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Comprehensive Review on Organogel: As a New Formulation

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ABSTRACT:

A gel is a semi solid formulation having the solvent phase which is organogel (apolar) or hydrogel (polar) that immobilized this inside the voids contained in 3-D network structure. Organogel are composed of two continus system of gelators and polar solvents that may or may not the water molecule is trapped may or may not be they self assembled structure of gelators.when concentration is around 14-16 % used. The gelators undergoes chemical or physical interaction, in the resulting the formation of self assembled fibrous structure that become with each one another,in the result they formed three dimensional network structure. In the resulting three dimensional network like structure are block the flow of a polar phase. Lecithin, sorbitan monosterate, cholesteryl anthraquinone derivative and sterol are examples of gelators. The some special characteristic such as viscosity, thermo-reversibility and versatility impart longer shelf life of organogel and ease to preparation of organogel. The characteristic are easily to be adjust by simple formulation, in that the result highly-structured architectures. The organogel have capacity to trap the hydrophobic and hydrophyllic compound within the structure have also wide scope to use of organogel in different delivery system. These characteristic make the structures of high quality matrices with ability to deliver an effective drug concentration over a long period of time, they increase the chance of patient difference. Hence this article discuss the various aspects of it.

Key Word : Topical Delivery System, Organogel, lecithin, Organogelator

Background:

Organogel is the part of polymer chemistry , which is made by organic liquid phase in presence of three dimensional , that also have cross-linked network Organogels are an important class of gels, and are similar to hydrogels owing to their residences as liquid-infused tender substances. no matter the giant preference of liquid media and well matched networks that can provide a broader variety of properties, highly few research are pronounced on this vicinity. This review presents the applicability of organogels concerning their preference of additives, unique homes, and packages. Their specific capabilities compared to other gels are mentioned, which include multi-stimuli responses, affinity to a vast variety of materials, thermal and environmental balance, digital and ionic conductivity, and actuation. The active position of solvents is highlighted inside the versatility of organogel houses. to distinguish between organogels and other gels, these are categorised as gels full of unique organic drinks, such as especially polar organic solvents and binary solvent systems. maximum promising packages of organogels as state-of-the-art multipurposeful substances are mentioned in mild in their particular features. The gadgets are of sure together through robust kinds of vanderwaal forces to be able to shape crystalline amorphous regions throughout the whole device. The organogels have decrease hydrations, the drug dissolving polymer and is transported among the chains. pass linking will increase hydrophilicity of gels & diminishes the diffusion rate of drug

Introduction :

Topical dosage form which are formulated for applied on topically like skin. these formulation are applied to skin for its therapeutic effect or physical effect that for it capable to act as skin protection or protectants , drying agent , emollients , lubricants, localized effect , etc. for their specialized effect in presence of medicinal agent. the formulation must be sold the over the counter which contain mixtures or combination of medicinal substance that are used in the preparation of such condition as major or minor like skin infection ,surgery, itching , bruise , acne, psoriasis , and skin allied infection. that medication is carried out all over body via the circulatory system in a topical drug delivery system the skin location has been identified as a significantly channel in the topical drug delivery system , its make for essential and extensivelyaccessible organ for topically administration or application. The main benefits of applying formulation topically that include delivering the medication directly to the target of activity and long duration action of effect. By avoiding first pass and second pass metabolism of the drug from irritating the gastrointestinal tract, topically medication or formulation improves the drug's bioavailability . which can be maximise the local effect while minimizing the systemic absorption that provide satisfactory limitation or penetration of the drug throught the skin as part of a topical dosage form.In that topical formulation or skin application must required a prescription which generally contain a single dosage form for intended to diagnosed and treatment on that condition [1]

1. Material and method

1.1 Materials :

Gelator compounds which kindly denoted by ceras marti (Barcelona spain), and its main properties or composition shown in table. The virgin olive oil basically use commercial origin (Azeite Gallo, Lisbon, Portugal) and was purchased at local supermarket.

Natural waxes	Melting point	Acidity Value	Saponification Value	Ester Content
Bees wax	60-64	13-23	81-103	69-79
Euphorbia Cerifera Wax	68-72	12-21	42-62	30-42
Vegitable Wax	79-85	02-07	77-94	70-87

1.2 Methods of organogel Preparation :

In order to obtain a dispersion mixture, organogels are prepared by heating a mixture of gelato and an organic liquid or organic solvent after cooling. The temperature in the room leads to the formation of a jelly structure. Organogelator molecule interactions induce a gelator organization into well-defined aggregates, such as tubular rods, fibrils and threads. The preparation of organogel is carried out mainly by three methods: fluid filled fiber mechanism, solid method.[2]

1.2.1 Fluid –Filled Fiber Mechanism

In gelation process takes place with addition of amount of water in the solution of polar solvent and surfactant like lecithin molecule.before addition of water firstly prepare the surfactatnt dispersed in the organic medium then addition the small amount of water. The surfactant molecule assemble themselves in the form of micelles. Further the addition of waater then makes short tubular or cylindrically micellar aggregates. Water molecules is bind stoichiometrically to the hydrophyllic head of the molecules. One water molecule is linked with two surfactant molecules this forms a linear network with hydrogen molecule bonds between the phosphate group of lecithin molecule and polar molecule. In further addition of little amount of water in which the result is formation of worm like and flexible tuvular micellar structure. The tubular micellar micro structure is formed interwine and overlap with other formed by 3-D gel fibers and fibrils network, which possesses viscoelasticity and thermo-reversibility properties. [3]

1.2.2 Solid fiber Mechanism :

The solid fiber mechanism is involved in the dispersion of solid organogelators in to polar solvent bt the hot emulsification then the formation of a polar lmixture of organogelator in liquid form. After cooling at room temperature, organogelator molecules. These solif fiber physical interaction each other is three dimentional fibrillar network structure. The polar solvent is immobilized by the semi solid organogel and fibers is formed [4,5,6,7,57]

1.2.3 Hydration Mthod :

In that method the gel is prepared by directly hydration inorganic chemical, which are produced a dispersed phase of the dispersion in the addition of water vehicle or other agent such as propylene glycol , hydroxyl propyl cellulose and propyl gallate it may be used for the enhance gel formation

2 Type of Organogel

2.1 Lecithin organogel :

Lecithin oganogel is formed when the small amount of polar substances and water is added polar substances such as ethylene glycol , formaamide and glycerol are added to the non aqueous solution of lecithin [8,9,10,11]The molar ratio of water $w_o = [H_2O]/[Lecithin]$ is typically 2:10 it depend on the organic solvent. Excessive leads to stabilization of the gel and separation of phase. A long range of non aqueous solution as fatty acid, amine, ether, esters, cyclic alkanes and branched or linear containing lecithin gel is adiing the small amount of water. Gell formation is thought to change in the structure of the micelles in the non aqueous medium . if the add the water to cause the axial growth of the micelles in to cylindrical micelles, it overlap and entangle or formed the three dimenstional network [12] they increase the viscocity and they found the result in gel formation are these result [11,13]Drug incorporation in the lecithing organogels.[57]

2.2 Pluronic Lecithin Organogel :

Pluronic lecithing gel is derived from the organogels. It is opaque, yellow gel, PLO is composed of soy lecithin, isopropyl palmitate, water and pluronic F127 ,hydrophyllic polymer. PLO in that the main contain of is pluronic F-127 or poloxomer 407 it is tri block copolymer in main contain is polyethylene (70%) molecular weight is 12500Dalton [14,15,57]

PLO was devloped by the compounding In US by pharmacist Marty Jones and woek mate Lawson kloesel in the early 1990s as a topical vehicle for transdermal and topical drug delivery pluronic F127 was added to the lecithin organogel in order to stabilise the formulation. [16,17] about that PLO formed a many theory they claims PLO has unique in nature that theypenitrate the barrierlayer of the skin and it give much more theraputicv effect it mainly used for NSAIDs, Antifungal, antipsychotic, opioids, antifungal, antiemetics and hormonal drug [18] it absorbs quickly and not found any irritation allergy in the skin. Hence on the basis of literature review we say PLO is a promising vehicle in the transdermal drug delivery system. According to the International journal of Pharmacutical compounding (IJPC) currently 85s PLOs formulation are available in the market. Transdermal PLO cream are very popular.Depend upon the patient requirement in themarketed PLOs creams and gels which are loaded with with drugs.[19]

2.2.1 Mechanism of action PLOs through the skin

Stratum corenum (SC) is main barrier barrier for the drug permeation in the skin hence the limitation of chemical penetration enhancers are widely used for the transdermal drug delivery system, The chemical penetration enhancers are create the skin irritation and sensitization. Because the chemical enhancers after they penetration is distruped the lipid layer of the skin. Lecithin structure is disorganised of the skin, enduring it open the skin pores and increase the drug penetration.[20]Fig.1

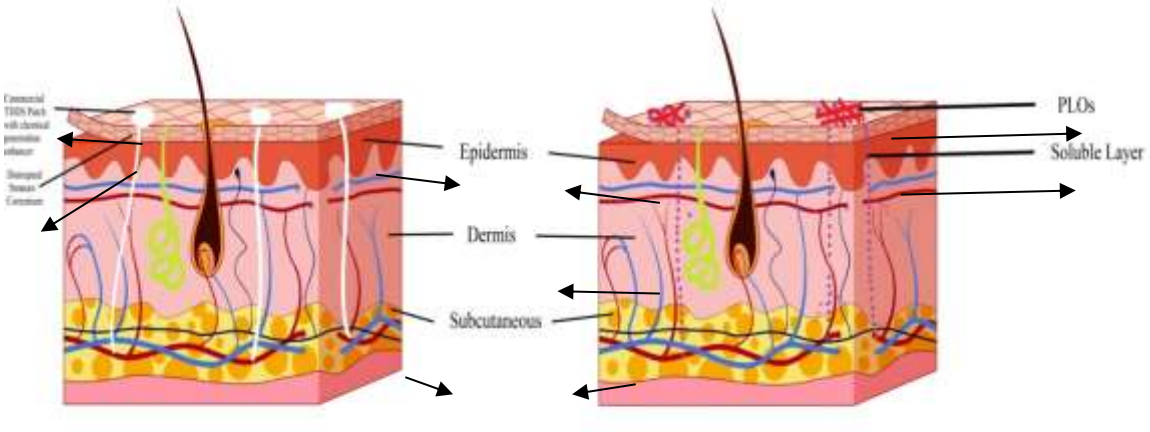


Fig. 01 MECHANISM ACTION OFPLOs WITH RESPECT TO OTHER TRADITIONAL TRANSDERMAL DRUG DELIVERY SYSTEM[20]

2.3 Micro Emulsion Based organogel(MGB) :

Micro emulsion based organogel are different form but most of the organogels are used the gelator,gelatine, it is hydrophilic polymer in nature. Micro emulsion based organogel are prepared by dissolving solid gelatine in hot water in oil W/O micro eulsion by cooling. [21] in the research studies researchers expected the gelatine was dissolved in the water droplet of the W/O microemulsion but after cooling of the system would result in gelation of water droplets,which leads toclouding of the system or phase separation, they whole MGBs are transparent and semi solid with high viscocity or high electro-conductivity. In water by oil MGB comparing 80-9-% of oil phasehas been gelled[22] topically applied to the skin.in the investigational study the MEBo are iontophoretic transdermal drug delivery system[23]

2.3.1 Mechanism of Micro Emulsion Based Organogel :

The first of microemulsion based organogelwas entrapment of the enzyes,lipase, for catalysis and esterification [24]. Application in drug delivery system, they formulated with pharmaceutically acceptable oil (eg.isopropyl)

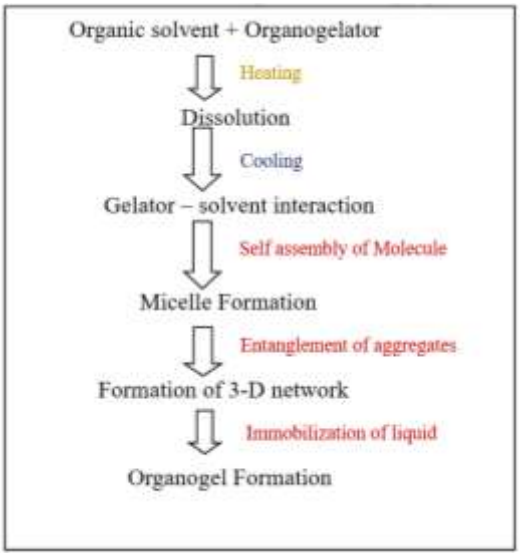
2.3 Eudragit organogel :

Eudragit organogel: Eudragit organogel is formed the different types which use some mixtures of Eudragit. It contains (30-40%w/w) of high concentration of Eudragit in containing polyhydric alcohol, glycerol, propylene glycol, and liquid polyethylene glycol this mixture is used in these organogel. In that,

the organogel preparation method drug (Salicylic acid, sodium salicylate, Ketoprofen) are dissolved in the prepared gel in which containing propylene glycol. They are poured into eudragit powder and quickly mixed with the mortar pestle for 60 seconds. [25,26] These eudragit organogel viscosity was measured by the instrument of penetrometer and spreadmeter [25]Gel viscosity was determined to increase with increasing concentrations of Eudragit and to lower with growing drug content material. [25,57]

2.3.1 Mechanism of organogelation:

Organogelation is generally induced by the insert of polar solvent in to the organogel. If lecithin is present in then it assemble self in to reverse spherical micelles at conc of 0.01 mM. This is triggered by addition of minimum and critical amount of polar additives which bind the hydrophyllic head in lecithin. They create linear networks. If the polar additives is increased, then it result the formation of adjustable, long tub shape micelles of 2.0 to 2.5 nm in radius and 100 to 1000 nm in length. After the overlapping each other they entangle themselves and build the 3D network.[27,28,29]



3 Properties of organogel :

3.1 Viscoelasticity :

Viscoelasticity term is related to the two properties is that viscosity and elasticity. This properties is also authenticated by stress relaxation studies [30,31,6,42] this also act s solid at lower shear stress (elasticity) and a flowing fluid at escalated shear stress [27,32, 38]. In that the lower shear rates, there no pressure acting over that so it behave like solids with intact structure but at higher stress they behave like 3D mesh network with start structure rupturing,permitting this flow. Hence the observation of the organogel appear to follow the Maxwell model of viscoelasticity. Organogel are also similar to other gel system and it observed the retain plastic flow behaviour. Organogel are obtained a 3D network in the solvent, interfere with the activity of the flow of liquid. The rheological way of acting the gelator solution and it interact with the solvent and it influence the flow properties of organogel [30,27]

3.2 Optical clarity :

Optical clarity is the transparency of organogel which depends on the chemical makeup. For example PLOs are the opaque and sorbitan monostearate organogel wher the lecithin organogel are transpaprent in colour in nature[33,34]

3.3 Thermostability :

The nature of the organogel make them thermostable. The gelators are undergo to assemble in suitable condition to produce organogel it responsible for therostability of the organogel. The overall free energy of the system they decrese the gelation undergo self assembly,yielding a low energy and make thermostable. At the raised temperature, the organogel molecule aquire kinetic energy to reduce or loss in their structure, and little temperatue they regain its original structure. This integral properties of the organogel is responsible for to make it longer shelf life, thereby making it ideal for the delivery of the bioactive compound.[27,35,36]

3.4 Thermoreversibility :

Orgranogel is distorted the matrix structure when the temperatature is extent from its critical point hence it start the flowing. In that added the thermal energy that cause interaction of the organogel is disrupted in the structure. But the temperature decreased,the interaction of that molecules is also retarded, in that the result rebersily back of its original function. This phenomenon called as thermo reversibilityproperty of organogel for example, PLOs when

heated above the 25^0c this is the critical temperature of this organogel, they lost solid matrix configuration and after the cool they return to the itsstable configuration. [37,35]

***3.5 Biocompatibility* :**

In previously , the organogel is formulated by different non biocompatible components, which result in non biocompatible organogels [38,39] currently , research on organogel involved the different biocompatible components such as coca butter, vegitable oil has icreased their potential for extend use in biomedical formulation.[27,32,36,40]

***3.6 Non – Birefringence* :**

This is the optical properties of the material that allows propagation of light passing the polarized light. Organogel are the non-birefringent, that they does not allow the prapogation of polarised light in the matrix. In the result organogel are observed under the polarised light, they appear as dark matrix. That is attributed to isotropic property[32,35,41,42]

4 Evaluation Parameter :

4.1 Physical Examination :

It is a preliminary test in this test they inspected the colour, phase separation, texture, appearance and odour etc.[41]

4.2 Water content:

Evaporation of water it cause viscosity to drop, which impair the stability of the gel. They measure the water content in organogel by use NIR Spectroscopy (NIR,1800-2200)[43]

4.3 Stability study :

The organogel formulation are tested by stored away from in light tube at 40^0C and 75%RH at 3 month the n the sample are tested their pH,viscosity,% of drug release, physical appearance and drug conent. [44,45]The stability study of organogel is also determine at different temperature and different relative humidity condition as per ICH guidelines i) 25^0c ± 2^0c at 75 ± 5%RH ii)) 40^0c ± 2^0c at 75 ± 5%RH.[56]

4.4 pH :

pH is concentration of the H+ ion negative logaritham of the formulation is determines the indirectly of the skin. pH is determine by using the pH meter which are standardized with standard buffer of pH 4 and pH 7. This is measured by using electrode which are deep in to the sample 10-15 min prior to taking the reading.[31]

4.5 Drug Content :

When the deteremination of drug content take 1 gm of prepared gel and mix with 100 ml of solvent. A stock solution of different concentration prepared with suitable diluation after the stock solution was prepared and measured. Drug content is calculation by using the equation of linear regression calculation by using calibration curve[46]

4.6 Viscosity :

The measurement of organogel viscosity by the Brookfield viscosity. The sample is rotated up to 10 rpm by using instrument at 0.3,0.5 and 10 rpm after the rotated then settled for 5 min then reading the value of viscosity. Viscosity is determined by the value of cps form.[46]

4.7 Spreadability :

In these parameter the the area of organogel is how much area spread and it determined the spread area. Organogel is spreads with uniformly when apply on skin or affected area. Spreadability is measured by time (second) take by two slide to flip of from gel is placed between the slides under the influence of load. Spreadability is expressed by gm.cm^2/second. This is calculated by using the formula S=M.L/T where, M= weight tied to upper slide L= Length of glass slides T= Time taken to separate the slide.[46]

4.8 Homogeneity :

Homogenesity is tested after the container is filled, all developed organogel is inspected by visual inspection. Appearance and any aggregation is presence is also observed by visual inspection[46]

4.9 In vitro diffusion studies

These study can be carried out by Franz diffusion cell. Take gel sample (0.5 gm) was take in the cellophane membrane and diffusion study is carried out by at 37 ± using 250 ml of buffer solution at 7.4pH (Phosphate buffer) then withdrawl 5ml of sample and dissolve the medium periodically at 1 to 8 hour at every one hour and the n sample is replaced with the equal volume of fresh dissolution medium. Then the sample is analyse the percent of drug is release in phosphate buffer solution as blank sample[46,47,56]

4.10 Globular size is distribution in organogel :

Globular size and its distribution is determined by Malvern Zetasizer. Approximately 1.0 gm sample is dissolved in doubled distilled water and agitated to the homogenious dispersion medium. Sample is injected in to photocell of zetasizer. Mean distribution and globular diameter is obtained [48]

4.11 Stability studies :

The organogel is stored away from light in collapsible tube at 40 ^{0}c and 75% RH for 3 months. After the storage sample is tested for their viscosity,pH,physical appearance, % drug release and drug content [49,50]

5. Factor affecting on organogels:

5.1 Temperature:

Organogel are less stable in increased temperature, that cause disruption of the 3D mesh network like structure is formed. Temperature is also affect on viscosity. When the temperature is increased then the viscosity of the the organogel is decrease 4 hence the temperature range during their storage should be closely maintained [27,32,48]

5.2 pH:

A pH change minor the reversible transition is formed a gel state to solution state [51] hence , pH can change the physical state of the gels

5.4 Purity:

The component used in organogel it should be in pure form. If they have any impurity in the component may lead to instability in the network matrix, for example lecithin is unable to induce gelation if not used in pure[52,53]

5.5 Moisture:

Organogel is swell when it exposed to moisture as they absorb the water molecule from it this aid in the instability of the organogel [32]

6 Application of organogel :

6.1 A) Application in topical drug delivary system:

The skin is the largest tissue organ in the body which provide the good bioavability of the drug,that mean to enter the systemic circulation by the permeation through in the skin it passes the first-pass metabolism. Pluronic lecithin organogels (PLOs) it contain isopropyl pamitate/myristate as an apolar solvent it used in NSAIDs as a vector (diclofenac,ketoprofen,flurbiprofen),used as analgesic. Organogels loaded with piroxicam are used in the treatment of rheumatoid arthritis. Organogel forming in situ condition L-alanine injectableused for the releasing of macromolecular drugs. PLO with with mometasone furoate used in the treatement of psoriasis and fluconazole loaded organogel on olive oil for the treatment of fungal infection, have positive result is exhibited[54,55,56]

6.2 B) oral and trans-mucosal drug delivery system:

In these system drug are delivered through oral cavity with the help of bio-adhesive organogels, this drugs is administered by implants. These drug are dissolved with organic solvent and mixed with muco-ashesive polymer.12-HSA-soyabean oil in organogel was used for the ibuprofen[27]oral organogel is prepared by incorporating an NSAIS to achievetheraputic effect[56]

Conclusion:

Organogel is visco-elastic substance made by gelling organic solvent with a bio active compound. The potential for to change or execrete several compounds and restraint procedure for various formulation types due to their special features and explore to all aspect of their application due to their properties. The organogel have a vast area of application, although possess rare limitations and drawbacks. These are administered the body via various drug delivery route, the most of used as topical route for many more reasons. A stable organogel designed all the bio-compatible compounds might attract the commercial market in professional choice of different formulation and consumer

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