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EMULGEL: A COMPREHENSIVE REVIEW

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ABSTRACT

When comparing semisolid formulations, gels are often considered more advantageous in both cosmetics and pharmaceutical preparations. Combining gel and emulsion creates a formulation known as emulgel, which shows promise as a drug delivery system specifically for hydrophobic drugs. Emulgel offers a dual release control system by combining the properties of gel and emulsion. It provides several benefits such as being non-greasy, easy to spread and remove, moisturizing, and transparent. Emulgel is typically prepared using the incorporation method. It is commonly used for delivering analgesics, anti-inflammatory, anti-fungal, anti-acne drugs, and various cosmetic formulations. Studies on emulgel demonstrate its potential for delivering a wider range of topical drugs due to its advantages over other drug delivery systems. Gels are a relatively recent type of dosage form that involve trapping significant quantities of aqueous or hydroalcoholic liquid within a network of colloidal solid particles. Gel formulations generally offer faster drug release compared to conventional ointments and creams. Despite the many advantages of gels, a major limitation lies in effectively delivering hydrophobic drugs. To overcome this limitation, emulgels are prepared. Emulgels refer to combined forms of gels and emulsions. Emulsions possess a certain level of elegance and can be easily washed off when desired. They also have a high capacity to penetrate the skin. Emulgels formulated for dermatological use offer several desirable properties, such as thixotropic behavior, non-greasy texture, easy spreadability, easy removal, emollient effects, non-staining properties, water solubility, longer shelf life, biocompatibility, transparent appearance, and aesthetically pleasing appearance. Another important factor is the ability to prolong drug release, even for hydrophilic drugs, by developing water-in-oil (w/o) emulgels.

KEYWORDS: Emulgels, polymers, emulsion, gel, topical drug delivery.

INTRODUCTION

The topical drug delivery system refers to a dosage form that is applied to the skin, often used when other routes of drug delivery are ineffective or for treating skin disorders. One advantage of the topical drug delivery

system is its ability to bypass first-pass metabolism. Additionally, it helps avoid the risks and inconveniences associated with intravenous therapy. Topical formulations can be prepared in various consistencies, including solid, semisolid, and liquid. However, the topical delivery system may face challenges when administering hydrophobic drugs. In each formulation, active ingredients are combined with several excipients. Sometimes, multiple formulations can be combined to enhance drug delivery, and emulgel is an example of such a combination. Emulgel is formed by combining an emulsion and a gel [1]. Emulgel can be prepared using both oil-in-water and water-in-oil type emulsions mixed with gel. The oil-in-water type emulsion is suitable for delivering lipophilic drugs, while the water-in-oil type emulsion is used for delivering hydrophobic drugs [2]. Emulgel offers numerous advantages, including being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, environmentally friendly, visually appealing, transparent, and cosmetically acceptable. Additionally, emulgel exhibits good skin penetration and has a long shelf life [3]. Emulsion and gel preparations each have their own distinct properties. However, gels have certain limitations when it comes to delivering hydrophobic drugs. These limitations can be overcome by using emulgel. Emulgel is created by incorporating a gelling agent into a classical emulsion, transforming it into an emulgel [4].

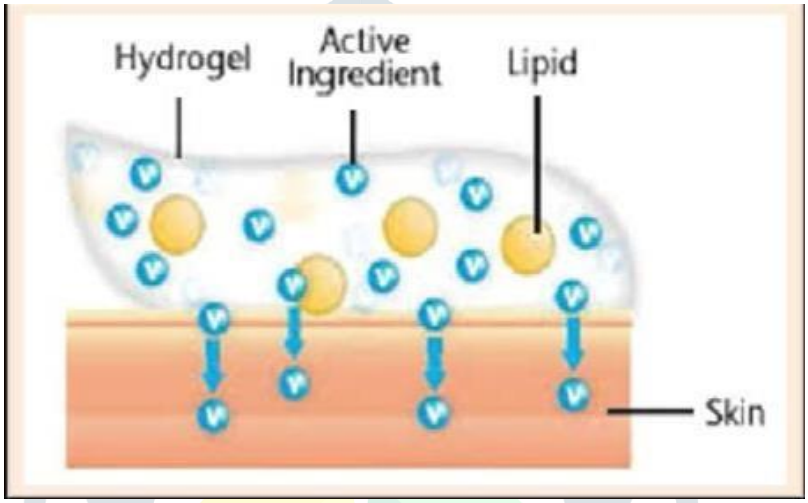

Fig. 1: Emulgel structure [5]

There are two categories of topical delivery products: external and internal [6]. Topical preparations are administered by applying them to the surface of the skin or mucous membranes, either by spreading or spraying. On the other hand, internal preparations are meant for oral, vaginal, or rectal administration. These routes involve taking the medication through the mouth, inserting it into the vagina, or administering it via the rectum [7]. Topical preparations can be categorized based on their textures, including solid preparations, liquid preparations, semi-solid preparations, and miscellaneous preparations [8].

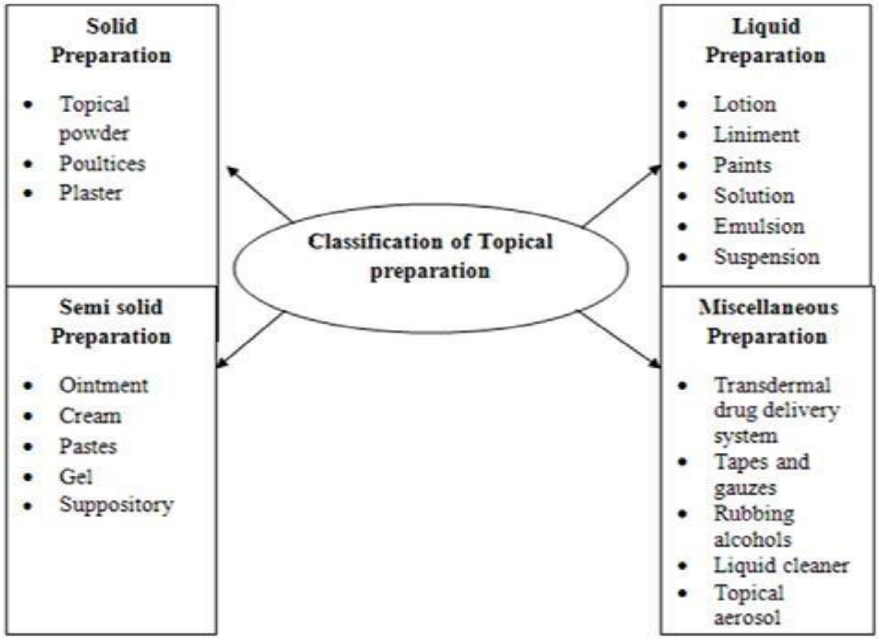

Fig. 2: Classification of topical preparation [9].

The absorption of drugs through different routes can be influenced by various factors. For topical administration, factors such as skin thickness, skin pH, hydration, inflammation, partition coefficient, and molecular weight can affect drug absorption. Topical delivery systems have both advantages and disadvantages. One of the main advantages is that they allow for the avoidance of first-pass metabolism and gastrointestinal incompatibility. Topical preparations are typically applied to the skin, where they can penetrate and exert their therapeutic action at the desired site. The skin, which is the largest sensory organ in the body, has an approximate surface area of 2 m2 and a pH of 4.0 to 5.6. It consists of four layers: the non-viable epidermis (stratum corneum), viable epidermis, viable dermis, and subcutaneous connective tissue.

Non-viable epidermis[stratum corneum]: The non-viable epidermis, or stratum corneum, is the outermost layer of the skin, measuring 10-20 cells thick. The cells in this layer are approximately 34-44 μm long, 25-36 μm wide, and 0.5-0.20 μm thick, with a surface area of 750-1200 μm.

Viable epidermis: The viable epidermis is located between the stratum corneum and the dermis and has a thickness of 10-50 μm. The tonofibrils in this layer help to connect the cells.

Dermis: The dermis is situated beneath the viable epidermis and is a structural fibrin. It has a thickness ranging from 2000-3000 μm and contains loose connective tissue.

Subcutaneous connective tissue: The subcutaneous connective tissue is classified as a genuine connective tissue, characterized by a lax structure consisting of fibrous connective tissue as well as blood and lymph vessels.

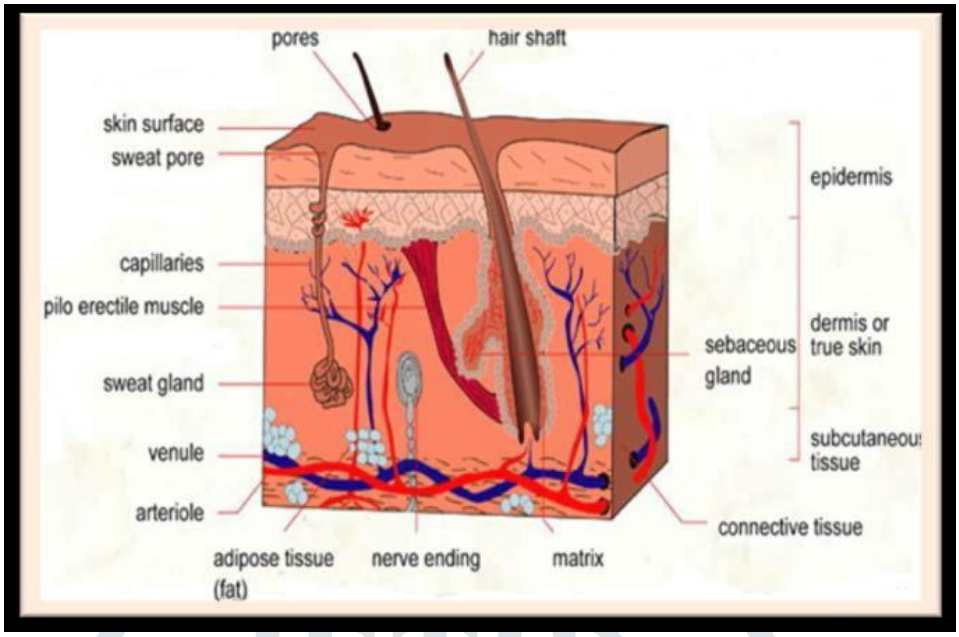

Fig. 3: Structure of skin [10]

Topical drug absorption occurs through three mechanisms: transcellular, intercellular, and follicular. Passive diffusion allows drugs to penetrate the outermost layer of the skin, known as the stratum corneum [11]. The rate limiting steps in this process are diffusion and dissolution. Topical medications serve three purposes: epidermal formulation, endodermal formulation, and transdermal formulation. The transcellular mechanism is the most direct route, while the intercellular mechanism is the commonly used pathway. The follicular mechanism involves the use of hair follicles and sweat glands [12].

Drug penetration is improved through various methods, including chemical means such as surfactants, water, solvents, and others. Physical techniques like stripping, iontophoresis, and ultrasound can also enhance penetration. Additionally, biochemical approaches involving peptides and metabolic inhibitors can be employed. Another method is super saturation enhancement[13].

Pros and Cons of Emulgel: Pros of emulgel:

- Enhanced loading capacity
- Enhanced stability
- Regulated release
- Elimination of intensive sonication
- Prevention of first-pass metabolism
- Prevention of gastrointestinal incompatibility
- Increased selectivity for a specific site

• Enhanced patient compliance

• Convenient and user-friendly application[14] **Cons of emulgel:**

- Skin irritation caused by contact dermatitis
- Potential for allergic reactions
- Inadequate skin permeability for certain medications
- Difficulties in absorption for drugs with larger particle sizes
- Formation of bubbles during the emulgel formulation process [15]

FORMULATION OF EMULGEL CONSTITUENTS:

Vehicle: Vehicle should follow the ideal characters given in the Pharmacopeias.

Aqueous material: The aqueous phases used are water, alcohol, rose water, sterile water,etc[16].

Oil: Mineral oil, different oils of vegetable origin or fish liver oil may be used and liquid paraffin are used either alone or in combination[17],[18].

Table no.1: Use of oils

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

Emulsifiers: span 80, tween 80, stearic acid, sodium stearate. Tween-20, 40, 60, 80, PEG-300, 400, 600, Acrysol K-140, 150, 160, Glycerine,Span-20, 40, 60, Transcutol®-P, Sepineo™ SE68, etc.

Gelling agents: Sepineo™ P 600, carbomer 934,934P, 940, sodium alginate, HPMC, sodium, CMC, Gellan gum, etc[19],[20].

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

pH adjusting agent: NaOH, triethanolamine[21].

Penetration enhancers: Propylene glycol, cloveoil, isopropyl myristate, olive oil, urea,DMSO, lauracapram, isopropyl palmitate,oleic acid, SLS, SDS, STGC, SDC, etc. [22].

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 formulations are created by combining a gel and an emulsion. The emulsion and gel are prepared independently and then blended together. To prepare the emulsion, separate aqueous and oil phases are taken and mixed. The gel is then prepared using a gelling agent. Once the gel and emulsion are ready, they are gently stirred together. Commonly used chemicals for the oil phase include castor oil, clove oil, and liquid paraffin. Water and alcohol are typically used as the aqueous phase [23].

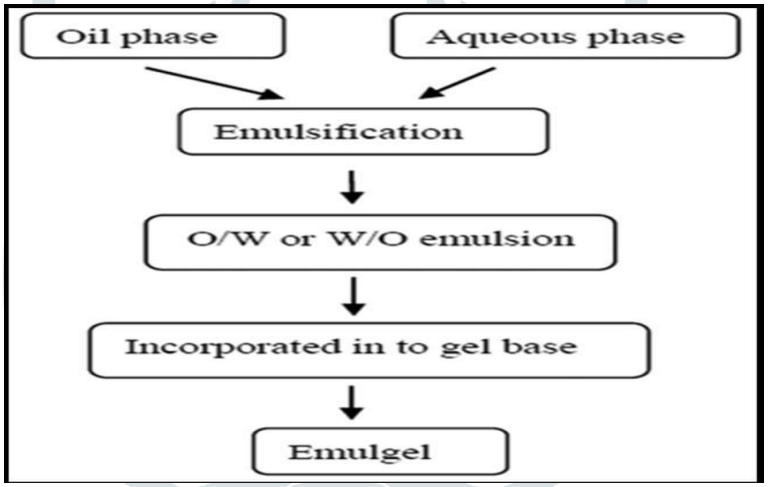

Fig. 4 : Flow chart of emulgel preparation[24]

The water phase is created by combining tween 80 and water, while the oil phase is formed by mixing paraben and propylene glycol. The drug is dissolved in ethanol, and the two phases are blended together with constant stirring. Subsequently, the polymers are dissolved in water with a pH range of 6.0-6.5. After separately preparing the emulsion and gel, they are combined to form the emulgel.

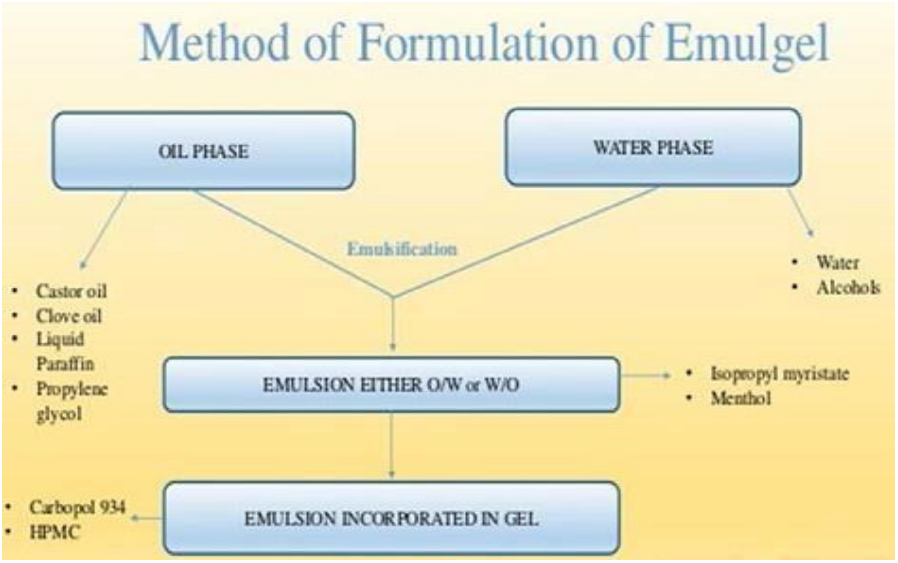

Fig. 5. : Method of formulation of emulgel [25]

EVALUATION TECHNIQUES

❖ **Physical examination:**

The color, homogeneity, consistency and phase separation are checked here[26].

❖ **Spreadability:**

The spreadability of emulgel is assessed by evaluating its "slip" and "drag" characteristics. To measure spreadability, a wooden block apparatus is utilized, which is equipped with a pulley at one end. The block contains a fixed ground glass surface. A quantity of 2 g of emulgel is applied onto the glass surface and covered with another glass, creating a sandwich-like structure. A weight of one kilogram is then placed on top, and the spreadability is evaluated based on the observed results.

❖ **Determination of pH:**

The determination is carried out using a digital pH meter. The pH meter is immersed into the emulgel, and the pH is measured. This process is repeated three times to ensure accuracy. ❖ **Rheological study:**

In rheological studies, the viscosity is measured at a temperature of 25 ºC. The cone and plate viscometer is the instrument utilized for this purpose[27] ❖ **In vitro drug release study:**

It is carried out by using Franz diffusion cell. It helps to determine the drug release[28].

❖ **Microbiological assay:**

The Ditch plate technique is employed for this method. It is utilized to assess the bacteriostatic or fungistatic activity.

❖ **Accelerated stability studies:**

Stability testing is performed in accordance with the guidelines established by the International Council for Harmonisation (ICH). This testing procedure entails exposing the samples to controlled temperatures within a hot air oven, specifically at 37 ± 2 ºC, 45 ± 2 ºC, and 60 ± 2 ºC, for a period of 3 months [29].

❖ **Drug content:**

The drug concentration in the Gellified Emulsion was analyzed using a spectrophotometer. To determine the drug content, a known quantity of the emulsion was dissolved in methanol with the aid of sonication. Subsequently, the absorbance of the solution was measured using a UV/VIS spectrophotometer (UV_1700 CE, Shimadzu Corporation, Japan) after suitable dilution [30].

❖ **Swelling Index:**

To assess the swelling index of the prepared topical emulgel, we took 1 gram of gel and placed it on a porous aluminum foil. Then, each sample was individually placed in a 50 ml beaker containing 10 ml of 0.1 N NaOH. After certain time intervals, the samples were taken out of the beakers and allowed to dry. They were then reweighed. The swelling index was determined using the following formula:

Swelling Index (SW) % = [(Wt – Wo) / Wo] × 100.
Where, (SW) % = Equilibrium percentage swelling,
Wo = Original weight of emulgel at zero time after time t,
Wt = Weight of swollen emulgel[31]

❖ **Drug Release Kinetic Study:**

To analyze how drugs are released from the topical gel, the data on drug release were fitted to the equations mentioned below:

- **Zero-order equation:** The amount of drug released at a specific time, denoted as Q, is given by the equation

$$Q = K_0 t.$$

where, Q= The percentage of drug release at time t K_0= The zero-order release rate.

- **First-order equation:** The percentage of drug release at a specific time, denoted as Q, is related to time (t) by the equation

$$In(100 - Q) = In\ 100 - K_1 t.$$

where, Q= The percentage of drug release at time t K_1= The first-order release rate constant.

- **Higuchi's equation:** The percentage of drug release at a specific time, denoted as Q, can be calculated using the equation

$$Q = K_2 \sqrt{t}.$$

Where, Q= The percentage of drug release at time t, K_2= The diffusion rate constant[32].

❖ **Globule size and its distribution in emulgel:**

The dimensions and arrangement of globules were measured using the Malvern Zetasizer. To ensure a consistent distribution, a 1gm sample was dissolved in purified water and thoroughly agitated. The resulting mixture was then inserted into the photocell of the Zetasizer. The analysis offered the mean diameter and dispersion of the globules [33].

SUMMARY:

Topical drug delivery systems encompass a wide range of formulations, but they also possess certain drawbacks. However, these shortcomings can be effectively addressed through the use of emulgel preparations. Emulgels have emerged as a highly convenient, superior, and efficient delivery system in our project. By combining an emulsion with a gel, emulgels establish a dual control release mechanism that helps overcome issues such as phase separation and creaming associated with emulsions, while also enhancing stability. The constituents required for emulgel preparation are similar to those used in emulsion and gel formulations. The preparation process for emulgels involves three steps: emulsion preparation, gel preparation, and incorporation of these two preparations. It is crucial to thoroughly evaluate every formulation, and there are approximately twenty-five evaluation methods available, including photo microscopy, spreadability assessment, rheological studies, in-vitro drug release studies, and more. Emulgels have gained widespread usage in recent times, with commonly employed examples including Miconaz-H-emulgel, Isofen emulgel, Diclon emulgel, among others. Anti-inflammatory drugs are often administered via emulgels.

Conclusion:

Topical drug delivery is expected to be widely utilized in the future to improve patient adherence. Emulgel, a novel method for delivering drugs to the skin, is particularly effective for hydrophobic medications. Its ability to enhance spreadability, adhesion, viscosity, and extrusion makes it a desirable drug delivery system. Additionally, emulgels offer a solution for incorporating hydrophobic drugs into a water-soluble gel base, further increasing their popularity.

References:

1. Purushottam Sonaje Sumeet, Bhaskarrao Gondkar Sheetal, Bhandudas Saudagar Ravindra., 2013. Gellified Emulsion: A New Born Formulations For Topical Delivery of Hydrophobic Drugs A Review, World Journal of Pharmacy and Pharmaceutical Sciences, 3(1), pp 233251.
2. Shah A. Arpan, Kamdar Kamal, Shah Rushabh, Keraliya A. Rajesh., 2013. Emulgel: A Topical Prepartions for Hydrophobic Drugs. Ph Tech Med, 2(5), pp 370-376.
3. Bhatt Preeti, Gnanarajan. G, 2013. Emulgels: A Novel Formulation Approach for the Topical Delivery of Hydrophobic Drugs A Review. International Research Journal of Pharmacy, 4(2), pp 12-16.
4. Panwar AS, Upadhyay N, Bairagi M, Gujar S, Darwhekar GN, Jain D,2011. Emulgel: A Review. Asian Journal of Pharmacy and Life Science, 1(3), pp 333-343.
5. K.P. Mohammade Haneef, Sherry Easo, P.V. Hafsa, Guru Prasad Mohanta, Chandini Nayar, 2013. Emulgel: An Advanced Review. Journal of Pharmaceutical Science and Research, 5(12), pp 254-258.

6. Haedenia Anu, Jayronia Sonali and Jain Sanjay,2014. Emulgel: An emergent tool in topical drug delivery. A review International Journal of Pharmaceutical Science and Research, 5(5), pp 1653-1660.

7. Kute S.B and Saudagar R.B. Emulsified Gel a Novel approach for delivery of hydrophobic drugs,2013. A review on emulgel. Journal of Advanced Pharmacy Education and Research, 3(4), pp 368-376.

8. Joshi Baibhav, Singh Gurpreet, Rana A.C, Saini Seema, Singla Vikas, 2011, Emulgel: A Comprehensive Review on the Recent Advances in Topical Drug Delivery. A Review International Research Journal of Pharmacy, 2(11), pp 66-70.

9. Vikas Singla, Seema Sanil, Baibhav Joshi and A.C. Rana, 2012. Emulgel: A New Platform for Topical Drug Delivery. International Journal of pharmaceutical and biological sciences, 1 (3), pp 485-498.

10. Anu Hardenia, Sonali Jayronia and Sanjay Jain, 2014. Emulgel: An emergent tool in topical drug delivery. International Journal of Pharmaceutical Science and Research, 5(5), pp 16531660.

11. Pathan, I.B, Setty C.M, 2009. Chemical penetration enhancers for transdermal drug delivery systems. Tropical Journal of Pharmaceutical Research, 8, pp 173-179.

12. Vats S, Saxena C, Easwari T, Shukla V, 2014. Emulsion based gel technique: Novel approach for enhancing topical drug delivery of hydrophobic drugs. International Journal of Pharmaceutical Science and Research, 3, pp 2277-7873.

13. Kullar R, Saini S, Steth N, Rana AC, 2011. Emulgel A surrogate approach for topical used hydrophobic drugs. International Journal of pharmaceutical and biological sciences, pp 11728.

14. Jain NK, 2004. Progress in controlled and novel drug delivery st systems. New Delhi: CBS publishers and distributors, 1, pp 319-20.

15. Hardenia A, Jayronia S, Jain S, 2014. Emulgel: An emergent tool in topical drug delivery. International Journal of Pharmaceutical Science and Research, 5, pp 1653-60.

16. Pant S, Badola A, Baluni S, Pant W, 2015. A review on emulgel novel approach for topical drug delivery system. World Journal of Pharmacy and Pharmaceutical Sciences, 4, pp 172843

17. .Vyas, S.P.; Khar, R.K. Controlled Drug Delivery. 1st Ed. VallabhPrakashan; 2002. pp. 416417.

18. Bonacucina G, Cespi M, Palmieri GF. Characterization and Stability ofEmulsion Gels Based on Acrylamide/Sodium AcryloyldimethylTaurate Copolymer AAPS PharmSciTech. June 2009; 10 (2).

19. Mortazavi SA, Aboofazeli R. An Investigation into the Effect of VariousPenetration Enhancers on Percutaneous Absorption of Piroxicam.Iranian Journal of Pharmaceutical Research 2003; 135-140.

20. Kumar, L.; Verma, R. Int. J Drug Delivery 2010,58-63.

21. Ashara, K., Soniwala, M., & Shah, K. (2016). Emulgel: A novel drug delivery system. Journal of Pakistan Association of Dermatologists, 26(3), 244-249.

22. Jacob SW, Francone CA. Structure and Function of Man, (2). WBSaunders Co. Philadelphia, 1970, 55-60.

23. Khullar Rachit, Kumar Deepinder, Seth Nimrata, Saini Seema, 2012. Formulation and Evaluations of Mefanamic acid Emulgel for Topical Delivery. Saudi Pharmaceutical Journal, 20(1), pp 63-67.

24. Anil R. Phad, Nandgude Tanaji Dilip, R. Sundara Ganapathy, 2018. Emulgel: A Comprehensive review for Topical Delivery of Hydrophobic Drugs. Assian Journal of Pharmaceutics, 12 (2), pp 382 -393.

25. Singla et al, 2012. Emulgel: a platform for topical drug delivery. International Journal of pharmaceutical and biological sciences, 3, Issue 1.

26. George Eby and Mathews Manju Marai, 2014. Formulation and Evaluation of Topical Gel containing Hair Growth Promoters for the Treatment of Androgenic Alopecia A Research Article, Bulletien of Pharmaceutical Research, 4(1), pp 1-8.

27. Masmoudi H, Piccerelle P, Le Dréau Y, Kister J, 2006. A rheological method to evaluate the physical stability of highly viscous pharmaceutical oil-in-water emulsions. Pharm Res.,23(8), pp 1937–47.

28. Subranayam N, Ghosal SK, Moulik SP, 2005. Enhanced In Vitro Percutaneous Absorption and In Vivo Anti-Inflammatory Effect of a Selective Cyclooxygenase Inhibitor Using Microemulsion. Drug Development and Industrial Pharmaceutics,1(3), pp 12-19

29. Rutrer N, 1987. Drug absorption through the skin: a mixed blessing. Arch Dis Child. 62, pp 220-221.
30. Chaudhari P, Ajab A, Malpure P, Kolsure P, Sanap D, Development and in-vitro evaluation of thermo reversible nasal gel formulations of Rizatriptan benzoate, Indian J Pharm Edu Res,43: 55-62, (2009).

31. Patel RP, Patel G, Baria A. Formulation and evaluation of transdermal patch of aceclofenac, Int J Drug Del, 1(3): 41 – 51, (2009).

32. Jones DB, Woolfson AD, Brown AF. Textural, viscoelastic and mucoadhesive properties of pharmaceutical gels composed of cellulose polymers. Int J Pharm,151:223–33, (1997).

33. Gupta GD, Gound RS. Release rate of nimesulide from different gellants. Indian J Pharm Sci., 61, 1999, 229-234.