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EMULGEL: A NOVEL TREND IN TOPICAL DRUG DELIVERY SYSTEM

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ABSTRACT

For the treatment of local as well as systemic skin disorders, topical drug delivery systems have been used for centuries offering the advantage of delivering the drug directly to the site of action and also delivering the drug for extended period of time at the affected area. When gel and emulsion are used in combined form the dosage form are referred as Emulgel. Since they contain dual control release systems: a gel and an emulsion, emulgels have emerged as one of the most interesting topical delivery system. They are emulsions of either oil-in-water or water in oil type, which are gelled by mixing with a gelling agent. The major objective behind emulgel is delivery of hydrophobic drugs via skin. Thus emulgels have major advantages on novel vesicular system as well as on conventional systems in various aspects. They are referred for topical use due to their favorable properties such as being greaseless, non-staining, thixotropic, emollient, easily removable, water soluble, bio-friendly, long shelf-life, transparent and pleasant appearance. The use of emulgels can be expanded in different classification namely analgesics, anti-inflammatory, anti-fungal, antiacne drugs and various cosmetic formulations.

KEYWORDS: Emulgels, Topical drug delivery, Hydrophobic drugs, Emulsion, Gel.

INTRODUCTION

Drugs have been applied to human body via various routes namely oral, sublingual, rectal, parenteral, etc. for the treatment of illness over the last decades. The topical drug delivery system is generally used where these systems of drug administration fails or in local skin infection like fungal infection. Topical delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders (e.g. acne, psoriasis) with the intent of containing the pharmacological or other effect of the drug to the surface of the skin or within.Topical drug administration through various routes applies a wide spectrum of preparations for both cosmetic and dermatological, to their healthy and diseased skin.Topical preparations are applied to the surface of a part of the body and have effects only in a specific area of the body and are formulated in such a manner that the systemic absorption of the medicament is minimal.[1] The most common examples of topical dosage forms are solutions, suspensions, emulsions, semisolids (e.g. foams, ointments, pastes, creams and gels), sprays and solids (e.g. powders and aerosols) among them ointments, creams, and lotions have numerous disadvantages. They are usually very sticky and cause uneasiness to the patient when applied. Moreover, they also have less spreading coefficient and need to apply with rubbing. They also exhibit the problem of stability. Due to all these factors, a major group of semisolid preparation, transparent gel has expanded its use in both cosmetics and in pharmaceutical preparations. In spite of many advantages of gels a major limitation is their inability to deliver hydrophobic drugs. In order to overcome this limitation an emulsion based approach is being used so that a hydrophobic therapeutic moiety can be successfully incorporated and delivered through gels. When gels and emulsions are used in combined form the dosage forms are referred as emulgels. 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. Emulsions possess a certain degree of elegance and are easily washed off whenever desired. They also have a high ability to penetrate the skin.[2]

Advantages of Emulgel[3]

1. **Incorporation of hydrophobic drugs:** 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.
2. **Better loading capacity:** When compared to other novel approaches like niosomes and liposomes the gels due to vast network have comparatively better loading capacity

3. **Better stability:** Various other topical preparation shows less stability than emulgels. As creams show phase inversion or breaking, ointments show rancidity due to oily base and powders are hygroscopic in nature.
4. **Production feasibility and low preparation cost:** Preparation of emulgels consists of simpler and short steps which increases the feasibility of the production. There is no need for specialized instruments for the production of emulgels. Moreover, materials used are easily available and cheaper. Hence, decreases the production cost of emulgels.
5. **Controlled release:** Emulgels act as a dual control preparation and thus is good for release of drugs with short half-life.
6. **No intensive sonication:** When vesicular molecules like liposomes, niosomes are produced they need sonication which may result in drug degradation and leakage, but this is not required during the formulation of emulgels.
7. **Patient compliance:** Emulgels improve patient compliance as they can be self-applied and medication can be terminated whenever required.
8. **Other benefits:** Emulgels avoid first pass metabolism and provide site specific drug delivery.
9. Increases contact time and mean residence time of the drug.
10. It is a non-invasive mode of drug delivery with no trauma or risk of infection.

Disavantages of Emulgel[4]

1. Poor permeability of some drugs through skin.
2. Occurrence of bubble during formation of emulgel.
3. Drug which are of large particle size not easy to absorb through the skin.
4. Skin irritation or allergic reaction on contact dermatitis.

Types of Emulgels

1. **Macroemulsions gel:[4,5]** These are most common type of emulgels where the particle size of droplets of emulsion is more than 400nm. They are visually opaque but the individual droplets can be easily observed under microscope. Microemulsions are thermodynamically unstable, but can be stabilized using surface active agents.E.g. Mefenamic acid emulgel was prepared using Carbopol 940 as gelling agent. Liquid paraffin was used as oil phase. Mentha oil and clove oil was used as penetration enhancer.

2. **Nanoemulgel:[5,6]** When Nanoemulsion is incorporated into gel it is called as nanoemulgel. Nanoemulsions are thermodynamically stable transparent (translucent) dispersions of oil and water stabilized by an interfacial film of surfactant and co-surfactant molecules having a droplet size of less than 100 nm. Nanoemulsions have improved transdermal permeation of many drugs over the conventional topical formulations such as emulsions and gels. Nanoemulgel on contact with skin will release the oily droplets from the gel network. The oil droplets then will penetrate in to the stratum corneum of the skin and directly deliver thedrug molecules without a transfer via hydrophilic phase of Nanoemulsions.

3. **Microemulsion:[5]** Microemulsions are transparent and thermodynamically stable as their droplet size range from 10 to 100 nm and they do not coalesce. Microemulsions are composed of oil, surfactant, co-surfactant and water in specific proportions. The ingredients of microemulsion could facilitate the permeation rate of the drug by reducing the diffusion barrier of the stratum corneum. However, due to low viscosity of microemulsion, their less retention capacity in the skin restrains its application in the pharmaceutical industry, to overcome this disadvantage, gelling agents such as Carbopol 940, xanthan gum and carrageenan have been added into the microemulsion for forming microemulsion based gel in order to increase its viscosity which could be suitable for topical application. Moreover, microemulsion based gel prevents the absorption of drug in the blood stream and provide higher drug accumulation in the skin for efficient action.

Formulation considerations[1]

The challenges in formulating topical emulgels are:

1. Determining systems that are non-toxic, nonirritating, non-comedogenic and non-sensitizing.
2. The emulgel formulation must have low allergic potential, good physiological compatibility and high biocompatibility.
3. Formulating cosmetically elegant emulgel

The different excipients used in the formulation of emulgel includes:

1. Vehicle[7]

Some of the properties of vehicles is that

- Deliver the drug to the target site
- Sustain a therapeutic drug level in the target tissue for a sufficient duration to provide a pharmacologic effect.
- Release the drug so it can migrate freely to the site of action.

a) Aqueous Material: They constitute the aqueous phase of emulsion. The commonly used agents are water, alcohols etc.

b) Oil:[7,8] They constitute the oily phase of the emulsion. Most commonly used oils are mineral oils either alone or in combination with soft and Hard Paraffin. Non-biodegradable mineral oil and Castor oils can be used which provide local laxative effects. Oils extracted from different types of plant with various medicinal values can be employed in emulgel formulation.Mahesh et al (2014) carried one such a research work using lavender oil as oil phase for emulgel. Emulgel of Clotrimazole using lavender oil as oil phase. The inclusion of lavender oil has

supplemented antifungal action of Clotrimazole. It also possesses anti-inflammatory and antiseptic activity. The other examples include almond oil,Wheat germ oil, Sesame oil.

2. **Emulsifying agents:**[9] 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 preparationse.g.: Polyethylene glycol 40 stearate, Sorbitan mono-oleate (Span 80), Polyoxyethylene Sorbitan mono-oleate (Tween 80), Stearic acid, Sodium stearate.

3. **Gelling agent:**[5,7] These are used to increase consistency of dosage forms and provide gelled behavior. Gelling agent are of two types, natural and synthetic. Incorporation of gelling agent to a system makes it thixotropic. It is observed that there exists an inverse relationship between concentration of gelling agent and extent of drug released. The gelling agents like Carbomer readily absorb water, get hydrated and swell. Besides its hydrophilic nature, its cross-linked structure and its insolubility in water makes Carbopol a potential candidate for use in controlled release drug delivery system. HPMC based emulgel shows better drug release than Carbopol based emulgel. Various gelling agent used are Carbopol-934, HPMC 2910, HPMC K4M etc.

Examples of Gelling Agent

Gelling agent	Quantity	Dosage Form
Carbopol-934	1%	Emulgel
Carbopol-940	1%	Emulgel
HPMC-2910	2.5%	Emulgel

4. **Penetration Enhancers:**[7] These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability. In order to promote absorption of drugs thorough skin barrier, vehicles often include penetration enhancing ingredients which temporarily disrupts the highly ordered structure of stratum corneum skin barrier, fluidize the lipid channels between corneocytes, alter the partitioning of the drug into skin structures, and enhance delivery into skin. E.g. Oleic Acid, lecithin, Isopropyl Myristate, Urea, Eucalyptus oil, Chenopodium oil, Pyrrolidone, Laurocapran, Dimethyl Sulphoxide, Linoelic acid, Menthol etc.

5. **Preservatives:**[5] e.g. Propyl paraben, methyl paraben, Benzalkonium chloride, Benzoic acid, Benzyl alcohol etc.
6. **Antioxidants:** e.g. Butylated Hydroxy Toluene(BHT), Ascorbyl palmitate, Butylated hydroxyanisole(BHA), etc.
7. **Humectant:** Mostly used to prevent loss of moisture.e.g. Glycerin, Propylene gylcol, etc.

Method of preparation of emulgel[4]

It consists of three steps:

Step 1: Formulation of Emulsion either O/W or W/O

Preparation of oil phase of emulsion:

Oil phase of the emulsion is prepared by dissolving emulsifier e.g. span 20 in oil phase like light liquid paraffin.

Preparation of aqueous phase:

The aqueous phase is prepared by dissolving emulsifier e.g. tween 20 in purified water.

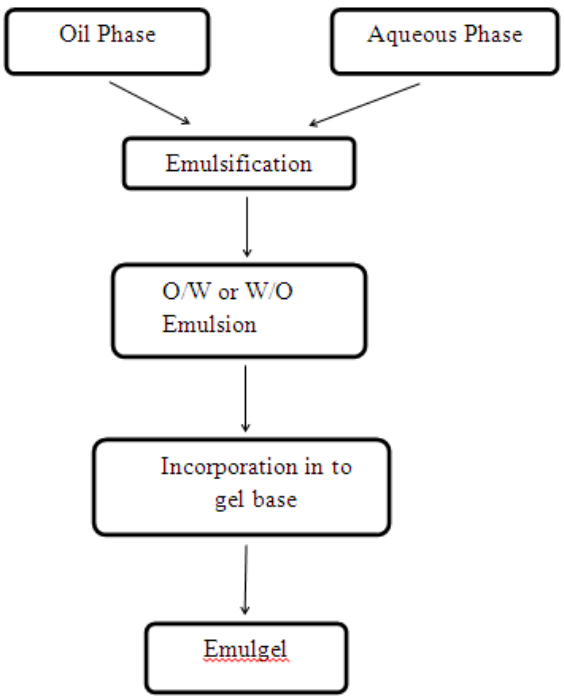
Step 2: Formulation of gel base

The gel phase in the formulations is prepared by dispersing polymer in purified water with constant stirring at a moderate speed using mechanical shaker, then the pH was adjusted to 6–6.5 using tri ethanolamine (TEA).

Step 3: Incorporation of emulsion into gel base

Add glutaraldehyde in during mixing of gel and emulsion in ratio 1:1 to obtain the emulgel.

Flowchart of emulgel preparation:



Evaluationparameters of emulgel[3,7,10,11]

1. **Physical Examination:** The prepared emulgel formulations are inspected visually for their color, homogeneity, consistency and phase separation.
2. **pH evaluation:** pH evaluation is the important criteria especially for the topical formulation. The pH of the emulgel should be between 5-7 to mimic the skin condition. If the pH of the prepared emulgel is acidic or basic, it may cause irritation to the

patient. pH of the prepared emulgel was measured using digital pH meter by dipping the glass electrode into an emulgel. The measurement of pH of each formulation was done in triplicate and average values were calculated.

3. **Compatibility studies by FT-IR:** Compatibility study of drug with the excipients was determined by FTIR Spectroscopy. By this we can confirm any chemical interactions between the excipients and the drug.
4. **Rheological Studies:** The viscosity of the gel during handling, transport and storage is important criteria. The viscosity of different emulgel formulations were measured using Brookfield viscometer at different rpm.
5. **Spreadability:** Spreadability is determined by apparatus 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 2gm) 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 1kg 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 80gm. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5cm be noted. Lesser time indicates 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 slide
   T = Time taken to separate the slides completely from each other.
6. **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 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 then calculated by using the following formula:
   Extrudability = Applied weight to extrude emulgel from tube (in gm) / Area (in cm2)
7. **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 beakercontaining 10 ml 0.1 N sodium hydroxide. 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
   Wt = Weight of swollen emulgel after time t,
   Wo = Original weight of emulgel at zero time.
8. **Drug Content Determination:** Take 1gm of emulgel. Mix it in suitable solvent. Filter it to obtain clear solution. Determine its absorbance using UV spectrophotometer. Standard plot of drug is prepared in same solvent. Concentration and drug content can be determined by using the same standard plot by putting the value of absorbance.
   Drug Content = (Concentration × Dilution Factor × Volume taken) × Conversion Factor.
9. **Determination of Globule Size and its distribution in emulgel:** The globule size analysis of the optimized formulation were determined by treating the emulgel sample with scarlet red dye and spreaded over as a thin film on the glass slide and observed under the 10X of the microscope. Measurements were carried at an angle of 90◦ at 25◦C. Micro emulsion was diluted with double distilled water to ensure that the light scattering intensity was within the instrument 's sensitivity range. All the measurement was carried out at 25˚C.
10. **Skin Irritation Test (Patch Test):** Formulation, 0.5 g of each is applied on the hair – free skin of rabbits by uniform spreading over an area of 4 cm2. The skin surface is observed for any visible change such as erythema (redness) after 24, 48 and 72 hours of the formulation application. The mean erythmal scores are recorded depending on the degree of erythema:
    No erythema = 0
    Slight erythema (barely perceptible – light pink) = 1
    Moderate erythema (dark pink) = 2
    Moderate to severe erythema (light red) = 3
    Severe erythema (extreme redness) = 4
11. **Syneresis measurement:** Upon standing sometimes gel system shrinks as bit and little liquid is pressed out. This phenomenon is known as syneresis. In this test, emulgel is put in cylindrical plastic tube with a perforated bottom which is covered with filter paper (whatmann No. 4). These tubes are then placed in centrifuge tubes and centrifuged for 15 min. the cylindrical plastic tube and liquid which had separated from emulgel is weighed. The percentage of syneresis is then calculated as the ratio of weight of liquid separated from the emulgel to the total weight of emulgel before centrifugation and

multiplied by 100. The data were reported as the average of five measurements.

12. **In Vitro Release/Permeation Studies:** In vitro release studies can be carried out using Franz diffusion cell having capacity of 10ml volume.
13. **Phase Separation:** All prepared formulations can be subjected to centrifugations at 10,000 rpm for 10 min and examined for any change in phase separation.
14. **Stability Studies:** The prepared emulgels is packed in aluminum collapsible tubes (5 g) and then 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.
15. **Drug Release Kinetic Study:** To analyze the mechanism of drug release from the topical gel, the release data were fitted to the following eq.
    Zero – order equation: Q = k0 t
    Where, Q is the amount of drug released at time t, and k0 is zero – order release rate.
    First – order equation: In (100 – Q) = In 100 – k1 t
    Where, Q is the percent of drug release at time t, and k1 is the first – order release rate constant.
    Higuchi's equation: $Q = k2\sqrt{t}$
    Where, Q is the percent of drug release at time t, and K2 is the diffusion rate constant.
16. **Microbiological assay:** Ditch plate technique is used. It is a technique which is 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 are used. 3 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 is observed and the percentage inhibition is measured as follows.
    Percentage inhibition = L2 / L1 × 100, Where L1 = total length of the streaked culture, and L2 =length of inhibition.

CONCLUSION

As the emulgel is the recent technique for the topical drug delivery it is better suitable for hydrophobic drugs and obviously it is a very good technique for drug delivery of combination of both hydrophilic and hydrophobic drugs. Mainly the hydrophobic drug formulation can be developed using emulgel technique. In future, topical drug delivery will be used extensively to impart better patient compliance. Since Emulgel is helpful in enhancing Spreadability, adhesion, viscosity and extrusion, this novel drug delivery will become a popular formulation in future.

REFERENCES

1. Vaishali Arora, Praveen Kumar, Rajni Sharma.Emulgels: a review for topical drug delivery of hydrophobic drugs, July-2015; 6(3): 1256-1262.
2. Patel Chirag J, Satyanand Tyagi, Anil Kumar Gupta, Prabhakar Sharma, Parimal M. Prajapati, Mrugendra B. Potdar. Emulgel: a combination of emulsion and gel. Journal of Drug Discovery and Therapeutics, 2013; 1(6): 72-76.
3. Anu Hardenia, Sonali Jayronia and Sanjay Jain. emulgel: an emergent tool in topical drug delivery. IJPSR, 2014; 5(5): 1653-1660.
4. Asish Dev, Reha Chodankar, Om Shelke.Emulgels: a novel topical drug delivery system.Pharmaceutical and biological evaluations, August 2015; 2(4): 64-75.
5. S. B. Kute and R.B. Saudagar.Emulsified gel A Novel approach for delivery of hydrophobic drugs: An overview. Journal of Advanced Pharmacy Education and Research, Oct-Dec 2013; 3(4): 368-375.
6. Padmadevi chellapa,aref t. Mohamed,eseldin i. Keleb, assad elmahgoubi, ahmad m. Eid,yosef s. Issa, nagib a. Elmarzugi. Nanoemulsion and Nanoemulgel as a Topical Formulation. Iosr journal of pharmacy, october 2015; 5(10): 43-47.
7. Surender Kumar, Neeraj Singh and Satish Chander Arora. Emulgel: an insight. European Journal of Pharmaceutical and medical research, 2015; 2(4): 1168-1186.
8. Vaishali Potnis, Mahesh Khot, Mangesh Kahane, Sindhu Mohite, Pradnya Bhongale, Suchita Dhamane.Formulation of gellified emulsions of Clotrimazole using essential oil from Lavendula angustifolia Miller. World J Pharm Sci, 2014; 2(10): 1316-1322.
9. Eswaraiah S, Swetha K, Lohita M, P. Jaya Preethi, B. Priyanka, Kiran Kumar Reddy. Emulgel: Review on Novel Approach to Topical Drug Delivery. Asian J. Pharm. Res, 2014; 4(1): 4-11.
10. Shaik. Shaheda Sultana, P. Parveen, M. Sri Rekha, K. Deepthi, Ch. Sowjanya, Dr. A. Seetha Devi.Emulgel – a novel surrogate approach for transdermal drug delivery system. Indo American Journal of Pharm Research, 2014; 4(11): 5250-5263.
11. Sonam Vats, Charu Saxena, TS Easwari, VK Shukla.Emulsion Based Gel Technique: Novel Approach for Enhancing Topical Drug Delivery of Hydrophobic Drugs. International Journal for Pharmaceutical Research Scholars (IJPRS), 2014; 3(2): 649-658.
12. K.P.Mohammed Haneefa, Guru Prasad Mohanta, Chandini Nayar.Emulgel: An Advanced Review.J. Pharm. Sci. and Res, 2013; 5(12): 254–258.
13. A. S. Panwar, N. Upadhyay, M. Bairagi, S. Gujar, G. N. Darwhekar, D. K. Jain.Emulgel: a review.Asian Journal of Pharmacy and Life Science, July-Sept, 2011; 1(3): 333-340.