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A REVIEW ON HERBAL EMULGELS

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ABSTRACT

Herbal molecules are known for their potent action and fewer side effects but they have draw backs like low bioavailability, High molecular weight, Low lipophilicity etc. To overcome such drawbacks novel drug delivery systems are employed. One of such an approach is Emulgel. Gel formulations commonly offer faster drug release than conventional ointments and creams. Major limitation of gel is in the difficulty of hydrophobic drugs delivery. So to solve these limitations, emulgels formulations are considered. Combination of gels and emulsions dosage forms is called as Emulgels. Recently, Emulgels is used for topical drug delivery systems. The use of emulgels includes analgesics and antifungal drugs. This review article is focused on herbal formulation, emulgel containing essential oils and herbal drugs. In fact presence of a gelling agent in water phase converts a classical emulsion in to emulgel. The emulgel for dermatological use has several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water-soluble, longer shelf life, bio-friendly, transparent & pleasing appearance.

KEYWORDS: Emulgels, topical delivery, Herbal drugs, penetration enhancers.

INTRODUCTION

Herbal medicines are the oldest form of health care known to mankind. World Health Organization (WHO) has defined herbal medicines as finished, labeled medicinal products that contain active ingredients, aerial or underground parts of the plant or other plant material or combinations. WHO estimates that 80% of the world populations presently use herbal medicine for primary health care. Herbal drugs have certain advantages over traditional

medicines such as lower risk of effects, widespread availability, low cost and efficacious for lifestyle diseases for prolonged period of time. suppress symptoms and ignore the underlying disease processes But these herbal extracts/plant actives suffer from various limitations such as stability in highly acidic pH, liver metabolism etc. led to drug levels below therapeutic concentration in the blood resulting in less or no therapeutic effect.[7] Also most of the plant actives such as glycosides, tannins, flavonoids, etc. are polar in nature and poorly absorbed due to large molecular size limiting the absorption via passive diffusion, poor lipid solubility hence preventing their ability to cross the lipid-rich biological membranes. These limitations lead to reduced bioavailability and hence, low therapeutic index of plant actives.[8] Hence considerable attention has been given to development of novel drug delivery system for herbal drugs. The novel carriers should ideally fulfill two requirements, Firstly; it should deliver the drug at a rate directed by the needs of the body, over the period of treatment. Secondly, it should channel the active entity of herbal drug to the site of action. Novel drug delivery attempts to either sustain drug action at a predetermined rate or by maintaining a relatively constant effective drug level in the body with minimization of undesirable side effects. Are gaining more attention for better therapeutic response.[11]

EMULGEL

Emulgel is emerging field for the topical drug delivery, and till date it has less marketed product, so it is interesting and challenging to focus on emulgel. Before going to emulgel we need to know the advantages of emulsion and gel that is being used for the topical drug delivery. Emulsions are controlled release systems containing two immiscible phase in which one is dispersed (internal or discontinuous phase) into other (external or discontinuous phase), with the use of emulsifying agent to stabilize the system. emulsion are of oil-in-water or water-in-oil type, where the drug particle entrapped in internal phase passes through the external phase and then slowly gets absorbed into the skin to provide controlled effect. USP defines gel as a semisolid system consisting of dispersions made up of either small inorganic particles or large organic molecules enclosing and interpenetrated by liquid. The gel contains the larger amount of aqueous or hydro alcoholic liquid in a cross linked network of colloidal solid particles where it captures small drug particles and maintain the controlled release of drug.

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

1. Poor absorption of macromolecules.
2. Entrapment of bubble during formulation.
3. Hydrophobic drugs are the best choice for such delivery systems.

Table for Emulgels Drug

S. No	Emulgel Drugs	Uses	Ingredient
1.	Hydrophobic Drug	Analgesic, Antifungal, Antinflammentory, Anti-acne, Various cosmetic formulation.	Geling Agent, Carbopol, Sodium CMC, Pentration inhancer- clove oil, menthol.
2.	Loratadine	Hypersensitivty, Itching, Redness, Sunburn, Insect bites.	Liquid paraffin, propylene glycol, cetrimide, Methyl paraben, propyl paraben, Distilled water.
3.	Metronidazole Emulgel	Acne vulgaris, Skin lesions, Wound drainage, Wound odor.	Capmul 908-P, Acconon MC-8 EP (polyoxyethylene (8) Propylene glycol
4.	Meloxicam	Treatment of Rheumatoid Arthritis	Tween20 and San20, gelling agents (HPMC K4 and Carbopol 934). liquid paraffin (5 and 7.5%) and Cetyl Alcohol

5	Sunscreen emulgel Cinnamomum burmannii stem bark	Protect to sun	extract, olive oil, sodium lauryl sulfate, methyl paraben, propyl paraben
6.	Terminalia chebula Retz. leaves exract,	Antibacterial, Fevers, cough, asthma astringent,	Carbopol 940, Methyl Paraban, Propyl Paraben, Propylene glycol-400
6.	Lantana camara leaves	itches, cuts, ulcers, swelling	Carbopol 934, Na CMC, HPMC, HPMC K15M, HEC, Span
7.	Emulgel of Pothos scandens Linn	Skin disease, boils,swellings, wound ulcers	HPMC K4M. Carbopol 934,
8.	Cosmeceutical herbal emulgel for skin care	Wrinkles, fight acne	*Cucurbita pepo* Seeds, Carbopol 940, Propylene glycol and liquid paraffin
9.	Herbal Anti Psoriatic Emulgel	Use in Anti Psoriatic drug	Commiphora mukul, babchi oil
10.	Cinnamomum burmannii Nees	Antioxidant, antibacterial	NA
11	Capsicum frutescent	Antioxidants, analgesic, rheumatoid arthritis pain and inflammation	NA
12	Cosmetical herbal emulgel for skin care	Reduce wrinkles, fight acne and to control oil secretion, skin anti-aging, nourishes the skin	NA
13	Jojoba oil	Anti-fungal activity: Dermatological research	Candistan and Canesten
14	Heracleum Siamicin	Anti-microbial activity:	NA
15	Pothos Scandes oil	Skin disease, boils, swellings, wound ulcers, dropsy, menorrhagia, vomiting, flatulence and burning sensations. The extract is also reported regarding its usage in the treatment of cuts and wounds. Wound Healing Activity: Wound Healing Activity	The study was conducted to formulate herbal emulgel of Pothosscandens using gelling agents like carbopol 934, Carbopol 940 and HPMC K4M.[13]
16	Lemongrass oil	Analgesic, Antidepressant, antimicrobial antipyretic, antiseptic, astringent, bactericidal, fungicidal, galactogogue, sedative and tonic substance.	cow ghee emulgel is superior to that of all formulation including marketed.
17	Cucurbita pepo oil	Vitamins. moistens and nourishes the skin, moistening and nourishing the skin[15]	NA
18	Camellia seed oil	anti-oxidant activities anti-ageing, improve skin barrier function and promote	NA

		keratinocyte differentiation, antioxidant and antimicrobial activities of rose oil	
19	Commiphora mukul and babichi oil	Anti-psoriatic activity:	
20	Lanata camara	wound healing activitys	Carbopol 934, Na CMC, HPMC, HPMC K15M, and HEC.
21	Menthe oil	Skin protective, sunscreen, antiacne, antiwrinkle and antiaging	Oil, Carbapol 940, mentha oil.
22	Ricinus Communis	Psoriasis	Ricinus Communis Extract, ethanol, propylene glycol, methyl paraben, propyl paraben, EDTA disodium, tri-ethanolamine and required amount of distilled water.

RATIONALE

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 preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations.

Factors Affecting Topical Absorption of Drug

Physiological Factors

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

Formulation of Emulgel Preparation

1. Aqueous Material

This forms the aqueous phase of the emulsion. Commonly used agents are water, alcohols.[28]

2. Oils

These agents form the oily phase if the emulsion. For externally applied emulsions, mineral oils, either alone or combined with soft or hard paraffins, are widely used both as the vehicle for the drug and for their occlusive and sensory characteristics. Widely Used oils in oral preparations are nonbiodegradable 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.[29-30]

3. 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.eg Polyethylene glycol 40 stearate, Sorbitan monooleate (Span 80), and Polyoxyethylene sorbitan. Monooleate (Tween 80), Stearic acid, Sodium stearate.

4. Gelling Agent

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

5. Permeation Enhancers

These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability.[38]

EMULGEL PREPARATION

Emulgel was prepared by the method reported by Mohammad et al (2004) 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 Tri ethanol amine (TEA). The oil phase of the emulsion were prepared by dissolving Span 20 in light liquid paraffin while the aqueous phase was prepared by dissolving Tween 20 in purified water. Methyl and Propyl paraben was dissolved in propylene glycol whereas drug was dissolved in ethanol and both solutions mixed with the aqueous phase. Both the oily and aqueous phases were separately heated to 70° to 80°C; then the oily phase were 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.

Characterization Emulgel

Physical appearance

The prepared Emulsion formulations were inspected visually for their color, homogeneity, consistency and pH. The pH values of 1% aqueous solutions of the prepared Gellified Emulsion were measured by a pH meter (Digital pH meter DPH 115 pm).

Spreadability

Spreadability is determined by apparatus suggested by Mutimer et al (1956) which is suitably modified in the laboratory and used for the study. It consists of a wooden block, which is provided by a pulley at one end. By this method, spreadability is measured on the basis of 'Slip' and 'Drag' characteristics of emulgels. A ground glass slide is fixed on this block. An excess of emulgel (about 2 gm) under study is placed on this ground slide. A pH meter (Digital pH meter DPH 115 pm).

Extrudability study

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 for evaluating emulgel formulation for extrudability is based upon the quantity in percentage of emulgel and emulgel extruded from lacquered aluminum collapsible tube on application of weight in grams required to extrude at least 0.5 cm ribbon of emulgel in 10 seconds. More quantity extruded better is extrudability. The measurement of extrudability of each formulation is in triplicate and the average values are presented. The extrudability is than calculated by using the following formula:

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

Globule size and its distribution in emulgel

Globule size and distribution was determined by Malvern zetasizer. A 1.0 gm sample was dissolved in purified water and agitated to get homogeneous dispersion.

Rheological Study

The viscosity of the different emulgel formulations is determined at 25°C using a cone and plate viscometer with spindle 52 (Brookfield Engineering Laboratories,) and connected to a thermostatically controlled circulating water bath.

Swelling Index

To determine the swelling index of prepared topical emulgel, 1 gm of gel is taken on porous aluminum 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 dry place for some time after it reweighed. Swelling index is calculated as follows:

$$\text{Swelling Index (SW) \%} = [(Wt - Wo) / Wo] \times 100.$$

(MICE SHAVEN SKIN): The modified method is used 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 wooden piece 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 at 200 mg/ min to the left-hand pan until the patch detached from the skin surface. The weight (gram force) required to detach the emulgel from the skin surface gave the measure of bioadhesive strength.

Drug Content Determination

Drug concentration in Gellified Emulsion was measured by spectrophotometer. Drug content in Gellified Emulsion was measured by dissolving known quantity of Gellified Emulsion in solvent (methanol) by Sonication. Absorbance was measured after suitable dilution in UV/VIS spectrophotometer (UV-1700 CE, Shimadzu Corporation, Japan).[46]

In Vitro Release Study

Franz diffusion cell (with effective diffusion area3.14 cm2and 15.5 ml cell volume) was used for the drug release studies. Gellified Emulsion (200 mg) was applied onto the surface of egg membrane evenly. The egg membrane was clamped between the donor and the receptor chamberof diffusion cell. The receptor chamber was filled with freshly prepared PBS (pH 5.5) solution to solubilize the drug. The receptor chamber was stirred by magnetic stirrer. The samples (1.0 ml aliquots) were collected at suitable time interval. Samples were analyzed for drug content byUV visible spectrophotometer after appropriate dilutions. Cumulative corrections were made to obtain the total amount of drug release at each time interval .The

cumulative amount of drug released across the egg membrane was determined as a function of time.

Microbiological assay

Ditch plate technique was used. It is a technique used for evaluation of bacteriostatic or fungistatic activity of a compound. It is mainly applied for semisolid formulations. Previously prepared Sabouraud's agar dried plates were used. Three grams of the Gellified Emulsion are placed in a ditch cut in the plate. Freshly prepared cultureloops are streaked across the agar at a right angle from the ditch to the edge of the plate. Afterincubation for 18 to 24 hours at 25°C, the fungal growth was observed and the percentage inhibition was measured as follows. % inhibition = L2 / L1 × 100

Where L1 = total length of the streaked cultureL2 =length of inhibition.

Skin irritation test

A 0.5 gm 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 are applied on the skin of rabbit. Animals were returned to their cages. After a 24 hour exposure, the Gellified Emulsion are removed. The test sites were wiped with tap water to remove any remaining test article residue

Accelerated stability studies

Stability studies were performed according to ICH guidelines. The formulations were stored in hot air oven at 37 ± 2°, 45 ± 2° and 60 ± 2° for a period of 3 months. The samples were analyzed for drug content every two weeks by UV-Visible spectrophotometer. Stability study was carried out by measuring the change in pH of gel at regular interval of time.

Marketed Preparations

Drug	Product Name	Manufacturer
Miconazole nitrate Hydrocortisone	Miconaz – H emulgel	Medicinal union pharmaceutical
Diclofenac diethyl ammonium	Voltaren emulgel	Novartis pharma
Metronidazole	Lupigyl gel	Lupin pharma
Benzoyl peroxide	Pernox gel	Cose Remedies Ltd

CONCLUSION

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.

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