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FORMULATION AND EVALUATION OF HERBAL ORAL EMULGEL

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Abstract:

Emulgel is used to treat aches and pains caused by colds, headaches, muscle aches, backaches, arthritis and other conditions and injuries. The patient adherence to topical formulations is significant in relation to chronic skin diseases, like fungal infections, acne, psoriasis. Emulgel is one of the recent technology in NDDS used topically having characteristics of dual control release i.e. emulsion as well as gel. Emulgels have emerged as one of the most interesting topical delivery systems as it has dual release control system i.e. gel and emulsion. When gel and emulsion are used in combined form, the dosage form are referred as Emulgel.

Keywords: Emulgel, Gelling agents, Topical drug delivery, Skin diseases

INTRODUCTION:

Herbal medicines are the oldest known form of human health care. Even today herbal medicines are widely used. About 80% of the population still uses herbal medicine, and it uses plant extracts and active ingredients in traditional therapy. Emulgel is a combination of "emulsion'' and "gel'' which is a new approach for topical deliver drugs. These formulations range in consistency from solid through semisolid to liquids. It has a double control release like emulsion and gel. Emulsion and gels are have importance due to many reasons; they have better application property in comparison to classical formulation as creams and ointment, they have faster and more complete release of the drug from the vehicle to the skin, also they are convenient to apply on hairy skin due to the absence of greasiness and lack of residue upon application. These are superior in terms of use and patient acceptability. Emulgels have several complimentary properties for topical use such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, long shelf life, bio friendly, transparent and pleasing appearance. Sometime the two formulations are combined to increase drug delivery. Most of the topical preparations are used for the localized effects by virtue of drug penetration into the underlying layers of skin or mucous membranes. Gels are a relatively newer class of dosage form created by entrapment of large amounts of aqueous or hydro alcoholic liquid in a network of colloidal solid particles, which may consist of inorganic substances, such as aluminum salts or organic polymers of natural or synthetic origin. The term of medicinal plants include a various types of plants used in herbalism and some of these plants have a medicinal activities. Such herbal medicines that are easily available, cheaper, time tested and considered safer than most of modern synthetic drugs.

Type of Emulgel Based on the type of emulsion-

- **Macroemulgel**: Size of dispersed phase droplets more than 400 nm and prepared by High Energy and Low Energy Method.
- **Micro Emulgel**: Droplet Size between 1 nm to 100 nm. Prepared by Phase Inversion And Phase Titration Method.
- **Nano Emulgel**: Droplet size is less than 1 nm

Advantages of Emulgel

1. Increased patient acceptability.
2. Provide targeted drug delivery.
3. Easy termination of the therapy.
4. Improve bioavailability and even the low doses can be effective in comparison with other conventional semi solid preparation.
5. Stable formulation by decreasing surface interfacial tension resulting in increase in viscosity of aqueous phase, more stable than Transdermal preparations that are comparatively less stable, powders are hygroscopic, creams shows phase inversion or breaking and ointment shows rancidity due to oily base.

6. Hydrophobic drug can be incorporated in emulgel using emulsion as the drug carrier that is finally dispersed in the gel.
7. Provide the controlled effect of that enhance the prolong effect of the drug with short half life.
8. Easy and cost-effective preparation.
9. Drug loading capacity is better than other novel approaches like niosomes and liposomes

DISADVANTAGES of Emulgel

- Skin irritation on contact dermatitis
- The possibility of allergenic reactions
- The poor permeability of some drugs through the skin
- Drugs of large particle size are not easy to absorb through the skin
- The occurrence of the bubble during formulation of Emulgel
- Hydrophobic drugs are the best choice for such delivery systems.

Rationale of Emulgel as a topical drug delivery system

Many widely used topical agents like ointment, cream, lotion have many disadvantages. They have very sticky causing uneasiness to the patient when applied. Moreover, they also have lesser spreading coefficient and need to apply with rubbing. And they exhibit the problem of stability also. Due to all these factors within the major group of semisolid preparation, the use of transparent gels has expanded both in cosmetics and in a pharmaceutical preparation. A gel is a colloid that is typically 99% wt. liquid, which is immobilized by surface tension between it and a macromolecular network of fibres built from a small amount of a gelatin substance present. In spite of many advantages of gels, a major limitation is in the delivery of hydrophobic drugs. So to overcome this limitation an emulsion based approach is being used so that even a hydrophobic therapeutic moiety can be successfully incorporated and deliver through gels . Numbers of medicated products are applied to the skin or mucous membrane that either enhances or restores a fundamental function of skin or pharmacologically alters an action in the underlined tissues. Such products are referred as topical or dermatological products. Many widely used topical agents like ointments, creams lotions have many disadvantages. They are sticky in nature causing uneasiness to the patient when applied, have lesser spreading coefficient so applied by rubbing and they also exhibit the problem of stability. Due to all these factors within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations. In spite of many advantages of gels, a major limitation is in the delivery of hydrophobic drugs.

Classification of topical preparation

Solid preparation	Semisolid preparation	Liquid preparation	Miscellaneouspreparation
1.Topical powder	1.creams	1.Liniment	1.Taps and Gauzes
2.Plasters ointment	2.Poultics	2.lotion	2.Rubbing alcohols
3.Poultics	3.Gels	3.solution	3.Liquid cleaner
	4.Suppositories	4.tinctures	4.topical aerosol
	5.ointment	5.Emulsions	
	6.pastes	6.Suspensions	
		7.Paints	

Factors affecting topical absorption of drug

Physiological factors

1. Skin thickness.
2. Lipid content.
3. The density of hair follicles.
4. The density of sweat glands.
5. Skin pH.
6. Blood flow.
7. Hydration of skin.
8. Inflammation of skin.

Physicochemical factors

1. Partition coefficient.
2. The molecular weight

Emulgel preparation

Aqueous material

This forms the aqueous phase of the emulsion. Commonly used agents are water, alcohols.

Oils

These agents form the oily phase if the emulsion. For externally applied emulsions, mineral oils, either alone or combined with soft or hard paraffin, are widely used both as the vehicle for the drug and for their occlusive and sensory characteristics. Widely used oils in oral preparations are non-biodegradable mineral and castor oils that provide a local laxative effect, and fish liver oils or various fixed oils of vegetable origin (e. g., Arachis, cottonseed, and maize oils) as nutritional supplements

.

Table 1: Use of oils

Chemical	Quantity	Dosage form
Light Liquid Paraffin	7.5%	Emulsion and Emulgel
Isopropylmyristate	7-7.5%	Emulsion
Isopropyl stearate	7-7.5%	Emulsion
Isopropyl palmitate	7-7.5%	Emulsion
Propylene glycol	3-5%	Gel

Emulsifiers

Emulsifying agents are used both to promote emulsification at the time of manufacture and to control stability during a shelf life that can vary from days for extemporaneously prepared emulsions to months or years for commercial preparations. e. g. polyethylene glycol 40 stearate , sorbitan monooleate (span 80) , polyoxyethylene sorbitan monooleate (tween 80) , stearic acid , sodium stearate.

Gelling agent

These are the agents used to increase the consistency of any dosage form can also be used as thickening agent .

Table 2: Use of gelling agents

Gelling agent	Quantity	Dosage form
Carbopol-934	0.5%-2%	Emulgel
Carbopol-940	0.5%-2%	Emulgel
HPMC-2910	2.5%	Emulgel
HPMC	3.5%	Gel
Sodium CMC	1%	Gel

Permeation enhancers

These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability

Table 3: Use of penetration enhancers

Penetration enhancer	Quantity	Dosage form
Oleic acid	1%	Gel
Lecithine	5%	Gel
Urea	10%	Gel
Isopropyl myristate	5%	Gel
Linoleic acid	5%	Gel
Clove oil	8%	Emulgel
Menthol	5%	Emulgel
Cinnamon	8%	Emulgel

Preparation of Emulgel

Emulgel was prepared by the method reported by [28] with minor modification. The Gel in formulations were prepared by dispersing Carbopol 934 in purified water with constant stirring at a moderate speed and carbopol 940 in purified water with

constant stirring at a moderate speed then the pH are adjusted to 6 to 6.5 using triethanolamine (TEA). The oil phase of the emulsion was prepared by dissolving Span 80 in light liquid paraffin having the drug in ethanol solution while the aqueous phase was prepared by dissolving Tween 80 in purified water. Methyl and Propylparaben was dissolved in propylene glycol and was mixed with the aqueous phase. Both the oily and aqueous phases were separately heated to 70 ° to 80 °C; then the oily phase was added to the aqueous phase with continuous stirring until cooled to room temperature. And add glutaraldehyde in during of mixing of gel and emulsion in ratio 1:1 to obtain the Emulgel.

Evaluation of emulgel

Fourier transforms infrared spectroscopy (FTIR)

The primary objective of this investigation was to identify a stable storage condition for the drug in solid state and identification of compatible excipients for formulation.

Physical examination

The Prepared emulgel formulations were inspected visually for their colour, homogeneity, consistency and phase separation.

Determination of pH

pH of the formulation was determined by using digital pH meter. pH meter electrode was washed by distilled water and then dipped into the formulation to measure pH and this process was repeated 3 times.

Measurement of viscosity

The viscosity of the formulated batches was determined using a Brookfield Viscometer (RVDV-I Prime, Brookfield Engineering Laboratories, USA) with spindle 63. The formulation whose viscosity was to be determined was added to the beaker and was allowed to settle down for 30 min at the assay temperature (25±1 °C) before the measurement was taken. Spindle was lowered perpendicularly into the centre of emulgel taking care that spindle does not touch the bottom of the jar and rotated at a speed of 50 rpm for 10 min. The viscosity reading was noted.

Spreadability

To determine spreadability of the gel formulations, two glass slides of standard dimensions were selected. Formulation whose spreadability was to be determined was placed over one slide and the other slide was placed over its top such that the gel is sandwiched between the two slides. The slides were pressed upon each other so as to displace any air present and the adhering gel was wiped off. The two slides were placed onto a stand such that only the lower slide is held firm by the opposite fangs of the clamp allowing the upper slide to slip off freely by the force of weight tied to it. 20 g weight was tied to the upper slide carefully. The time taken by the upper slide to completely detach from the lower slide was noted.

Globule size and its distribution in emulgel

Globule size and distribution is determined by Malvern zeta sizer. A 1.0 g sample is dissolved in purified water and agitated to get homogeneous dispersion. The sample was injected to photocell of zeta sizer. Mean globule diameter and distribution is obtained.

Swelling index

To determine the swelling index of prepared topical emulgel, 1 g of gel is taken on porous aluminium foil and then placed separately in a 50 ml beaker containing 10 ml 0.1 N NaoH. Then samples were removed from beakers at different time intervals and put it on a dry place for some time after it reweighed.

In vitro drug release study

The in vitro drug release studies of the Emulgel were carried out on Diffusion cell using egg membrane. This was clamped carefully to one end of the hollow glass tube of dial y sis cell. Emulgel (1g) was applied onto the surface of egg membrane dialysis membrane. The receptor chamber was filled with freshly prepared PBS (pH 7.4) solution to solubilize the drug. The receptor chamber was stirred by a magnetic stirrer. The samples (1 ml aliquots) were collected at suitable time interval sample were analysed for drug content by UV-visible spectrophotometer after appropriate dilutions. Cumulative corrections were made to obtain the total amount of drug released at each time interval. The cumulative amount of drug release across the egg membrane was determined as a function of time. The cumulative % drug release was calculated using standard calibration curve.

Microbiological assay

Ditch plate technique was used. It is a technique used for evaluation of bacteriostatic or fungi static activity of a compound. It is mainly applied for semisolid formulations. Previously prepared Sabouraud's agar dried plates were used. Three grammes of the Gellified emulsion are placed in a ditch cut in the plate. Freshly prepared culture loops are streaked across the agar at a right angle from the ditch to the edge of the plate.

Skin irritation test

A 0.5 g sample of the test article was then applied to each site (two sites per rabbit) by introduction under a double gauze layer to an area of skin approximately 1" x 1" (2.54 x 2.54 cm2). The Gellified Emulsion was applied on the skin of a rabbit. Animals were returned to their cages. After a 24 h exposure, the Gellified emulsion is removed. The test sites were wiped with tap water to remove any remaining test article residue

Stability studies

The Gellified Emulsion was applied on the skin of a rabbit. Animals were returned to their cages. After a 24 h exposure, the Gellified emulsion is removed. The test sites were wiped with tap water to remove any remaining test article residue [32]. The prepared emulgels were packed in aluminium 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 mo. Samples were withdrawn at 15-day time intervals and evaluated for physical appearance, pH, rheological properties, drug content, and drug release profiles.

CONCLUSION

The topical drug delivery system will be used extensively due to 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 a water soluble gel bases.

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