International Standard Serial Number (ISSN): 2319-8141
International Journal of Universal Pharmacy and Bio Sciences 8(2): March-April 2019
INTERNATIONAL JOURNAL OF UNIVERSAL PHARMACY AND BIO SCIENCES
*IMPACT FACTOR 4.018****
*ICV 6.16****
Pharmaceutical Sciences **Review Article……!!!**

EMULGEL: A REVIEW

A. U. Kamble*, V.K. Khot, F.I.Mevekari, U.M. Khumber, S. D. Tipugade,
S.D.Patil Institute of pharmacy Urun Islampur, S.D Patil nagar, Islampur-415409, India.

KEYWORDS:

Emulgel, Thixotropic, non-staining, Antioxidant and Skin Anti-aging Properties.

FOR CORRESPONDENCE:

A. U. Kamble*

ADDRESS:

S.D.Patil Institute of pharmacy Urun Islampur, S.D Patil nagar, Islampur-415409, India.

.

ABSTRACT

The principal objective of dosage form design is to achieve a predictable therapeutic response to a drug include in a formulation which is capable of large-scale manufacture with reproducible product quality. There are numerous dosage form into which a drug substances can be incorporated for the convenient and efficacious treatment of disease. Generally herbal cosmetics also called as natural cosmetics. Cosmetics are developed to reduce wrinkles, fight acne and to control oil secretion. Plant materials with antioxidant and skin anti-aging properties have been widely used in cosmetic products for many years. Emulgel have several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining and pleasing appearance.

INTRODUCTION:

Many extensively used topical agents like ointments, creams, lotions have numerous disadvantages. They are generally very sticky causing discomfort to the patient when applied. Likewise they also have a reduced amount of spreading coefficient and necessitate to apply with rubbing. They also show evidence of the problem of stability. Due to all these factors, within the major group of semisolid preparations, the use of transparent gels has increased both in cosmetics and in pharmaceutical preparations.**1**

A gel is colloid that is typically 99% by weight liquid, which is immobilized by surface tension between it and a macromolecular network of fibers built from a small amount of a gelating substance present. In spite of many advantages of gels a major limitation is their inability to delivery hydrophobic drugs. When gels and emulsions are used in combined form the dosage forms are referred as **Emulgel.** The presence of a gelling agent in the water phase converts a classical emulsion into an emulgel. Direct (oil-in-water) system is used to entrap lipophilic drugs whereas hydrophilic drugs are encapsulated in the reverse (water-in-oil) system.**2**

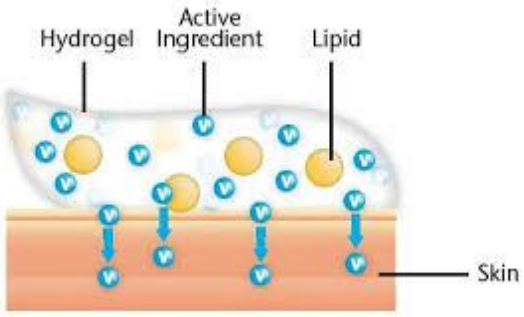

Fig.; Emulgel structure

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

Physiochemical Factors

1. Partition coefficient.
2. Molecular weight (<400 Dalton).
3. Degree of ionization (only unionized drugs gets absorbed well).
4. Effect of vehicles **3,4**

Factors to be Considered When choosing a Topical Preparation

1. Effect of the vehicle e.g. an occlusive vehicle enhances penetration of the active ingredient and improves efficacy. The vehicle itself may have a cooling, drying, emollient or protective action.
2. Match the type of preparation with the type of lesions. For example, avoid greasy ointments for acute weepy dermatitis.
3. Match the type of preparation with the site. (e.g., gel or lotion for hairy areas)
4. Irritation or sensitization potential. Generally, ointments and w/o creams are less irritating, but gels are irritating. Ointments do not contain preservatives or emulsifiers if allergy to these agents is a concern.**5,6**

ADVANTAGES

1. **Hydrophobic drugs** can be easily incorporated into gels using 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 hydrophobic drugs into the oil phase and then oily globules are dispersed in aqueous phase resulting in o/w emulsion. 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 preparations are comparatively less stable than emulgels. Like powders are hygroscopic, creams shows phase inversion or
breaking and ointment shows rancidity due to oily base.
3. **Better loading capacity:** Other novel approaches like niosomes and liposomes are of nano size and due to vesicular structures may result in leakage and result in
lesser entrapment efficiency. But gels due to 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 instruments needed 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 needs 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 to prolong the effect of drugs having shorter t1/2. It can be used for both hydrophobic (o/w emulgel) and hydrophilic drugs (w/o) emusion.**7,8**

METHOD OF PREPARATION

STEP1: Formulation of Emulsion either O/W or W/O

STEP2: Formulation of gel base

STEP3: Incorporation of emulsion into gel base with continuous stirring

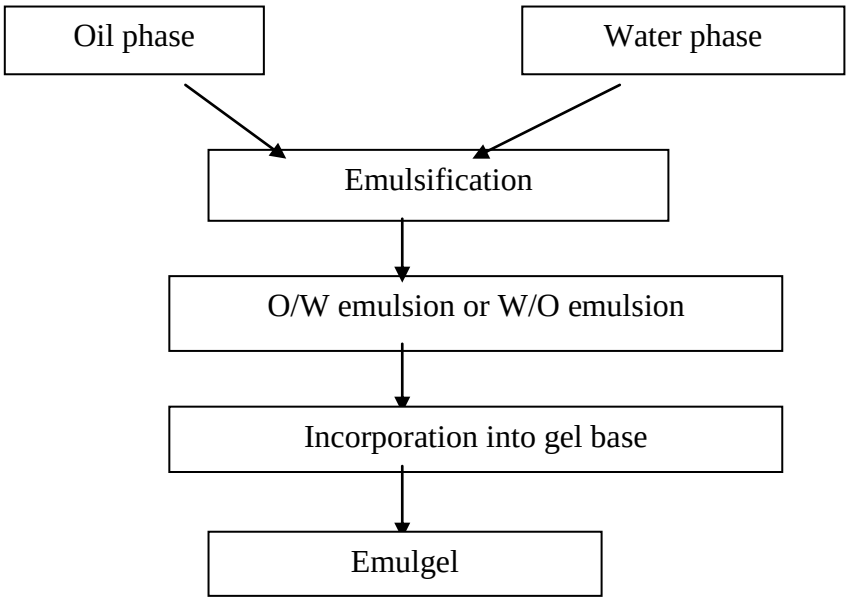

Figure.2 ***Flow chart of Emulgel formulation***

Important Constituents of Emulgel Preparation

1. Aqueous Material:

This forms the aqueous phase of the emulsion. Commonly used agents are water, alcohols.**9**

2. Oils:

These agents from 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.**10,11**

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 **12,** stearate, Sorbitan monooleate (Span 80)**13**, Polyoxyethylene sorbitan monooleate (Tween 80)**14**, Stearic acid**15**, Sodium stearate**16**.

4. Gelling Agent:

These are the agents used to increase the consistency of any dosage form can also be used as thickening agent.**17,18**

5. Permeation Enhancers:

These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability.**19**

CHARACTERIZATION OF GELLIFIED

EMULSION

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).**20**

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. The emulgel is then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with the hook. A 1 Kg weight is placed on the top of the two slides for 5 minutes to expel air and to provide a uniform film 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 gms. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance

of 7.5 cm be noted. A shorter interval indicate better spreadability. Spreadability was calculated by using the formula S= M.L/T

Where, S = spreadability,

M = Weight tied to upper slide,

L = Length of glass slides

T = Time taken to separate the slides completely from each other.

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. Sample was injected to photocell of zetasizer. Mean globule diameter and distribution was obtained.

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:

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

Where, (SW) % = Equilibrium percent swelling,

Wo = Original weight of emulgel at zero time

after time t, Wt = Weight of swollen emulgel

***Ex–vivo* Bioadhesive strength measurement of topical emulgel:**

(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 tothe 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. The bioadhesive strength is calculated by using following:

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

Figure :1 Setup for bioadhesive test 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).

In Vitro Release Study:

Franz diffusion cell (with effective diffusion area 3.14 cm2 and 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 chamber of 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 by UV 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 culture loops are streaked across the agar at a right angle from the ditch to the edge of the plate. After incubation 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 culture, and

L2 =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 of Gellified Emulsion:

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.**21,22**

Conclusion: There is great potential lied in development of novel drug delivery system for herbal formulation as its safe, effective, convenient and economically affordable drug delivery. Since emulgel possesses an edge in terms of spreadibilty, adhesion, viscosity and extrusion, they will become a popular drug delivery system. the new concept of formulation emulsion in gel has shown better delivery as here the drug are incorporated in oil phase of emulsion and emulsion is better stabilize in the gel and the combination of both of the phase provide the controlled release effect, that improves the bioavailability of that drugs. Such advantages of emulgel provide the big scope in future for the delivery of hydrophobic drug topically with more efficacy and less production cost. Oils with medicinal value provide the Synergistic effect to emulgel.

REFERENCES:

1. Rieger M, Lachman L, Lieberman H, Kanig J; The Theory and Practice of Industrial Pharmacy: 3rd ed. PA Lea and Febiger: Philadelphia: 1986, 502-33.
2. Khullar R, Saini S, Seth N, Rana A; Emulgels: A surrogate approach for topically used hydrophobic drugs. International Journal of Pharmacy and Biological Sciences. 2011, 1:117-28.
3. Kalia YN, Guy RH. Modeling transdermaldrug release. Adv Drug Deliv Rev. 2001, 48:159-72.

4. Ayub, CA, Gomes ADM, Lima MVC, Vianna- Soares CD, FerreiraLMA. Topical Delivery of Fluconazole: In Vitro Skin Penetration and Permeation Using Emulsions as Dosage Forms Drug. Dev. Ind. Pharm. 2007; 33:273- 280.
5. Gaur PK, Mishra S, Purohit S, Dave K. Transdermal Drug Delivery System: A Review. AJPCR 2009; 2: 14-20.
6. Subranayam N, Ghosal SK, Moulik SP. Enhanced In Vitro Percutaneous Absorption and In Vivo Anti-Inflammatory Effect of a Selective Cyclooxygenase Inhibitor Using Microemulsion. Drug Dev. And Industrial Pharm., 2005.
7. Rashmi, MS. Topical Gel: A Review, 2008. Available from: http://www.pharmainfo.net/reviews/topic algel- review. 28.
8. Djordjevic J, Michniak B, Uhrich, Kathryn E AAPS PharmSciTech 2003; 5(4):1-12.
9. Lachman, L.; Lieberman, H.A. The Theory and Practice of Industrial Pharmacy. 3rd Ed. Varghese Publishing house; 1990. pp. 534.
10. Vyas, S.P.; Khar, R.K. Controlled Drug Delivery. 1st Ed. Vallabh Prakashan; 2002. pp. 416-417.
11. Bonacucina G, Cespi M, Palmieri GF. Characterization and Stability of Emulsion Gels Based on Acrylamide/Sodium Acryloyldimethyl Taurate Copolymer AAPS PharmSciTech. June 2009; 10 (2).
12. Curr AEB. Transdermal Drug Delivery: Penetration Enhancement Techniques Heather. Drug Deliv. 2005; 2:23-33.
13. Rutrer N. Drug absorption through the skin: a mixed blessing .Arch Dis Child 1987; 62:220-221.
14. Zhang XL, Zhao R, Qian W. Preparation of an emulgel for treatment of aphthous ulcer on the basis of carbomers. Chin. Pharm. J. 1995; 30:417-418.
15. Swarbrick, J. Encyclopedia ofpharmaceutical technology, 3rd ed., 1551.
16. Gibson, M. Pharmaceutical formulation and preformulation , Interpharm 2004.
17. Mortazavi SA, Aboofazeli R. An Investigation into the Effect of Various Penetration Enhancers on PercutaneousAbsorption of Piroxicam. Iranian Journal of Pharmaceutical Research 2003; 135-140.
18. Kumar, L.; Verma, R. Int. J Drug Delivery 2010,58-63.
19. Jacob SW, Francone CA. Structure and Function of Man, (2).
20. WB Saunders Co. Philadelphia, 1970, 55-60.

21. Schreier H, Bouwstra JA. Liposomes and Niosomes as topical drug carriers: Dermal and Transdermal delivery. J Contr Rel 1985;30:863–68.

22. Varma VNSK , Maheshwari PV, Navya M, Reddy SC, Shivakumar HG, Gowda DV. Calcipotriol delivery into the skin as emulgel for effective permeation. Saudi pharm J 2014;22:591-99.