

**EMULGELS: RECENT DEVELOPMENTS****Chandel Mehak and Sharma Chandan\***

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Pharma Sciences, Gharauan,  
Mohali, Punjab.**ABSTRACT**

It is not very long back that creams and gels were the mainstay in the topical drug delivery segment. But with the limitations of gels and creams calling for medication in the topical dosage form led to breakthrough development of emulgel as a topical dosage form. Emulgel had the obvious advantage of delivering hydrophobic drugs that gave them an extra edge over creams or gels which mainly could deliver only hydrophilic drugs. This review provides information regarding rationale and advantages of emulgels over other topically administered semisolids. Various gelling agents that could be incorporated in emulgels have been explored and discussed in this

review. Other ideal drug candidates for emulgels have also been discussed. The possible oils and penetration enhancers that may be added have also been explained through this review. At the end few marketed formulations also have been mentioned like Voltaren. Further the review discusses the current research scenario and developments in field of emulgel preparation.

**KEYWORDS:** Emulgel, topical drug delivery, gelling agents.**INTRODUCTION**

Emulgel is a recent new technology, it is used as topically and its characteristics of dual control release. Emulgel is emulsion as well as gel and they followed both the characteristics. Emulsion and gel are combined with the drug (mostly hydrophobic as well as hydrophilic) they referred as a emulgel. Emulgels are really good prospects for topical route for the lipophilic drugs. Oil containing aqueous phase are employed for entrapping lipophilic drugs and lyophilic drugs are loaded in water loaded oil phase. Emulgel are used to treat the topical diseases.(D. Kumar et al., 2016).

Topical route of delivering drugs may be explained as applying dosage form for treatment of dermal ailments. Dermal application can be considered better than the other route of administration (other route like oral, sublingual, rectal, parenteral) and the main benefit of this route is avoiding the first pass metabolism. Application of drug on skin provides many advantages like selective and site specific delivery of medicaments. They increase the bioavailability. (Phad et al., 2018).

Biggest organ in the body of human beings is skin. Skin is the outermost covering on body of human beings. The major functions of the skin is protection, regulation, and sensation. Human skin consists of three layers and these are as follows.

- ❖ Epidermis: It is the outermost layer.
- ❖ Dermis: This layer underlies beneath epidermis.
- ❖ Hypodermis: it is not the part of skin. Hypodermis is present below the dermis and the main purpose of this layer is attach the skin to underlying bone and muscle and supplying it with blood vessels and nerves. (shailendra panwar, sayantan mukhopadhyay, 2015)

Emulgel for dermatological use for having many useful characteristics as they are not greasy, spread gently without stains, exhibit prolonged storage life and ecofriendly.

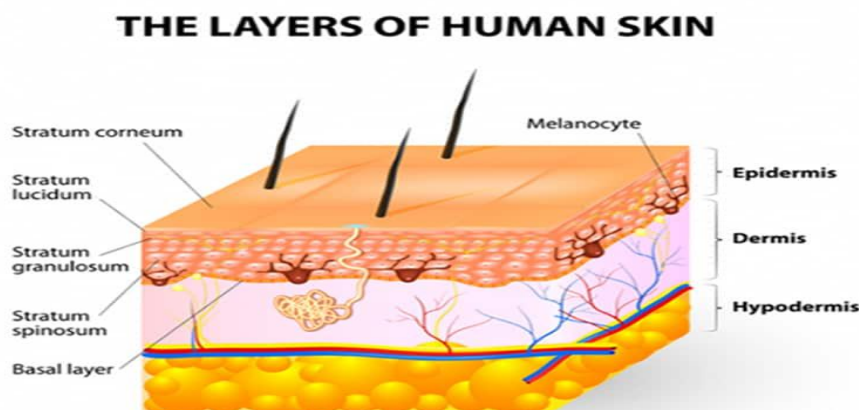
## OBJECTIVES

- ❖ To increase patient compliance
- ❖ Better stability
- ❖ Controlled release of drug
- ❖ superior loading capacity
- ❖ production utility
- ❖ low preparation cost
- ❖ non irritant.

## Advantages of emulgel

- ❖ Incorporation of hydrophobic drugs
- ❖ Superior loading capacity
- ❖ Better stability
- ❖ No intensive sonication
- ❖ Controlled release
- ❖ Production utility and low preparation cost

- ❖ Bypassing first pass hepatic metabolism



**Figure 1: Layers of skin.**

- ❖ Preventing incompatibility issues of gastrointestinal tract
- ❖ Improve patient compliance and suitability for self medication
- ❖ Convenient and easy to apply.
- ❖ Providing utilization of medication with short biological half-life and narrow therapeutic window.
- ❖ Ability to easily terminate medication when needed.(K.Raju et al., 2019)

### **Disadvantages**

- ❖ Skin irritation on contact dermatitis
- ❖ The possibility of allergenic reaction.
- ❖ Medication of large particle size not easy to absorb through the skin.
- ❖ Poor permeability of some medication through the skin
- ❖ The occurrence of bubble during formation of emulgel.(shailendra panwar, sayantan mukhopadhyay, 2015)

### **Rational**

There are many dosage forms for dermal application. Topical formulations such as ointments, creams, lotion and they also have some advantages as well as disadvantages. They are sticky, greasy, and less spreadable that are uneasiness to the patient. Emulgels show stability issues. Application of gels in field of cosmeceuticals and pharmaceuticals have gained increasing demand and popularity. But lipophilic drugs are not easily delivered by gel dosage form. Thus emulsion based methodology has been employed to get rid of this problem.

The challenges in formulating a topical emulgels are

- Determine the system are non-toxic, non-irritating, and non-sensitizing.
- Formulating physically stable emulgel.(Preeti et al., 2013)

Characteristics to be considered for dermal medicaments:

- Vehicle characteristics must be considered, for example a vehicle that occlusive will improve penetration of drug across skin.
- Assessing permeability features as per requirement depending on type of lesions.
- Any chance of irritancy should be considered.
- Avoiding inclusion of preservatives to avoid irritation.(Preeti et al., 2013)

## FORMULATION OF EMULGEL

For the preparation of emulgel some constituents are used including drug, they are:

- **Vehicle:** Vehicle should follow the ideal characters given in the pharmacopeias. Deliver the drug to the target site.
- **Aqueousmaterial:** The aqueous phases used are water, alcohol etc.
- **Oil:** These are used in preparation of emulsion. This medium is required for dispersing hydrophobic drugs.
- **Emulsifying agents:** These are employed for the purpose of emulsifying aqueous and oil medium for stability purpose. Emulsifying agent are maintain the stability while they thermodynamically unstable.
- **Gellingagent:** Gelling agent are employed for gel formation that is intended for dispersing in for altering thixotropy characteristics.
- **Penetrationenhancer:** These substances help in increasing permeation characteristics of drug so that it passes across skin.(Serena & Bruce Smoller, 2015)

**Table 1: Constituents for Emulgels(D. Kumar et al., 2016).**

Consituents	Examples
Aqueous materials	Rose water, sterile water, alcohol.
Oils	Mineral oil, different oils of vegetable origin or fish liveroil, balsam oil, castor oil etc.
Emulsifiers	Tween 20, tween 40, tween 80, PEG-300,400,600, span 20, Span 80, sodium stearate etc.
Gelling agent	Carbomer934,934P,940, sodium alginate, HPMC, sodium CMC(carboxymethyl cellulose), gellan gum etc.
Penetration enhancer	Propylene glycol, clove oil, isopropyl myristate, olive oil, urea, isopropyl palmitate, oleic acid, SLS(sodium lauryl sulphate), SDS(Sodium dodecyl sulphate) etc.
pH adjusting agent	NaOH, triethanolamine.

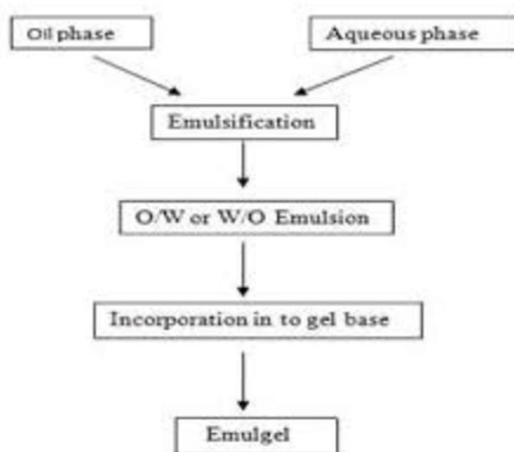
Method of preparation of emulgel.

Step 1 : formulation of emulsion either oil-in-water, water-in-oil.

Step 2 :Preparing base of gel.

Step 3 : Including emulsion in base by rapid and prolonged mixing. (Ashara, 2016)

Oil phase and water medium was heated at temperature about 75 °C. To the water medium, then oil medium was added. Continuous stirring was performed till cooling to room temperature was achieved. Glutaraldehyde was added as cross linking agent.



**Figure 2: Steps involved in emulgel preparation.**

### Evaluation techniques

#### Parameters for physical testing

Color, homogeneity, consistency, and phase separation are checked here.

**Spreadability:** Spreadability is checked by “slip” and “drag” character of emulgel.

**Determination of pH:** pH meter is employed to assess pH of formulation.

**Rheological study:** In this, viscometer is employed to analyze the viscosity.

**In vitro drug release study:** It is carried out by using Franz diffusion cell. It helps to determine the drug release.

**Microbiological assay:** For this method Ditch plate technique is used. Through this method the bacteriostatic or fungistatic activity is evaluated.

**Accelerated stability studies:** It is performed by ICH guidelines. The stability test is done in hot air oven at  $37 \pm 2^\circ\text{C}$ ,  $45 \pm 2^\circ\text{C}$  and  $60 \pm 2^\circ\text{C}$  for 3 months.

**Drug content:** The drug content is determined by UV spectroscopic analysis.

**Dispersed phase size in emulgel:** Malvern Zetasizer is employed for globules size study.

**Centrifugation study:** This method is used to determine the stability of emulgel. It is done only after one week of preparation. This study was done by using minicentrifuge at 3000rpm for 30 minutes.

**Swelling index:** This parameter is used to determine the swellability of prepared emulgels.

**Skin irritation test:** This test is very important because the preparation is a topical formulation. The test is carried out on the animal skin. The emulgel is applied to the animal skin and then the animals are returned in to their cages. After 24 hr the animals are tested . then the emulgel are removed from the site and wiped with tap water.

**Study of Stability:** Prepared emulgel is stored in extreme conditions and the stability checked.(Serena & Bruce Smoller, 2015)

Study of literature reveals that following criterion should be met for being incorporated into emulgel

- Half life should be less than 10 hours.
- Preferably mass of drug should be less than 800 Daltons.
- Log P should vary between 0.8-5.
- Permeability coefficient should be greater than or equal to 0.005 cm/hour.
- Drug should not be irritating to skin
- High value of pKa should be there. (Foldvari, 2000)

While considering excipients for emulgel, following properties must be there.

- Excipient to be included should be non-irritating.
- There shouldn't be any effect on stability of formulation.
- Excipients must be biologically safe.
- Concentration of excipient must be below specified standards.
- It must be compatible with drug to be incorporated.(Foldvari, 2000)

Three different kinds of penetration enhancers are available:

- Chemical penetration enhancers: like solvents, surfactants.
  - Biochemical penetration enhancers: eg. Peptides, metabolic inhibitorsetc.
  - Physical penetration enhancing methods: eg. Electroporation, ultrasound, iontophoresis.
- (Farris et al., 2016; Sharma et al., 2020)

Researchers have explored various gelling agents in their findings. Carbopol-934 is one frequently used for emulgel preparation.(Jaiswal et al., 2016) Carbopol 940 also has been used quite often as gelling agent.(Khullar et al., 2012) Hydroxy propyl methyl cellulose has been employed as gelling agent for insulin delivery via emulgel dosage form. (Akram et al., 2013).

Nowadays, emulgel formulations have become quite popular due to their efficiency in delivering hydrophobic drugs. Voltaren emulgel is marketed emulgel formulation (Voltaren Emulgel Extra Strength | Our Products, n.d.) Following section of review focusses on recent research in the field of emulgel.

Jain et al prepared and ketoconazole emulgel. They employed Carbopol 940 and Carbopol 934 in the form of gelling agent. Various evaluation tests performed indicate that emulgels were stable and possessed acceptable characteristics. (Jain et al., 2010) Sahana et al investigated the effect of various liquids for formulating terbinafine hydrochloride emulgel. The emulgels consisting of Carbopol 934 and HPMC were evaluated for various characteristics. It was shown by results that efficient release was obtained with such emulgels. (Shrestha et al., 2017) Khullar prepared emulgels for mefenamic acid. Carbopol 940 was employed as gelling agent. Mentha oil as well as clove oil was incorporated as permeation enhancer. The emulgel produced acceptable characteristics and analgesic activity.(Khullar et al., 2012) Emulgel of Chlorphenesin was prepared and optimized by Magdy. Carbopol as well as HPMC were employed as gelling agent. Prepared emulgels were then characterized which showed that emulgel of chlorphenesin followed diffusion model. Antifungal activity of the drug was also efficient.(Mohamed, 2004) Vani developed emulgel of Piroxicam. Xanthum gum and Carbopol 934 were used as gelling agents. Triethanolamine was used to adjust pH of dosage form. Various evaluation tests for emulgels were carried out. It was confirmed from the results that the drug release followed zero order pattern. (formulation and in vitro evaluation of piroxicam emulgel | international journal of pharmaceutical sciences and drug research, n.d.) Chaudhary prepared and evaluated and optimized gel of diclofenac. Results showed that emulgel formed using HPMC as gelling agent were safe and effective.(Chaudhary et al., 2011).

Joshi prepared emulgel of clotrimazole. Various evaluation tests for the emulgels were done to characterize the properties of emulgel. Methyl cellulose and Carbopol 934 were used as the gelling agents. Results indicated that emulgel were more effective as compared to the cream



of clotrimazole.((pdf) preparation and evaluation of physical and, rheological properties of clotrimazole emulgel, n.d.) Joshi prepared emulgel of Clarithromycin. Carbopol 934, HPMC K4M and Carbopol 940 were used as various gelling agents. Various evaluation tests were also carried out. Results also proved that the developed emulgel had comparative response like azithromycin marketed gel. Also Higuchi model was applicable in the emulgel. (Baibhav et al., 2012).

Priya prepared and evaluated ciprofloxacin emulgel employing Carbopol 934 as gelling agent. Triethanolamine was used for adjusting pH of emulgel. Various evaluation tests were carried out to establishment stability and characteristic features of emulgel. Ciprofloxacin emulgel exhibited good physicochemical characteristics. ((PDF) *Formulation and In-Vitro Evaluation of Ciprofloxacin Loaded Topical Emulgel*, n.d.) Prajakta and coworkers prepared emulgel of itraconazole drug. Naturally occurring gelling agents were employed like guar gum and xanthum gum. Various evaluation tests were done to evaluate physicochemical characteristics of emulgel. The outcomes of tests carried out shown that emulgel was acceptable in all physicochemical characteristics. (Khule et al., 2019).

Arti and coworkers prepare emulgel of meloxicam and evaluated them. Carbopol 934 was used as gelling agent. Oleic acid, menthol and dimethyl sulphoxide were the other excipients used in the formulation. It was intended for rheumatoid arthritis treatment. Various evaluation tests provided the conclusion that emulgel was stable and had exhibited acceptable characteristics.(Pednekar A, Dandagi P, Gadad A, 2015).

Snehal and coworkers prepared characterized emulgel of indomethacin. HPMC K4M, Carbopol 934 and xanthum gum were explored for potential use as gelling agent. Propylene glycol was used as penetration enhancer. Various evaluation tests carried on prepared emulgels confirmed that the emulgel was stable and acceptable in the physical appearance and other properties. (Mulye et al., 2013).

Vijay and coworkers prepared emulgels of Loratadine. Gelling agent used was Carbopol 940. Prepared emulgels were tested for in vivo and skin irritancy test. The results exhibited that the formulation produced was stable and acceptable with zero order of drug release pattern.(V. Kumar et al., 2014).



Study	Drug	Polymer	Enhancer	Purpose	Reference
Development and characterization	Ketoconazole	Carbopol 934,940	Propylene glycol	Comparative study of polymer and drug release	(Pranali et al., 2019)
Formulation development and in-vitro evaluation	Terbinafine hydrochloride	Carbopol 934	Propylene glycol	Fungal infection	(Sabu & Basarkar, 2013)
Preparation characterization and pharmacodynamic evaluation	Ketoprofen	HPMC	Propylene glycol	Anti-inflammatory	(Fahmy, 2015)
Formulation and evaluation	Mefenamic acid	Carbopol 934	Propylene glycol	Anti-inflammatory	(Khullar et al., 2012)
Formulation and optimization	Chlorphenesin	Carbopol 934	Propylene glycol	Antifungal	(Mohamed, 2004)
Formulation design and development	Piroxicam	Carbopol 934	Propylene glycol	Anti-inflammatory	(Khunt et al., 2012)
Development and optimization	Diclofenac	HPMC	Propylene glycol	Anti-inflammatory	(Pakhare et al., 2017)
Preparation and evaluation	Clotrimazole	Carbopol 934	Propylene glycol	Antifungal	(Mengesha, 2015)
Development and characterization	Clarithromycin	Carbopol 934	Propylene glycol	Broad spectrum antibiotic	(Baibhav et al., 2012)
Formulation and in-vitro evaluation	Ciprofloxacin	Carbopol 934	Propylene glycol	Antimicrobial	(Ranga Priya M & Kumar Mohan K, 2012)
Optimization	chlorphenism	Catbopol 934,HPMC	Propylene glycol	Effect of gelling agent on release	(Mohamed, 2004)
Development study	Miconazole	Carbopol 934,940	Propylene glycol	Controlled delivery , antifungal	(S. Nagalakshmi, Radhika Ramaswamy, Renuga, Sowjanya, Premalatha, 2015)
Formulation, design,development, evaluation	Meloxicam	Carbopol 934	DMSO, Menthol, clove oil,oleic acid	Treatment of rheumatoid arthritis	(Pednekar A, Dandagi P, Gadad A, 2015)
Formulation , evaluation	Indomethacin	Carbopol 934,xantham gum	Propylene glycol	Using two type of polymer	(Mulye et al., 2013)

### Future prospective and Conclusion

Hydrophobic drugs have posing many problems during the formulation and development of any new formulation. Their hydrophobic behaviour are responsible for the poor water solubility and bioavailability of the drugs. Delivery of these drugs are posing challenges in biological system. Topical drug delivery system have many delivery system like ointments, lotion, creams, and pastes. They exhibit topical emollient characteristics. Emulgel is the good topical drug delivery system makes more effective, productive and profitable.

Topical drug delivery system is most convenient route of administration, and it provides the better patient compliance. Many topical formulation having advantages but they also a disadvantages and the disadvantages are overcome by the formulation of emulgel. Emulgel is the recent and novel technique to deliver the hydrophobic drugs but they also deliver the hydrophilic drugs. Emulgel are thixotropic, greaseless and easily spreadable, helpful in increasing the spreadability, adhesion, viscosity, extrusion, and increase patient compliance. The novel drug delivery system are famous formulation in future.

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