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Emulgel: An opportunity in topical drug delivery development

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Abstract
An extraordinary part of dermatological pharmacology is the immediate openness of the skin as an objective organ for analysis and treatment. The blend of hydrophilic cells in hydrophobic intercellular material gives a hindrance to both hydrophilic and hydrophobic substances. Inside the significant gathering of semisolid arrangements, the utilization of straightforward gels has extended both in beautifiers and in drug arrangements. Despite numerous benefits of gels a significant impediment is in the conveyance of hydrophobic drugs. Many benefits of gels a significant limit is in the conveyance of hydrophobic medications. An extraordinary perspective of dermatological pharmacology is the immediate openness of the skin as an objective organ for analysis and treatment. The mix of hydrophilic cells in hydrophobic intercellular material gives a barrier to both hydrophilic and hydrophobic substances. Truth be told, the presence of a gelling specialist in the water stage changes over a classical emulsion into an emulgel. These emulgel are enjoying significant benefits on novel vesicular frameworks just as on conventional frameworks in different aspects. Various pervasion enhancers can potentiate the impact, So emulgels can be utilized as better skin drug conveyance frameworks over present systems. The utilization of emulgels can be expanded in analgesics and antifungal medications.

Keywords: emulgels, topical drug delivery system, penetration enhancer

Introduction

Emulgels are emulsions, both of the oil-in-water or water in-oil type, which are gelled by blending in with agelling specialist. They have a high understanding accept ability since they have the beforehand mentioned advantages of the two emulsions and gels. Therefore, they have been as of late utilized as vehicles to deliver different medications to the skin. They are additionally called as creamed gel, quassi emulsion and gelled emulsion. (Joshi Baibhav *et al*, 2012) Both oil-in-water and water-in-oil emulsions are widely utilized for their remedial properties and as vehicles to convey different medications to the skin. Emulsions have a specific level of polish and are handily washed off at whatever point wanted. They likewise have a high capacity to infiltrate the skin. What's more, the formulator can handle the consistency, appearance, and level of oiliness of corrective or dermatological emulsions. Oil-in-water emulsions are generally helpful as water-launderable medication bases and for general corrective purposes, while water-in-oil emulsions are utilized all the more broadly for the treatment of dry skin and emollient applications. Gels for dermatological use have a few great properties, for example, being thixotropic, greaseless, effectively spreadable, effectively removable, emollient, nonstaining, viable with a few excipients, and water-dissolvable or miscible. (Magdy I Mohammad, 2004)

So emulgels have a high understanding adequacy since they have, recently referenced benefits of the two emulsions and gels. In this way, they have been as of late utilized as vehicles to convey different medications to the skin.(Joshi Baibhav *et al*, 2012) In the neighborhood Egypt ianmarket, 2 emulgels are accessible: Voltaren emulgel (Novartis Pharma, Basle, Switzerland), containing diclofenac diethylamine, and Miconaz-H emulgel (Medical Union Pharmaceuticals, Abu-Sultan, Ismailia, Egypt), containing miconazole nitrate and hydrocortisone.(Magdy I Mohammad, 2004)

Emulgel forming components

1. Drug

In emulgel, the drug component is either oil or liquid phase and it is rarely as insoluble solid.

2. Oil phase

It contributes oil phase in microemulsion. Mineral oils alone or in combinations with soft or hard paraffins are widely used for vehicle for the drug consequently non-biodegradable mineral and castor oil which provide local laxative effect and fish liver oil or various vegetable origin oils like arachis, cottonseed and maize oils as a nutritional supplements are used for oral preparations.

Table 1: Some of examples used for the oil phase

Oil	Quantity	Dosage Form	References
Isopropyl myristate	According to phase diagrams	Emulsion	Subramaniam, N. Drug Dev. Ind. Pharm.
CAPMUL	According to phase diagrams	Emulsion	Subramaniam, N. Drug Dev. Ind. Pharm.

Clove oil	According to phase diagrams	Microemulsion	Syamasri G., Ind. J. Of Biochem. & Biophysics
Light liq. paraffin	7.5%	Emulgel	Mohammed M.I., AAPS
Propylene glycol	3-5%	Gel	Arellano A., European J. Pharma. Sci.
Isopropyl myristate	According to phase diagram	Microemulsion	Doaa Ahmed, J. Pharmacy & Pharmacology
CAPMUL MCM L8	According to phase diagram	Microemulsion	Hyun J. Cho, Int. J. Pharmaceutics
Clove oil	According to phase diagram	Microemulsion	N. Chandrashekharan, IJPER

Emulsifiers

These are the agents which used both to facilitate emulsification at the time of manufacture and control stability during shelf life that can vary from days for prepared emulsion to months or years for commercial preparations. Some of the examples are polyethylene glycol 40 stearate, sorbitan mono-oleate (span 80), polyoxyethylene sorbitan monooleate (tween 80), stearic acid, sodium stearate, Polyoxyethylene (20) sorbitan monolaurate**.**

Gelling agent

These are the agents which increase the consistency of formulation and also used as thickening agent.

Table 2: Examples of Gelling agent

Gelling Agent	Quantity	Dosage Form	References
Carbopol 934	1%	Emulgel	Mohamed M.I.,AAPS
Carbopol 940	1%	Emulgel	Dignesh K.,I.J.P.Tech
HPMC 2910	2.5%	Emulgel	Mohamed M.I.,AAPS
HPMC	4%	Gel	Varun T., Drug Inv.Today
Xanthan gum	1%	Gel	Varun T., Drug Inv.Today
HPMC K_4M	1.3%	Emulgel	Baibhav J., IJDDR

Permeation enhancers

These are the agents which interact with the skin constituents to produce a temporary and reversible increase in skin permeability. (Joshi Baibhav *et al*, 2011) (Panwar A. S. *et al*, 2011) [18] (Khullar R. *et al*, 2012)

Table 3: Examples of Permeation enhancers

Permeation Enhancer	Quantity	Dosage Form	References
Oleic acid	1%	Gel	Mortazavi, SA, IJPS
Mentha oil	6%	Emulgel	Rachit K., Saudi Pharma. Journal
Clove oil	10%	Emulgel	Rachit K., Saudi Pharma. Journal
Olive oil	6%	Gel	Abid H., P. J. Pharma. Sci.
Oleic acid	10%	Gel	Varun T., Drug Inv. Today
Propylene glycol	10%	Gel	Varun T., Drug Inv. Today
Tween 80	5%	Gel	Varun T., Drug Inv. Today
Brij 92	0.5%	Emulgel	Doaa Ahmed, J. Pharmacy & Pharmacology

4. pH Adjusters

These agents are used to adjust final pH of the formulation near to skin pH. Eg. Diethanolamine, lactic acid, monoethanolamine, triethanolamine, sodium hydroxide, sodium phosphate, citric acid.

5. Antioxidants

These are used to prevent oxidation of the formulation and make formulation stable over shelf life. Eg. Butylated hydroxyl toluene (BHT).

6. Preservative

Preservatives are added to prevent microbial growth. eg. Propyl paraben, methyl paraben, etc. (Gibson M., 2008)

Advantages of using Emulgel as a Topical Drug Delivery System

1. Hydrophobic drugs can be easily incorporated into gels using d/o/w emulsions

Most of the hydrophobic drugs cannot be incorporated directly into gel base because solubility act as a barrier and problem arises during the release of the drug. Emulgel helps in the incorporation of hydrophobicdrugs into the oil phase and then oily globules are dispersed in aqueous phase resulting in o/wemulsion. And this emulsion can be mixed into gel base. This may be proving better stability and release of drug than simply incorporating drugs into gel base.

2. Better stability

Other transdermal preparationsare comparatively less stable than emulgels. Like powders are hygroscopic, creams shows phase inversion or breaking and ointment shows ranciditydue to oily base.

3. Better loading capacity

Other novel approacheslike niosomes and liposomes are of nano size and due to vesicular structures may result in leakage and result in lesser entrapment efficiency. But gels dueto vast network have comparatively better loading capacity.

4. Production feasibility and low preparation cost

Preparation of emulgels comprises of simpler and short steps which increases the feasibility of the production. There are no specialized instrument sneeded for the production of emulgels. Moreover materials used are easily available and cheaper. Hence, decreases the production cost of emulgels.

5. No intensive sonication

Production of vesicular molecules need intensive sonication which may result in drug degradation and leakage. But this problem is not seen during the production of emulgels as no sonication is needed.

6. Controlled release
Emulgels can be used toprolong the effect of drugs having shorter t1/2. (Joshi Baibhav *et al*, 2011) (Panwar A. S. *et al*, 2011) [18] (Khullar R. *et al*, 2012)

Method of Preparation Emulgel (Singla v.*et al* 2012) [3]
Step 1: Formulation of Emulsion either O/W or W/O
Step 2: Formulation of gel base
Step 3: Incorporation of emulsion into gel base with continuous stirring
The flow chart of emulgel preparation is shown in figure 3.

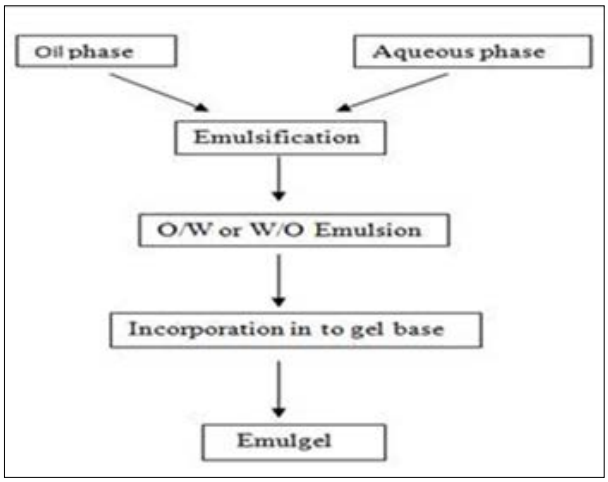

Fig 1: Flow chart of emulgel preparation

Characterization of Emulgel
1. Physical Examination
The prepared emulgel formulations areinspected visually for their color, homogeneity, consistency and phase separation.

2. Rheological Studies
The viscosity of the different emulgel formulations is determined at 25°C using a coneand plate viscometer with spindle 52 (Brookfield Engineering Laboratories,) and connected to athermostatically controlled circulating waterbath.

3. Spreading Coefficient
Spreadibility is determined by apparatus suggested by Mutimer *et al* (1956) which issuitably modified in the laboratory and used forthe study. It consists of a wooden block, which his provided by a pulley at one end. By this method, spreadibility is measured on the basis of 'Slip' and 'Drag' characteristics of emulgels. Aground glass slide is fixed on this block. Anexcess of emulgel (about 2 gm) under study isplaced on this ground slide. The emulgel is the nsandwiched between this slide and another glass slide having the dimension of fixed groundslide and provided with the hook. A 1 Kg weightis placed on the top of the two slides for 5minutes to expel air and to provide a uniformfilm of the emulgel between the slides. Excess of the emulgel is scrapped off from the edges. The top plate is then subjected to pull of 80 gm.With the help of string attached to the hook andthe time (in seconds) required by the top slide tocover a distance of 7.5 cm be noted. A shorterinterval indicates better spreadibility.

4. Extrudability Study of Topical Emulgel (Tube Test)
It is a usual empirical test to measure the force required to extrude the material from tube. The method applied for determination of applied shear in the region of the rheogram corresponding to a shear rate exceeding the yield value and exhibiting consequent plug flow.In the present study, the method adopted forevaluating emulgel formulation for extrudabilityis based upon the quantity in percentage ofemulgel and emulgel extruded from lacqueredaluminum collapsible tube on application ofweight in grams required to extrude at least 0.5cm ribbon of emulgel in 10 seconds. Morequantity extruded better is extrudability. The measurement of extrudability of eachformulation is in triplicate and the averagevalues are presented. The extrudability is thancalculated by using the following formula:

Extrudability = Applied weight to extrudeemulgel from tube (in gm) / Area (in cm2)

5. Swelling Index
To determine the swelling index of preparedtopical emulgel, 1 gm of gel is taken on porousaluminum foil and then placed separately in a50 ml beaker containing 10 ml 0.1 N NaoH. Then samples were removed from beakers at different time intervals and put it on dry place for some time after it reweighed. Swelling index iscalculated as follows:

Swelling Index (SW) % = [(Wt – Wo) / Wo] ×100.

Where (SW) % = Equilibrium percentswelling,
Wt = Weight of swollen emulgel aftertime t,
Wo = Original weight of emulgel at zerotime

6. Drug Content Determination
Take 1gm of emulgel. Mix it in suitable solvent. Filter it to obtain clear solution. Determine it sabsorbance using UV spectrophotometer. Standard plot of drug is prepared in the same solvent. Concentration and drug content can be determined by using the same standard plot by putting the value of absorbance in the standard plot equation

Drug Content= (Concentration×Dilution Factor× Volume taken) × Conversion Factor.

7. Skin Irritation Test (Patch Test)
The preparation is applied on the properly shaven skin of rat and its adverse effect like change in color, change in skin morphology should be checked up to 24 hours. The total set of 8 rats can be used of the study. If no irritationoccurs the test is passed. If the skin irritationsymptom occurs in more than 2 rats the study should be repeated.

8. Ex–Vivo Bioadhesive StrengthMeasurement of Topical Emulgel
The modified method isused for the measurement of bioadhesive strength. The fresh skin is cut into pieces and washed with 0.1 N NaoH. Two pieces of skin were tied to the two glass slide separately from that one glass slide is fixed on the woodenpiece and other piece is tied with the balance on right hand side. The right and left pans were balanced by

adding extra weight on the left –hand pan. 1 gm of topical emulgel is placed between these two slides containing hairless skin pieces, and extra weight from the left pan is removed to sandwich the two pieces of skin and some pressure is applied to remove the presence of air. The balance is kept in this position for 5 minutes. Weight is added slowly at200mg/min to the left- hand pan until the patchdetached from the skin surface. The weight (gram force) required to detach the Emulgel from the skin surface gave the measure of bioadhesive strength. The bioadhesive streng this calculated by using following formula

Bioadhesive Strength = Weight required (in gm)/ Area (cm2)

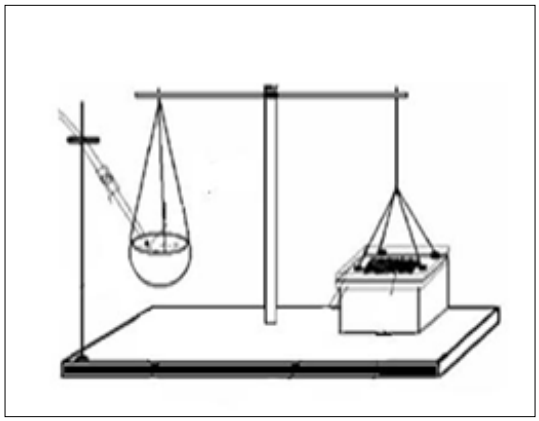

Fig 2: Setup for bioadhesive test

9. *In vitro* Release/Permeation Studies

In vitro release studies were carried out using Franz diffusion cell [singala *et al* 2012].

10. Stability Studies

The prepared emulgels were packed in aluminum collapsible tubes (5 g) and subjected to stability studies at 5°C, 25°C/ 60% RH, 30°C/65% RH, and 40°C/75% RH for a period of 3 months. Samples were withdrawn at 15-day time intervals and evaluated for physical appearance, pH, rheological properties, drug content, and drug release profiles. (Joshi B. *et al* 2011) [4].

Conclusion

As the emulgel is the recent techniques for the topical drug delivery it is better suitable for hydrophobic drugs and obviously it is very good techniques for drug delivery of combination of both hydrophilic and hydrophobic drugs mainly the hydrophobic drug formulation can developed with emulgel techniques because it contain both oil and aqueous (i.e gel phase) In the coming years, topical drug delivery will be used extensively to impart better patient compliance. Since emulgel possesses an edge in terms of spreadibilty, adhesion, viscosity and extrusion, they will become a popular drug delivery system. Moreover, they will become a solution for loading hydrophobic drugs in an water soluble gel bases.

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