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FORMULATION AND EVALUATION NEW DRUG DELIVERY SYSTEM PHARMACEUTICAL ORGANOGEL: A REVIEW

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ABSTRACT

Topical administration is applied to deliver a drug instantaneously at the point of application, so enough drugs is depleted into the systemic circulation to cause medicinal effects. To develop an effective drug absorption through an intact skin, several topical preparations are used one of that is "Gels". Gels basically used for the purpose of topical dosage form a lot which is to deliver drug across a localized area of the skin. Gel formulation contributes for better approach concept and product stability in respect to ointment, paste and cream. Administration of topical gel drug has a limited drug delivery process anywhere in the body system through skin route, vaginal route, rectal route and ophthalmic route as darmal routes. Generally gels used in wide range as applications in food products, cosmetics products, biotechnology. Most of the gels may be designed according to their nature of the liquid phase, for example, Organic solvent containing are organogels (oleogels) and water as solvent phase called hydrogels. Recent research studies have reported many types of gels for topical drug application, like aerogel, bigel and emulgel. Topical dosage forms like Gels are evaluated with following standard parameters such as pH of formulation, homogeneity of preparation, grittiness of active drug content, extrudability and spreadability of formulation, skin irritation studies, in-vitro release and Stability studies.

INTRODUCTION

Topical route of drug delivery is an Effective route for local and systemic treatment. The local delivery of drugs on the skin is known as dermal or topical route of administration for

local and dermal diseases. Topical dosage form can penetrate most inner and deeper into the skin and gave better systemic absorption of drug content. The skin is the largest sensitive organ of human body. It covers all the entire body parts and serves as defense line against the external environmental stress and microorganisms. Since the skin is the organ that is the most exposed with the environmental factors and the risk of damage of its mechanism and structural defense line may increase the disease chances.

Topical application has many advantages over the conventional dosage forms. In general, they are deemed more effective less toxic than conventional formulations due to the bilayer composition and structure. In the formulation of topical dosage forms, attempts are being made to utilize drug carriers that ensure adequate localization or penetration of the drug within or through the skin in order to enhance the local and minimize the systemic effects, or to ensure adequate percutaneous absorption.

Hydrogels:- Hydrogel is a 3-dimensional (3D) network of hydrophilic polymers that can be swollen in water and hold large amounts of water while maintaining structure due to the chemical or physical bonding of each polymer chain. Hydrogels were first reported by Wichterle and Lím (1960). By definition, water must make at least 10% of the total weight (or volume) for an object to be a hydrogel. Hydrogels also have a level of flexibility very similar to natural tissue due to their important water content. Network hydrophilicity is caused by the presence of hydrophilic groups such as -NH2, -COOH, -OH, -CONH2, -CONH -, and -SO3H.[2]

Organogel: - Organogel is thermodynamically stable, clear, viscoelastic, biocompatible and isotropic gels composed of phospholipids, a suitable organic and polar solvent. The formation of three-dimensional networks at organogel is the result of a change in the micellar level fluid in a low viscous network that includes a span that causes micelles in natural fluids that are not cool.

These reversible circular structures of microcarbid lipid aggregates, the twins progressively form micelles long tubular with background addition, followed by interference to create a three-dimensional temporary network with multiple solutions.

Advantage of organogels

1. **Template vechicle: -** Organogel offers the opportunity to combine a variety of materials. with different physicochemical properties namely: chemical environment, melting, molecular weight, size etc.[4]

2. **Processbenefits:** - Automatic organogel formation due to super molecular self-assembled the arrangement of the surfactant molecule makes the process much easier and easier to manage.
3. **Structural /Physical stability:-** Thermodynamically stable, Structural integrity. The organogels are stored for a long time.[5]
4. **Chemicalstability: -** Organogels are sensitive to moisture and being organic are also microbial resistant pollution.[5]
5. **Topical delivery potential:** - A good balance of hydrophilic and lipophilic character, canproperly separates from the skin and thus improves skin penetration and molecular transport.[6]
6. **Safe:-** The use of biocompatible, biodegradable and non-immunogenic materials makes them safe for long-term use.[6]

Disadvantage

- Should be stored in a proper condition.
- The organogel has greasy property
- Less stable to temperature.

Classification of organogels

1) Lecithin organogels

Lecithin is a phospholipid, extracted from various plants and animal tissues separately from the egg cell. Lecithin derived from natural sources can forms gelled structures and has been caused by the presence of incomplete chemicals within its structure. Synthetic lecithin and hydrogenated soy lecithin failed develop organogels. Apart from the chemical structure, the purity is excluded Lecithin also plays a key role in the formation of organogel. Experimentalresults show that lecithin fails to initiate the gellification process of apolar solvent when lecithin contains <95% phosphatidyl content. Lecithin-based organogels were found to be thermodynamically strong, thermoreversible (solto-gel transition temperature at 40◦C), transparent, viscoelastic, biocompatible.[6,7]

2) Pluronic Lecithin Organogel (PLO):- PLO is an organogel based on soy lecithin containing isopropyl palmitateorisopropylmyristate, water and Pluronic F127 (also known as Poloxamer 407). PLO may or may not contain sorbic acid, which acts as a preservative, in both stages. It occurs as a yellow, odorless and invisible gel that is absorbed by the skin quickly.[8,9]

3) **Premium Lecithin Organogels (PrLOs):-** PrLO is the second most common organogel of lecithin and is able to glide high without its oily and non-tacky nature, providing beauty pleasant reception. This gel does not have a Pluronic derivative, which leads toto avoid skin irritation and thus reactions to the skin intolerance. This gel has been used successfully to detoxify various bioactive agents, namely, diclofenac, ibuprofen, ketoprofen and progesterone, and has been considered the vehicle of choice for the delivery of intradermal drugs.[10,11]

4) **Limonene GP1 / PG Organogel:-** Limonene, terpene, has been found to be an excellent entry enhancer as welltherefore it has been incorporated into various types of transdermal formulations to improve the penetration of bioactive agents across the transdermal layer, thus to improve the bioavailability of the bioactive agent within the skin tissues.[11]

Properties of organogels

a) **Viscoelasticity:-** Viscoelastic materials mean, materials with both viscous and elastic properties. Organogel exhibits a flexible material in a solid state, where it has a low shear rate. As the shear rate increases, the elastic material decreases, because excessive shear stress will disrupt the physical interaction between the fibers present at organogel.[15,16,17]

b) **Non-Birefringence:-**Organogels are naturally isotropic, meaning that bright light cannot pass through them. This organogel character is called a non-birefringent. To look like a dark matrix when tested under polarized light.[18,19]

c) **Thermo reversibility:-** Organogels are more stable than critical temperatures, so that if the system temperature rises above critical temperature it will flow due to the disruption of the solid matrix as a structure. However, it can be reversed by cooling down.[20]

d) **Temperature:-** Generally, organogels are stable in temperature. The stability of the organogel thermo depends on the gelator, which will build a structure that binds itself together in the right conditions and forms a gel system. The free energy of organogel may be reduced due to the gelator molecules that bind to each other and provide stable, less powerful organogels.[21]

e) **Visual clarity:-** Like other gels, organogels may not always be obvious in nature. These can be opaque or transparent. The visual acuity of these systems depends on the

composition of the gel. Egorganogels prepared with sorbitanmonostearate will appear opaque and lecithin appears naturally.[22]

f) Chirality:- The emergence of chiral center in gelator molecules enables them to pack active cells, so that these are thermodynamically and kinetically stable in nature.23

g) Biocompatibility:- Initially, a variety of non-biocompatible materials were used in the manufacture of organogel and made organogel as non-biocompatible. Later organogel was developed with several biocompatible drug delivery.[24]

Application of organogels

a) Organogel as a matrix for transdermal transport for drugs: - Organogel have been successfully investigated as dermal drugs. Example- Aceclofenac [forosteoarthritis, rheumatoid arthritis, and ankylosing spondylitis causes stomach upset when taken orally that is avoided topical transdermal delivery with Ethyl oleate-based lecithin organogel [EO / Lecithin] aceclofenac can be avoid delivery of topical transdermal drugs [applicable to regular hydrogel]. Topical Microemulsion for Aceclofenac is also formulated but with no side effects as needed a large number of surfactants and co-surfactants of solidification of nano-droplets, poor viscosity and dispersion. Although lecithin organogels do not require such a type surfactant or penetration enhancer, as it has both properties. Organogel has a better spread as wellviscosity rather than microemulsion. Soyabean lecithin organogels are better than regular pieces of scopolamine as well broxaterol as it shows the rapid rate of delivery of transdermal drugs. Diclofenac and Indomethacin skin absorption have been found to be increase when used with isopropyl palmitate.25

b) Organogel as iontophoretic transdermal drug delivery system:- Drug delivery rate rises sharply byIntophoresis [especially large hydrophilic topical deliverytypes such as proteins, peptides etc. well-fitting during passive condition] .But, aeries problems if they occur on time application of the solution. This problem overcomes the loaded drugs gels [assists in drug administration] and hydrogels use as a reservoir of iontophorosis drugs but the biggest drawback is it microbial contamination of such aquatic systems. Which leads to cracking of the gel structure, redox reaction and pH change.This problem can be avoided by using organogels as the presence of a living solvent as a continuous phase therefore inhibiting microbial growth.

c) **Organogel as ophthalmic drug delivery systems:-** Eye drops are widely used for eye drug delivery however retreat when most of the drug is not absorbed targeted tissue due to rapid cleansing by the flow of tear therefore a double dose was required. Which leads to the unwanted side outcome and patient adherence. Suspension cannot help this condition as drug release depends on the degre elimination of different drug particles due to continuitychanges in the formation and release of lachrymal fluid. The effectiveness of treatment can be increased by increasing communication the duration of treatment which can be done by extension viscosity but the addition of a viscosity builder like CMC is not possible to improve the situation and in the state of water solubility oil visual acuity was affected. This is difficult can be overcome by oragnogel. High viscosity and organic the solvent as a continuous phase, makes it difficult to wash them. Due to the three-dimensional network of gel drug release in solid level.[26]

d) **Organogel in cosmetics:-** Skin care products in particular emulsion-based [contains water and oil phase respectively lipid]. Some products also contain oil category only.Fat but also organogel belong to this group. That's right It is mainly recommended for skin problem, so it is used in dermatological cosmetics. People with a skin boundary disruption depends on the high dose of life-sustaining lipids due to a certain group on organogel this problem is solved again gain more value. In this case, lip gels are recommended.In contrast to liquid-oils have the same consistency as emulsion cream [gel-like and semi-solid].[25]

e) **Nutraceutical applications:-** Scientists have synthesized fossil fuels and discovered themas an alternative to trans fats and saturated fats, so it can be use in many food products required a specific texture as well rheology without creating significant changes in the final product quality. This method can be completed by synthesis of certain molecules [polymers, amphiphiles, waxes become oily to make oleogels. A polymer similar to Ethylcellulose[is used as a basis for the preparation of many articles and chemicals stable than lubricating oils] that build up oleogels by binding oils at 10% levels have a variety of different properties. Sorbitantooglycerylmonostearatesolegogel with different types of vegetable oil [which can be biodegradabletraditional greasing grease]. Oils like rapeseed as well Soy bean oil [with low-viscosity] produces very strong gels high rates of direct viscoelastic operations.[25]

Preparation of gels: Gels are generally prepared at the industrial scale under room temperature. However few of polymers such-Synthetic and Natural need special treatment before processing. Gels are also prepared by following methods.

1. Thermal changes
2. Flocculation
3. Chemical process/ reaction

Evaluation of gels

Evaluation Parameters of the Formulated Gels:

Measurement of pH

The pH of various gel formulations determined by using digital pH meter. One gram of gel was dissolved in 100 ml water and stored for 2 hours. The measurement of pH of every formulation was done in triplicate and average values are calculated.

Drug content

1 g of the prepared gel was mixed with 100ml of suitable solvent. Aliquots of various concentrations were prepared by suitable dilutions after filtering the stock solution and absorbance was measured. Drug content was calculated using the equation, which was obtained by statistical regression analysis of calibration curve.

Viscosity study

The measurement of viscosity of the prepared gel was done with a Brookfield Viscometer. The gels were rotated at 0.3, 0.6 and 1.5 rotations per minute. At each speed, the corresponding readings were noted. The viscosity of the gel was obtained by multiplication of the dial reading with factor given within the Brookefield Viscometer catalogues3.

Spreadability

It show the extent of area to which gel readily spreads on application to skin or affected area. The therapeutic value of a gel formulation also depends upon its spreading value. Spreadability is expressed in terms of your time in seconds taken by two slides to slip movement from gel which is placed in between the slides under the direction of certain load. Lesser the time taken for the separation of two slides shows better the Spreadability. It's calculated by using the formula: S = M. L / T where, M = wt. tied to upper slide L = length of glass slides T = time taken to separate the slides

Extrudability study

After the gels were set within the container, the formulations were filled within the collapsible tubes. The Extrudability of the formulation determined in terms of weight in grams required to extrude a 0.5 cm. ribbon of gel in 10 second.

Skin irritation study

Guinea pigs were used for the testing of skin irritation. The animals were observed on standard animal feed and had free access to water. The animals were kept under standard and atmospheric conditions. Hair was shaved from back of guinea pigs and area of 4 cm2 was mark done both the edges, one side served as control while the other side was test. Gel was applied (500 mg / guinea pig) twice every day for 7 days and also the site was observed for any sensitivity and the reaction if any, was graded as 0, 1, 2, 3 for no reaction, slight patchy erythema, slight but confluent or moderate but patchy erythema and severe erythema with or without edema, respectively.

In vitro diffusion studies

The diffusion studies of the prepared gels may be concluding in Franz diffusion cell for studying the dissolution release of gels through a cellophane membrane. Gel sample (0.5g) was taken in cellophane membrane and also the diffusion studies were carried out at 37 ± 1° using 250 ml of phosphate buffer (pH 7.4) because the dissolution medium. Five milliliters of every sample was withdrawn periodically at 1, 2, 3, 4, 5, 6, 7 and 8 h and each sample was replaced with equal volume of fresh dissolution medium.

Stability

The stability studies were carried out for all the gel formulation by freeze - thaw cycling. Here, by subjecting the product to a temperature of 4° C for 1 month, then at 25°C for 1 month then at 40°C for 1 month, syneresis was observed. After this, the gel is exposed to ambient temperature and liquid exudate separating is noted 10.1. Homogeneity After the gels are set within the container, all developed gels were tested for homogeneity by visual inspection. They were tested for their physical appearance and presence of any aggregates. Grittiness all the formulations were evaluated microscopically for the presence of any appreciable particulate which was seen under microscope. Hence obviously the gel preparation fulfills the need of freedom from particular matter and from grittiness as desired for any topical preparation.[11]

DISCUSSION

Topical formulations include creams, ointments, pastes, gels etc. Out of which gels are getting more popular now a days because they're more stable and can also provide controlled release than other semisolid preparations. The gel formulation can provide better the absorption characteristics and hence the effective bioavailability of drug. It also provides the information regarding to the formulation and evaluation parameters of the novel herbal gel for anti-inflammatory activity and show the better therapeutic effects to patient compliance.

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