilized by surfactants or stabilizers. The resulting Nanoemul gel has several advantages over traditional emulsion-based gels, including improved stability, enhanced drug penetration, and increased bioavailability. Nanoemul gels have been studied for their potential in dermatology and drug delivery applications, showing promising results in reducing acne lesions and improving skin appearance, as well as enhancing drug delivery and reducing inflammation. Further research is needed to optimize the formulation and assess the safety and effectiveness of Nanoemul gels for different applications. Nanoemulgel consist two different systems in which drug containing nanoemulsion[9] is incorporated into a gel base. The fusion of these two systems makes this formulation advantageous in several ways. Lipophilic drugs can be easily incorporated and the skin permeability of the incorporated drugs can be enhanced in several folds due to the finely distributed oil droplets in gel phase. Simultaneously, it can be targeted more specifically to the site of action and can avoid first pass metabolism and relieve the user from gastric/systemic incompatibilities. The nanoemulgel drug [13]delivery system is a formulation related intervention to improve drug absorption and therapeutic profile of lipophilic drugs. An increasing trend in nanoemulgel use in recent years has been noticed because of the better acceptability of the preparation to the patients due to their non-greasy, convenience spreadability, and easy applicability and good therapeutic and safety profile. Despite having few limitations, nanoemulgel formulation can be considered as potential and promising candidates for topical[32] delivery of lipophilic drugs in the future.

Keywords: Nanoemulgel; Topical Formulation; Drug Delivery through skin[28].

INTRODUCTION:

A type of structural fluid known as a nanoemulsion gel combines the characteristics of nanoemulsions and gels. Nanoemulsions are clear or translucent, thermodynamically stable dispersions of oil and water, with typical droplet sizes ranging from 20 to 200 nm. Due to their large surface area and potential to improve drug solubility , bioavailability, and targeted distribution ,they are frequently used as drug delivery systems.

Gels, on the other hand, are semisolid systems made up of a three-dimensional network of crosslinked polymer chains, and they can offer advantageous qualities like increased adhesion, extended residence time, and improved skin penetration.

Nanoemulsions gels can offer a special set of benefits in drug delivery by combining these two systems, including increased stability, controlled release, and improved skin permeability. Nanoemulsions are a type of emulsion that has droplets in nanometer range. They are considered to have better stability and bioavailability than traditional emulsions due to their small droplet size. Nanoemulsions are commonly used in various industries, including the food, cosmetic, and pharmaceutical industries.

Nanoemulgels are topical gels contain nanoemulsions. They are commonly used in dermatology for the treatment of skin conditions such as eczema, relief, pscoriasis and acne[17]. They can also be used to deliver medications for pain relief, anti-inflammatory agents, and anti-infective agents. Nanogels are nanoparticles - based hydrogels that have been studied for their potential in drug delivery, tissue engineering and other biomedical applications. They are commonly used due to their biocompatibility , biodegradability and high drug loading capacity.

ADVANTAGES:

1.The ability to resist First-pass metabolism.

2.Effectiveness for a managed and long-term drug delivery system has been proven.

3.Skin friendly.

4.Appropriate for self-medication.

5.Patient accept it quickly.

6.Nanoemulsion provides large surface area and free energy which make an efficient delivery system.

7.Emulsion defect like Creaming, phase separation, flocculation, and coalescence is not found in nanoemulsion.

8.Nanoemulsion prepared in variety of formulations, foams, creams, sprays and much other cosmetic formulation.

9.It is safe on transdermal application due to its non-toxic nature.

10.By using biocompatible surfactant in nanoemulsion[31] formulation, it can be administered orally.

11.It shows better penetration of drug because the nano-sized particles can easily enter by the rough skin surface.

12.By the process of precipitation and interfacial poly-condensation of nanoemulsion, nanocapsule and nanosperes are prepared[23].

DISADVANTAGES:

1.Bubbles formed during emulgel formulation.

2.For utilization in pharmaceutical application, surfactant used ought to be non-poisonous.

3.Possibility of allergenic reactions.

4.Skin irritation on contact dermatitis.

Characterization of Nanoemulgel:

· Viscosity.

· Ph.

· Spread ability.

· Skin irritation test.

· Drug Content.

· In vitro Permeation Study.

· Study of drug release kinetics.

· Comparison of nanoemulgel with marketed products.

· Stability Study.

METHOD OF PREPARATION FOR NANOEMULGEL: -

Nanoemul gel is a type of gel formulation that incorporates nanosized droplets of oil or other hydrophobic substances in a hydrophilic matrix. The following are some general methods for preparing Nanoemul gel[33]:

1. High-pressure homogenization method: This method involves the use of a high-pressure homogenizer to break down the oil phase into nanosized droplets that can be easily dispersed in a hydrophilic gel matrix. The homogenization process generates high shear forces that help to reduce the droplet size and create a stable Nanoemul gel[27].

2. Ultrasonication method: In this method, ultrasonic waves are used to create Nanoemul gel. The oil phase and the hydrophilic matrix are mixed together, and the mixture is subjected to high-frequency ultrasound waves. The ultrasonic energy breaks down the oil phase into nanosized droplets, which are dispersed uniformly in the gel matrix.

3. Solvent evaporation method: This method involves the use of a water-miscible solvent to dissolve the oil phase and the hydrophilic matrix. The solvent is then evaporated under reduced pressure, leaving behind a Nanoemul gel with nanosized droplets of oil dispersed throughout the gel matrix.

4. Microfluidization method: In this method, the oil phase and the hydrophilic matrix are passed through a microfluidizer to create Nanoemul gel[26]. The microfluidizer generates high shear forces that break down the oil phase into nanosized droplets, which are dispersed in the gel matrix.

5. Self-emulsifying gel method: This method involves the use of a self-emulsifying drug delivery system (SEDDS)[34] that can create Nanoemul gel in situ. The SEDDS is a mixture of oil, surfactants, and co-solvents

that can spontaneously emulsify when in contact with water. When the SEDDS is mixed with a hydrophilic gel matrix, a Nanoemul gel is formed.

6. High-energy emulsification method: This method involves the use of high-energy input to create small droplets of the dispersed phase (oil) in the continuous phase (water). This can be achieved through various methods such as sonication, high-pressure homogenization, or microfluidization. The resulting emulsion can then be transformed into a gel by adding a gelling agent such as a polymer or a surfactant.

7. Phase inversion temperature (PIT) method: This method involves the use of a thermosensitive surfactant that undergoes a phase transition from a water-soluble to a water-insoluble state at a certain temperature. By adjusting the temperature of the system, the surfactant can be induced to form a gel-like structure that entraps the dispersed phase.

8. Sol-gel transition method: This method involves the use of a sol-gel transition system, where a gel is formed by the aggregation of a network of particles or polymers in a solvent. This can be achieved by adding a crosslinking agent or a thermosensitive polymer to the emulsion, which triggers the formation of a gel-like structure at a certain temperature or under certain conditions.

9. Electrostatic complexation method: This method involves the use of oppositely charged polymers or surfactants to create a stable emulsion, which can then be transformed into a gel by adding a crosslinking agent or a gelling agent.

10. Coacervation method: This method involves the use of two or more polymers that undergo phase separation in the presence of an electrolyte or a pH change, resulting in the formation of a gel-like structure. The dispersed phase can then be incorporated into the gel by high-energy emulsification or other methods.

Emulgel:-

Emulgel is a mixture of gel and emulsion the place emulsion used can be each kind W/O and O/W as a car for purpose to supply chosen drug to the skin. Water Phase containing the gelling agent converts a basic emulsion in emulgel [1]. Dermatological use of Emulgel has many favourable homes like effortless spreadable, greaseless, being thixotropic, water-soluble, convenient removal, longer shelf life, non-staining, and bio-friendly[30].

Drugs can penetrate into the pores and skin structure:

a. through thick stratum corneum, (SC)

b. Sebaceous follicle.

c. sweat ducts of skin,

Stratum corneum covers more than 99% of pores and skin handy for tablets to be absorbed. Passing thru this is the charge limiting step for drug percutaneous absorption. Establishment of a concentration gradient idea to be major steps involved in percutaneous absorption, which affords pressure vital for drug adsorption throughout the skin [2].

Nanoemulgel

Formation containing Nanoemulsion in gel base are referred to as nanoemulgel[6], is the addition of Nanoemulsion machine intergraded into gel matrix which influences a better skin permeation [3]. This mixture of nanomulgel acts as drug reservoirs, influencing the launch of drug from internal phase to outer phase and further. Nanoemulgel[25] on intact with skin launch the oil droplets from the gel and this oil droplets penetrate

into the SC of the pores and skin and supply the drug to supposed site. Nanoemulsion-gel[7] have a right adhesion property and excessive solubilising of drug in oil phase leads to large attention gradient closer to the pores and skin that in addition increase skin penetration of drug. Also affected person compliance is accelerated due to expanded spared potential compare to creams and ointments and decreased stickiness.

Important Component of Nanoemulgel:-

a. Oils: Oils used in Nanoemulsion are generally mineral oils used as the vehicle for drugs[22] E.g. castor oils and various fixed oils (cottonseed oil, maize oils, arachisoil) Olive Oil, Coconut Oil, eucalyptus oil, rose oil, clove oil etc.[14]

b. Aqueous Phase: Commonly distilled water is used as a aqueous phase for the preparation of Nanomulsion and hydrogel[35].

c. Surfactant and Co-Surfactant: urfactants are used both to give emulsification at the time of formulation and control day to day stability during shelf life of prepared Nanoemulsion. General selection of surfactant depends on the type of emulsion [15]. (O/W or W/O) E.g. Span 80 (Sorbitanmonooleate), Acrysol K 140, Polyethylene-glycol-40-stearate, Acrysol, Labrasol, Stearic acid, PlurolOleique, Tween 80 (Polyoxyethylene- sorbitan-monooleate), Labrafil, Sodium stearate, Where agents like Transcutol ,Captex, Cammul, Migyol, etc. can be use as cosurfactant or co-solvents[24].

d. Gelling Agent: Polymers essential to give the structural network for the preparation of gels are known as gelling agents E.g. Natural - Agar, Tragacanth, Guar gum, Xanthan Gum, Semisynthetic and Synthetic Carbapol, Poloxamer, HPMC (cellulose derivatives)

e. Permeation Enhancers: They interact with different skin constituents to produce a reversible temporary increase in permeability. They can act by one or more mechanisms like,

i. Disrupting the highly compact structure of SC.

ii. Improving partition of drug[21] or solvent or co-enhancer into the SC.

iii. Interacting intercellular protein.
Causing conformational changes in protein or solvent swelling is the key for alternating polar path. Some enhancers improve the fluidity of protein in SC, where some act on both pathways by disrupting multilaminate pathway. They can increase the diffusion of drug through skin proteins. Type of enhancer has a significant impact product designing [16] E.g. Eucalyptus oil, Linoleic acid, Lecithin, Oleic acid, Chenopodium oil, Isopropyl myristate, Urea.

Factors Affecting Topical Absorption of Drug:-

a. Physiological factors [10,11]

i. Lipid content of the skin - act as barrier for drug absorption and lowering this barrier property leads to increased penetration.

ii. Thickness of different skin layers -Greater the thickness lower the penetration rate, like palm and sole shows higher diffusion rate compare to other surfaces.

iii. Hair follicles density - large storage, about 10-12 times than SC.

iv. Skin pH.

v. Hydration of skin.

vi. Sweat gland density.

vii. Inflammation of skin disrupted stratum corneum has higher permeability.

viii. Blood flow.

ix. Skin temperature

b. Physicochemical factors [12]

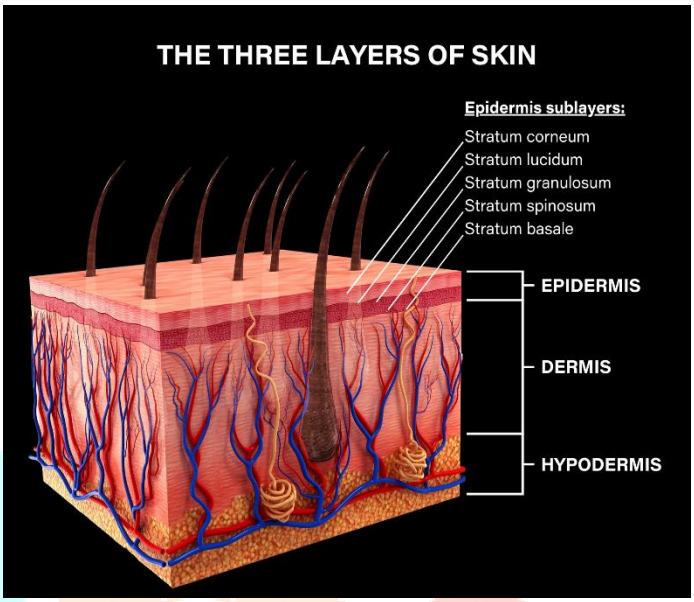
i. Partition coefficient - higher log p value give rise to absorption.

ii. Effect of vehicles - hydro alcoholic gel provides the most efficient absorption through skin.

iii. Degree of ionisation.

iv. Molecular Weight. (less than 400 Dalton)

DIFFERENT LAYERS OF SKIN:-



The skin is composed of three main layers, the epidermis, dermis, and hypodermis, each with unique characteristics and functions.

1.Epidermis :

The epidermis is the outermost layer of the skin in humans and many other animals[18]. It is composed of several layers of cells that provide a protective barrier between the internal tissues and the external environment. The main function of the epidermis is to prevent water loss and to protect against external damage, such as UV radiation, toxins, and microbes. The epidermis also contains cells that produce melanin, which is responsible for skin pigmentation, and cells that play a role in immune defence. The epidermis is the outermost layer of the skin and provides a protective barrier between the body and the external environment. It is composed of several layers of cells, including keratinocytes, melanocytes, and Langerhans cells, among others. The epidermis is responsible for the skin's colour, texture, and waterproofing, and contains sensory receptors that detect touch, pressure, and temperature.

2.Dermis :

The dermis is the second layer of skin that lies beneath the epidermis. It is a thick layer of connective tissue that contains collagen fibres, elastin fibres, blood vessels, nerves, and various other structures[20]. The dermis is responsible for providing strength, elasticity, and support to the skin. It also contains sensory receptors that are responsible for detecting touch, pressure, heat, and cold. The dermis plays a vital role in regulating body temperature and blood flow. Additionally, it contains cells that produce sweat and sebum, which are important for maintaining skin hydration and protection. The dermis is the middle layer of the skin and is composed of connective tissue, including collagen and elastin fibres. It contains blood vessels, nerves, and other structures that support the skin and provide it with nutrients and oxygen. The dermis is also responsible for regulating body temperature, detecting pain, and producing sweat and oil.

3.Hypodermis:

The hypodermis, also known as subcutaneous tissue, is the deepest layer of the skin located beneath the dermis. It is primarily composed of adipose tissue, which serves as a layer of insulation and padding to protect the body's internal organs. The hypodermis also contains blood vessels and nerves that supply the skin and regulate body

temperature. In addition, the hypodermis plays a significant role in energy storage, as it serves as a reservoir for excess calories in the form of fat. The thickness and composition of the hypodermis can vary among individuals and can change over time due to factors such as age, gender, genetics, and lifestyle. The hypodermis is the deepest layer of the skin and is primarily composed of adipose tissue. It provides insulation and padding, helps to regulate body temperature, and serves as a reservoir for energy storage.

CONCLUSION:-

Topical Nanoemulgels have proven to be a more advantageous choice for a dependable and practical drug transport mechanism. In comparison to previous formulations, the gel-like and non-greasy traits enlarge patient compliance and the absence of oil as a foundation improves drug release[19]. With more suitable Spread ability, problems with traditional emulsions such as creaming and phase separation are eradicated based on formulations of nanoemulsion-gel may additionally provide a higher and extra dependable approach for the administration of hydrophobic medications. Many of the tablets used to treat skin infections are hydrophobic in nature. These pills can be successfully delivered as Nanoemulgels by first being built-in into the oil section of the nanoemulsion and then being blended with the gel basis. Despite a few obstacles, nanoemulgel[29] has an accurate chance of being the main topical transport gadget for lipophilic drugs in the future. It offers a variety of transport options for topical medicines used to treat a vast vary of ailments, which includes the ability to adjust drug release as nicely as high drug loading owing to elevated solubilizing efficiency. In addition to the transdermal application, it may additionally be utilized for the ocular, vaginal, dental, and nose-to-brain delivery of medicinal drug for the therapy of quite a few neighbourhood and systemic disorders such as alopecia, periodontitis, and Parkinson's disease.

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