An Emerging Era in Topical Delivery: Organogels

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Abstract
Semisolid preparations for external application to skin have gained much demand, since it is easily absorbed through the skin layers. Many novel topical dosage forms have been discovered, among which organogels appears to play an important role. Organogels are thermodynamically stable, biocompatible, isotropic gel, which not only give localised effect, but also systemic effect through percutaneous absorption. Although different types of gelator molecules are being used for the development of organogels, both egg and soya lecithin are mainly focused. The purity of lecithin is also considered to be an important factor in gelation. Apart from lecithin, non-ionic surfactant based microemulsion gels and pluronic organogels are also being developed. Compared to conventional topical dosage forms, these novel formulations are found to be more advantageous and efficient. In future, organogels can give way to many promising discoveries in the field of topical dosage forms. The current review aims at giving an idea about organogels, its applications and importance in topical delivery.

Key words:
Percutaneous, Semisolid, Phospholipid, Lecithin

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INTRODUCTION
Skin being the largest organ is a vital part of human body. With an average surface area of 1.5 to 2 square meters, the skin holds numerous blood vessels which make the absorption of drugs easy through topical application. Topical dosage forms have always been a convenient method of drug delivery among which semisolid dosage forms have always proven to be the

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most effective dosage forms for localized drug delivery and these include creams, ointments, pastes, gels etc. Several novel drug carrier systems have been evolved, which offer sustained release of the drug or which provide a stable environment for the incorporation of APIs. The various properties which make semisolid dosage forms in demand are smooth texture, elegant appearance, non-grittiness, non-greasiness, non-irritating nature, miscibility with the skin secretion, ease of application, prolonged stability etc. Among the different topical applications available, gels have attained keen importance due to its easy absorption through skin layers. There has been much advancement in the field of topical delivery and many novel formulations have evolved. The novelty in ointments is related to its bases, eg: enhancement in absorption of water, high permeation and prevention of evaporation of moisture from the skin, inclusion of ingredients that prevent skin irritation and so on. They are even safer to use, compatible with a wide range of drugs and also release the drug in a controlled manner. In addition to ointments, the other novel semisolid dosage forms include creams incorporated with microspheres, produced by emulsion method for prolonged release and retention on skin, emulsion containing liquid paraffin as creams, creams with lipid nanoparticles which contains fats and oils, like liquid and semisolid paraffin which produces a high degree of occlusiveness, thereby preventing a rough feeling on application to the skin. Novel discoveries have also been done on gels, which have been explained below in detail. The objective of this review is to give an insight into the importance of topical drug delivery, the advancements made and also to give an idea about the novel semisolid preparations, emphasising mainly on organogels.

**TYPES OF CONVENTIONAL TOPICAL DOSAGE FORMS**

1. **Ointments**

They are soft semisolid preparations containing medicaments which are used for external application to the skin. It may be dermatological, ophthalmic, rectal, depending upon the area to which it is applied.

2. **Pastes:**

They are also semisolid preparations, which are used for external application but are usually stiffer, less greasy and more absorptive, but less penetrative compared to ointments.

3. **Creams:**

These are soft, semisolid emulsions of oil in water type or water in oil type emulsion containing medicaments, meant for external use. It is mainly used for cosmetic purposes and is considered as protective in nature.

4. **Gels:**

These are semisolid preparations, which have properties like transparency and non-greasiness, which make them highly absorptive. Usually a liquid phase would be entrapped inside a 3-dimensional polymer network which is formed as a result of high level of crosslinking.

5. **Poultices:**

They are soft semi-liquid preparations meant for external use. It is applied to the skin, when hot and should retain heat for a long time, so that it releases the medicament in the presence of heat, inorder to supply warmth to the concerned part of the body. eg: Kaolin Poultice B.P 58

6. **Plasters:**

Plasters are semisolid masses, which adhere to the skin. They are usually spread over a backing material from which the drug is released slowly.

7. **Rigid Foams:**

Semisolid preparations in which air would be emulsified in liquid phase. eg: shaving creams, aerosolised creams etc.

The above mentioned conventional formulations are being used from ancient times till today in different names and forms. It has some of the disadvantages like:
1. Drugs having high lipophilicity and partition coefficient can only be used.
2. Not suitable for drugs that cause irritation to the skin.
3. Can be effective only in case of localized delivery.
4. Stability problem

**IMPORTANCE OF ORGANOGELS**

For the delivery of drugs into the skin layers, many strategies and systems have been examined. Out of the topical applications available, gels are obtaining more popularity because of the ease of application and better absorption through the skin layers. Novel semisolid preparations in gels include, controlled release gels, organogels, extended release gels, amphiphilic gels, hydrophilic gels, non aqueous gels, bioadhesive gels etc.

**Controlled Release Gels:**
These are gels which control the release of drug substances from the respective formulations. Both charged and uncharged drug substances can be used.

**Extended release gels:**
Semi solid preparations in which drug core is surrounded by polymers which help in slow release of the drug.

**Amphiphilic gels:**
Here both the solid phase and the liquid phase would be mixed together and then heated to form a clear phase. On cooling the mixture would be jellified which is a result of aggregation of the gelator molecules.

**Hydrogels:**
These include incorporation of the drug with a suitable hydrophilic polymer and solvent, so that the polymer degrades slowly to release the drug present in the core.

**Organogels:**
These are semisolid preparations which include gelator substance, non polar solvent and a polar solvent. The addition of polar and non-polar solvent leads to the formation of 3 dimensional network which is formed due to the growth of reverse micelles. The above said mixture could be heated and then cooled to get a jellified structure.

Among these dosage forms, organogels can be prepared by the easiest method and also cost effective and thus can be considered as superior to the others. These are formed mainly by the fusion of phospholipids, appropriate organic solvent, along with a polar solvent. Here the organic phase would be entrapped inside a 3 dimensional network, which is formed due to the formation of reverse micelles, as a result of addition of polar phase to non polar phase. The phosholipid is dissolved in organic solvent and the addition of the appropriate amount of water, leads to the formation of gel. Here the phospholipids act as the gelator molecule, non-polar solvent as continuous phase and water as polar solvent.\[1-5\] The amount of organic solvent and the non polar solvent is critical for the formation of gel. Mainly lecithin (soya and egg), polymeric surfactant pluronic F 127, and other surfactants like Tween, Span, Sorbitan monostearate etc are being used for the preparation of organogels, as these have already proven to be good penetration enhancers, thereby rendering it a better chance to be used as a topical delivery system.\[6\] The type of organic solvent used is also considered as an important factor in organogelation. The various types of inorganic solvents which could be used is described by Scartazzini R and Luisi PL20 and Schurtenberger P et al. These differ from hydrogel in the sense that in the latter no non polar solvent is used. In a study conducted by I.M Shaik et al, lecithin organogel was proven to be more penetrative through the skin, when compared with that of the hydrogel.\[8\]

Organogels have been studied to have many applications in pharmaceuticals, nutraceuticals, cosmetics, food and so on. The scope of organogels, further increases, since the topical route becomes one of the convenient methods of drug delivery. Since it is
easy to manufacture the commercialization process may also become cost effective. Moreover it could also be able to cure chronic diseases like osteoarthritis, when appropriate analgesic drugs are incorporated. Now-a-days exposure to UV rays is giving way to skin cancer in people. Organogels can become a viable alternative, if anticancer agents are delivered through them, which has not been tried till date. The main disadvantage of these novel drug delivery systems include the toxicity through the non polar solvents and stability problems which may be cured by the usage of edible oils and other less toxic penetration enhancers.

MECHANISM OF SKIN PERMEATION OF ORGANOGELS AND ORGANOGELATION

Skin is made up of multiple layers of different types of tissue, which is protective in nature. The 3 main skin layers include: Epidermis, Dermis and Hypodermis

**Figure 1. Human Skin** [16]

For the efficient transfer of semisolid preparations to the skin, these have to be highly penetrative in nature. Due to the formation of cylindrical network, as a result of increase in area of lecithin polar region because of the addition of polar solvent, the gel formation takes place. Since the non polar solvent acts as penetration enhancer, organogels would penetrate through the skin easily. The steps involved in skin penetration include:

1. Formation of thin film on the skin surface.
2. Dissolution of drug in carrier system and diffusion to the skin surface.
3. Partitioning of drug through the epidermal layer.

MECHANISM OF ORGANOGELATION

As mentioned above the mechanism of gel formation occurs during the addition of polar solvent to lecithin non polar mixture, when 3-dimensional network of reverse micelles forms, which is shown in the figure.

**Figure 2. Mechanism of Organogelation** [15]

ADVANTAGES OF ORGANOGELS

1. Ease of preparation.
2. Cost reduction due to less number of ingredients.
3. Longer shelf life.
4. Thermodynamically stable.
5. Since it consists of both hydrophobic and hydrophilic components, both hydrophobic and hydrophilic drugs can be incorporated.
6. Organic solvents could be of natural origin, eg: sunflower oil, mustard oil, etc which have been already studied.

Recently an article has been published on organogels based on lecithin, which explains how it could be used for skin aging.[1] In addition to that, it could also
be used for the treatment of many skin disorders like psoriasis, skin cancer etc, because of the fact that it act as a viable carrier system for topical delivery. Research works on organogels have been done mainly in transdermal, percutaneous delivery of various drugs like NSAIDS. [8-11] Compared to the conventional topical delivery systems; organogels can have a better scope as a carrier system, due to the fact that it has numerous advantages.

### Table No.1: Organogel Formulations Used as Drug Delivery [8-14]

<table>
<thead>
<tr>
<th>No.</th>
<th>Formulation</th>
<th>Constituents</th>
<th>Drug used</th>
<th>Evaluation Techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lecithin Organogel</td>
<td>Soya lecithin, Ethyl Oleate, Water</td>
<td>Aceclofenac</td>
<td>Solubility Analysis of drug, Viscosity Measurement, Dynamic Light Scattering, Invitro efficacy, Histopathological studies</td>
</tr>
<tr>
<td>2</td>
<td>Surfactant and polymer based Organogel</td>
<td>Oil phase: Gelucire 44/14, Plurol oleique, Lauroglycol 90 Water phase: Sodium alginate, Glycerin, water</td>
<td>Ayclovir</td>
<td>Skin permeation studies, HPLC Analysis</td>
</tr>
<tr>
<td>3</td>
<td>Non-ionic surfactant based Organogel (microemulsion based)</td>
<td>Tween 80, Span 20, isopropyl myristate,n-butanol,water</td>
<td>Zidovudine</td>
<td>Physicochemical characterization, droplet size determination, determination of type of emulsion( dye test), FTIR, stability studies</td>
</tr>
<tr>
<td>4</td>
<td>Sorbitan monostearate Organogel</td>
<td>Sorbitan monostearate, Tween, water</td>
<td>Propanolol Hydrochloride</td>
<td>Invitro drug diffusion study, physicochemical characterization, stability studies</td>
</tr>
<tr>
<td>5</td>
<td>Sorbitan monostearate Organogel</td>
<td>Sorbitan monostearate, sorbic acid, tween 20, isopropyl myristate, potassium sorbate, water</td>
<td>Aceclofenac</td>
<td>Psychorheological characterization, drug content studies, Viscosity analysis, Spreadability, Invitro skin permeation, stability studies</td>
</tr>
<tr>
<td>6</td>
<td>Sorbitan monostearate Organogel</td>
<td>Sorbitan monostearate, isopropyl myristate, Different types of non polar solvents like Eucalyptus oil, n-octanol, propylene glycol, PEG (polyethylene glycol), ethyl alcohol, isopropyl alcohol</td>
<td>Oxytetracycline hydrochloride</td>
<td>Psychorheological characterization, drug content studies, extrudability, homogeneity, Invitro drug diffusion study, Anti-microbial study</td>
</tr>
<tr>
<td>7</td>
<td>Lecithin organogel</td>
<td>Egg and soya lecithin, Ethanol, triethanolamine, Ethyl oleate, water</td>
<td>Aceclofenac</td>
<td>Physicochemical characterization, photon microscopy, skin irritation, Drug content determination, Invitro drug release evaluation</td>
</tr>
<tr>
<td>8</td>
<td>Lecithin microemulsion gel</td>
<td>Soya lecithin, isopropyl palmitate (IPM),water</td>
<td>Indomethacin, diclofenac</td>
<td>Invitro skin permeation study, FTIR, Dynamic Light Scattering, Scanning Electron microscopy</td>
</tr>
<tr>
<td>9</td>
<td>Lecithin stabilised microemulsion based organogel</td>
<td>Soya lecithin, IPM, water</td>
<td>Ketorolac tromethamine</td>
<td>Invitro efficacy, drug content study, HPLC Analysis</td>
</tr>
<tr>
<td>10</td>
<td>Lecithin stabilised organogel</td>
<td>Lecithin, IPM, water, glycerol</td>
<td>Clobetasol propionate</td>
<td>Stability studies, Optimisation with Ternary phase diagram, Statistical analysis, Invitro studies.</td>
</tr>
<tr>
<td>11</td>
<td>Surfactant based organogel</td>
<td>Glyceryl monostearate, Glyceryl disteareate, Glyceryl stearate, IPM, fractionated coconut oil, glycerol caprate</td>
<td>Piroxicam</td>
<td>Invitro and Invivo efficacy studies.</td>
</tr>
<tr>
<td>12</td>
<td>Pluronic lecithin organogel</td>
<td>Soya lecithin, sorbic acid, IPM, Pluronic- P-127, potassium sorbate,water</td>
<td>Flurbiprofen</td>
<td>Drug content studies, viscosity determination, Diffusion study</td>
</tr>
</tbody>
</table>

### CONCLUSION
To summarize it can be said that organogels have evolved as one of the potential carrier system for topical delivery. When compared to other lipid based carrier systems, these prove to be better in terms of efficacy, feasibility and shelf life. Thus transforming drug molecules into novel formulations like organogels can help in cost effective and productive research. In future this carrier system can become a milestone in the field of topical delivery.

### ACKNOWLEDGMENT
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15) Http://www.google.co.in/imgres?q=human+skin&hl=en&safeflactive&biw=1366&bih=561&gbv=2&tbnm=isch&tbnid=3Cg4rvGuvDKoGM