

IJMPS
Section: Pharmaceutical
Sciences

Copyright@IJMPS

Emulgel Towards Novel Formulation Development: A Comprehensive Review

Eisha Ganju^{1*}, Susheel Deshmukh¹, Bhaskar Kumar Gupta¹¹School of Pharmacy & Research, People's University, Bhopal 462037, Madhya Pradesh, India.

ABSTRACT

Emulgels are an innovative topical drug delivery system that combines the properties of emulsions and gels to enhance the delivery and efficacy of pharmaceuticals. These systems leverage the advantages of both components: the solubilizing capabilities of emulsions and the stable, bioadhesive properties of gels. This review aims to summarize the development, formulation strategies, evaluation techniques, and therapeutic applications of emulgels. A comprehensive literature search was conducted across various scientific databases including PubMed, Scopus, and Web of Science. Studies focusing on the formulation, characterization, and clinical efficacy of emulgels were included. The review evaluates the methodologies used in the preparation of emulgels, including the choice of gelling agents, emulsifiers, and active pharmaceutical ingredients (APIs). Analytical techniques for assessing the physicochemical properties and stability of emulgels were also examined. The review identified key formulation parameters that influence the performance of emulgels, such as the type and concentration of gelling agents (e.g., carbomers, xanthan gum), emulsifiers (e.g., Tween, Span), and oils. Optimization of these components significantly affects the viscosity, spreadability, and drug release profile of emulgels. Studies demonstrated that emulgels exhibit improved drug penetration and sustained release compared to conventional topical formulations. Therapeutic applications of emulgels encompass a wide range of conditions including dermatological disorders, pain management, and microbial infections. The review also highlights novel advancements such as the incorporation of nanoparticles and the development of stimuli-responsive emulgels. Emulgels represent a promising platform for topical drug delivery, offering enhanced stability, bioavailability, and patient compliance. The versatility in their formulation allows for the incorporation of diverse APIs, making them suitable for various therapeutic areas. Future research should focus on the clinical translation of emulgels, exploring their potential in personalized medicine, and addressing regulatory challenges. Emulgels have the potential to revolutionize topical therapy and provide new avenues for effective and targeted drug delivery.

Keywords: Emulgel; Co-surfactant; Lipophilic; Gelling agent; Surfactant; bioavailability

INTRODUCTION

The term “topical drug delivery” describes the process of treating a skin problem by applying a formulation containing a medicine to the skin. When alternative methods of medication delivery (such as the mouth, under the tongue, in the rectal cavity, or via the parenteral route) are ineffective or when a fungal infection develops on the skin, this approach is used. For both local and systemic issues, topical medication administration is a typical therapy option. The medicine is absorbed by the skin and then goes to the site of action to have a therapeutic effect in the topical administration system. A topical preparation's medication release rate is directly

impacted by the carrier's physiological properties. Bypassing the first-pass metabolism is the main advantage of topical administration systems.¹ Particle size is the foundation of the word microemulsion. The tiny size of the medication particles makes it easy for them to diffuse through the skin and reach their target area. The gel's ability to retain the microemulsion for an extended period of time will facilitate the drug's prolonged release. An increasing number of fungal diseases are posing a serious threat to modern civilization. *Tinea capitis*, *Tinea pedis*, and *Tinea corporis* are fungal diseases that cause serious skin infections. The medicine may be more easily absorbed into the skin and its effects can be felt more quickly using a method like emulgel.²

Corresponding Author:**Dr. Eisha Ganju**, Professor, School of Pharmacy & Research, People's University, Bhopal 462037, Madhya Pradesh, India.Email: eishaganju26@gmail.com.

ISSN: 2231-2188 (Print)

ISSN: 2231-685X (Online)

Received: 13.11.2023

Revised: 15.12.2023

Accepted: 29.12.2023

Published: 10.01.2024

PHYSIOLOGY OF SKIN

Topical formulations are used to treat the skin. Designing topical dose formulations therefore requires an elementary familiarity with skin physiology and function.³ A third of the blood flow in the body goes via the skin, which covers an area of around 2 square metres. The human skin has about 40–50 hair follicles and 200–300 sweat ducts per square centimetre. The pH of human skin may vary from 4.7 to 5.7.⁴

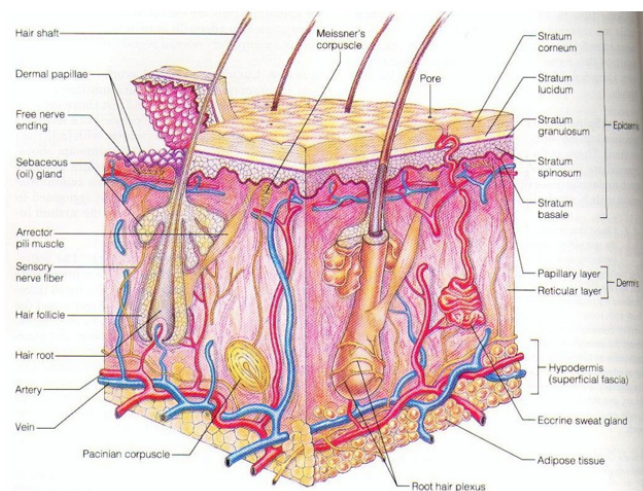


Figure 1: Anatomy of human skin.

PHYSIOLOGICAL FACTORS

Lipid Content: Percutaneous penetration rises when the stratum corneum of skin has a little lipid weight, despite the skin's crucial function as a water barrier.⁵

Skin Thickness: From the epidermis to the subcutis, the skin's thickness changes. The thickness of the epidermal layer ranges from 100 to 150 μm .

Hair Follicle Density: The infundibulum of a hair follicle has a storage capacity that is about 10 times more than the stratum corneum.⁶

The pH of Skin: An increase in perspiration and fatty acid release causes the skin's pH to rise.

Skin Temperature: A higher temperature causes the skin to permeate at a faster pace.

Hydration of Skin: Increase the drug's penetration.

Skin Inflammation: Damage to the stratum corneum causes an increase in permeability.⁷

EMULSION

The process of creating an emulsion involves mixing often incompatible substances. Here, an emulsifying agent is used to make the oil and water phases mix. To make emulsions more stable, emulsifying agents are used. They enter deeply and are simple to remove.⁸

GEL

To “gel” is to increase the viscosity of a liquid solution while keeping all other characteristics the same. In addition to thickening, gels may make a composition more uniform and easier to work with. Emulgel is made by mixing this ingredient with emulsion to form a gel basis. Polymers, the building blocks of gels, may swell both externally and inside when exposed to water or other fluids. The gel's stiffness is proportional to the volume of fluid it contains. The consistency of these gels is like melted butter; they're smooth and seemingly substantial. From their solid to liquid state, they may undergo substantial physical deformation.⁹

INTRODUCTION TO EMULGEL

An emulsion that has been gelled with the help of a gelling chemical is called an emulgel. They may be created with or without wire. When it comes to incorporating poorly water-soluble medications, Emulgel is a stable and excellent solution. A short explanation of what emulgel is: it's a hybrid of emulsion and gel.³ Gels have many benefits, but delivering hydrophobic medicines is a major drawback. Consequently, this constraint is being circumvented by using an emulsion-based solution, which enables hydrophobic therapeutic moieties to take advantage of the gel's distinctive features. Because it contains both water and non-water, emulgel is able to transport medications that are hydrophilic or lipophilic.¹⁰ They have found usage as a formulation for control releases in the last many years. Both the drug loading capacity and stability of these biphasic systems are improved. Compared to the standard topical formulation, Emulgel has a number of advantages, such as being easy to apply, not greasy, thixotropic, having a long shelf life, not smelling, and looking attractive. Emulgel is a dual-control release method that combines gel and emulsion characteristics.¹¹

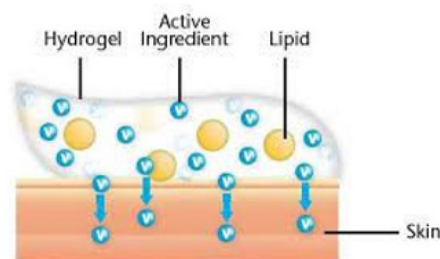


Figure 2: Structure of Emulgel.

TYPES OF EMULGEL

Microemulsion

Thermodynamically stable and optically transparent, microemulsions consist of an isotropic combination of a

biphasic oil-in-water systemic stabilised with a surfactant. Droplets don't combine and range in size from 10 to 100 nanometers. The components include water, surfactant, oil, and co-surfactant in measured proportions. Some unusual characteristics of microemulsions include a wide interfacial area, the capacity to dissolve substances in both water and oil, and very low interfacial tension. By reducing the stratum corneum's diffusion barrier, the microemulsion components may facilitate the drug's quicker penetration. Because of their poor skin retention ability and low viscosity, microemulsions have limited usage in the pharmaceutical sector. To overcome this drawback, microemulsion-based gels with a viscosity suitable for topical application are created by adding gelling agents such as guar gum, Carbopol 940, and HPMC K100M to the microemulsion.¹²

Nanoemulgel

Because they include surfactant and co-surfactant molecules with globule sizes ranging from 1 nm to 100 nm, nanoemulsions are thermodynamically stable oil-water dispersions that are transparent (translucent). Nanoemulgel is the name given to the emulsion when it is combined with gel. Nanoemulsion has a greater transdermal penetration than more conventional formulations, including emulsions and gels, for several medicines. In both *in vitro* and *in vivo* studies, the Nanoemulsion demonstrated improved transdermal and dermal transport capabilities. The medicine readily enters the skin and delivers a modest amount of therapeutic impact in a short amount of time due to its tiny globule size and high loading capacity.¹³

Macroemulsion gel

Use emulgel with droplet sizes of emulsion larger than 400 nm. While the droplets themselves are imperceptible to the naked eye, they become crystal distinct when seen via a microscope. While surface-active compounds may stabilize macroemulsions, they cannot withstand changes in temperature.¹⁴

ADVANTAGES OF EMULGEL

- It is possible to rapidly incorporate hydrophobic medications into the gel basis by using water/oil/water emulsions.
- Enhanced steadiness and capability to bear weight.
- A low-cost mechanism that is easy to produce.
- No sonication please.
- It stays away from the initial metabolism.
- Avoid anything that might cause stomach issues.
- Determine the optimal site on the body for medication administration.
- Patients were more likely to comply.
- Made self-medication more acceptable and suitable for patients.

- The capacity to discontinue medicine with ease.¹⁵

DISADVANTAGES OF EMULGEL

- People who already have contact dermatitis may have worsening symptoms from the medication and/or its excipients.
- Skin permeability is poor for certain drugs.
- The risk of adverse allergic responses.
- The skin is not an ideal delivery system for medications with larger particle sizes.¹⁶

The rationale of emulgel as topical drug delivery

For pharmacologically modifying an operation on the subcutaneous tissue or restoring the skin's basic function, there are a number of semisolids and other preparations on the market. Lotions, ointments, and creams are not without their flaws; for example, they are sticky, have a poor spreading coefficient, and have stability problems.¹⁷ The overall limits within semisolid preparations mean that only clear gels are exposed in pharmacological and cosmetic preparations. Consequently, this constraint is addressed via a solution based on emulsions. Therefore, gels should be used to integrate and provide the drug's hydrophobic moiety. To include hydrophobic medications into emulgel, drug/oil/water emulsions might be used. Problems with drug release might arise when most medicines cannot be directly introduced into gel bases due to their solubility.¹⁸ With the use of the emulgel system, hydrophobic drugs may be introduced into the oil phase, and then the oily globules can be readily disseminated into the water phase, creating an oil/water emulsion. The gel base may be combined with the emulsion. When compared to just adding the medication to the gel foundation, this method may improve drug stability and release.¹⁹

COMPONENTS OF EMULGEL

Oils

One way to get an emulsion ready is to employ oils as an oil phase. Emulsions made of mineral oil and either soft or hard paraffin are often used for topical applications. For instance, the majority of oral and topical remedies include laxative-effecting oils, such as castor and mineral oils.²⁰

Aqueous materials

These are the watery agents that make up the formulation and are hydrophilic; examples of these agents include water, polyethylene glycols, propylene glycols, alcohols, glycerine, and many more.

Vehicles

Oily and watery carriers are used in the emulgel formulation, along with hydrophobic and hydrophilic medications.

Aqueous phase emulsions employ carriers like water, alcohol, and other aqueous compounds.²¹

Emulsifiers

By increasing the emulsification of the preparation, an emulsifier is used to enhance the shelf-life stability. Span80, Tween 20, Tween 80, stearic acid, and other similar compounds are emulsifying agents.²²

Gelling agent

Any dosage form may be gelled with the use of a gelling agent. Any formulation benefits from its improved uniformity. Carbopol 940, Carbopol 934, HPMC-2910, and others are examples of gelling agents.²³

pH adjusting agent

The formulation's pH is controlled using these substances. Such compounds include triethylamine and sodium hydroxide, among others.

Permeation Enhancers

Chemical compounds called permeability enhancers are used to make medicine molecules permeability through the skin much more robust. The skin's chemical structure is changed by the interaction of permeability enhancer with the skin's components. Skin permeability changes, albeit brief and reversible, are a result of this shift in the skin's chemical composition.

Preservatives

Preservatives are chemical substances, either synthetic or non-synthetic, that extend the shelf life of drugs, excipients, and formulations by inhibiting the development of microorganisms. The antibacterial activity of each preservative falls within the range that has been provided. The antibacterial activity within a certain pH range should be considered when choosing preservatives. The final product needs a preservative that can ward off bacteria and other microbes, whether they are Gram-positive or Gram-negative. The most optimal medium for microbial development is purified water, which comprises 50.0-80.0% of the topical solution. Therefore, topical compositions cannot be complete without preservatives.

PREPARATION OF EMULGEL

Step 1: Formulation of gel base

For the gel base, dissolve a certain amount of polymer in dilute dimethyl urea (DME), mix well with a magnetic stirrer set at moderate speed, and then adjust the pH to between 5.5 and 6.5 using a combination of triethanolamine and sodium hydroxide.²⁴

Step 2: Formulation of O/W or W/O type of emulsion

Using a magnetic stirrer, combine the ingredients of Smix according to the recipe. To make a transparent emulsion, slowly pour the Smix into the oil phase while swirling constantly.²⁵

Step 3: Formulation of emulgel

To make emulgel, slowly pour the created emulsion into the gel base while stirring constantly with a homogenizer.^{26,27}

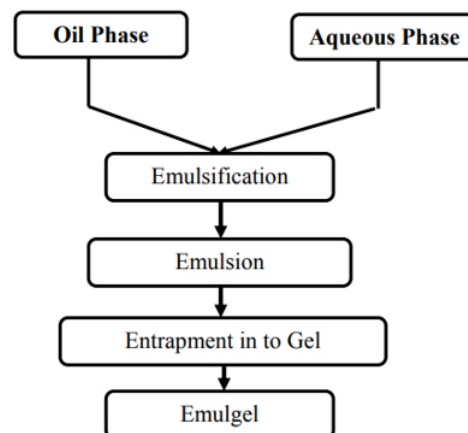


Figure 3: Method of preparation of Emulgel.

CHARACTERIZATION OF EMULGEL

Physical appearance

In order to observe the physical qualities of the created formulation, its colour, consistency, and homogeneity are visually examined.²⁸

pH measurement

We check the pH of every batch of created emulgel using a digital pH metre. Prior to utilising a standard buffer solution, the pH metre must be calibrated. A homogeneous suspension is made by dissolving 1 g of the formulation in distilled water and setting it aside for 2 hours. The pH is determined after 2 hours after dipping the glass electrode in the solution.²⁹

Rheological study

At 37°C, a cone and plate are used to determine the created formulation's viscosity. Viscometer.³⁰

Stability study

In order to conduct stability studies, a stability chamber is used along with the appropriate amounts of excipients (0.1 gm of API, 2.5 gm of oil, 6.665 gm of surfactant, 13.33 gm of co-surfactant, and 27.15 ml of double-distilled water) to

induce stress at various temperatures and humidity levels (room temperature of $30^{\circ}\text{C}\pm 2^{\circ}\text{C}$, RH of $65\%\pm 5\%$ and room temperature of $40^{\circ}\text{C}\pm 2^{\circ}\text{C}$, RH of $75\%\pm 5\%$). Physical changes, such as changes in clarity, turbidity, and particle development, are monitored over the one-month research.³¹

Skin irritation test

In most cases, researchers will get written agreement before conducting skin irritation tests on human subjects. Applying the prepared product to the skin of the hand and then watching for any negative effects is the standard procedure.³²

Zeta potential

This emulgel preparation's Zeta potential is found using zetasizer. The result is obtained by placing the formulation in a transparent, single-use zeta cell. Cuvettes are rinsed with methanol before each experiment, and the sample is then inserted into each cuvette.³³

Particle size and polydispersity index (PDI)

Using a zetasizer, the size of the emulgel globules is measured at 250C. Prior to the experiment, the material is diluted.³⁴

Swelling Index

In a 50 ml beaker containing 10 ml of 0.1 N NaOH, 1 mg of gel is put on porous aluminium foil individually. At regular intervals, the sample is taken out of the beaker and weighed again; then, it is preserved in a dry environment for a while.³⁵

$$\text{Swelling index (SW)} = \left[\frac{(\text{Wt}-\text{Wo})}{\text{Wo}} \right] \times 100$$

Where, (SW) %= Equilibrium percentage swelling; Wo= Original weight of emulgel at zero time where time t, Wt= Weight of swollen emulgel

Drug Content determination

The concentration of the medication in the emulsion may be determined using a spectrophotometer. By subjecting a known volume of emulsion to sonication in a solvent (methanol), one may ascertain the drug concentration of an emulsion. After the proper dilution, absorbance is measured in a UV/VIS spectrophotometer.³⁶

CONCLUSION

A revolutionary method, Emulgel has already shown to be the best delivery technique in terms of efficiency, effectiveness, and ease of use. Its gel-like qualities and superior drug release compared to traditional topical administration methods are a result of its non-greasy nature and absence of oily bases. Emulgel is an effective medication delivery vehicle with a high drug loading capacity. Because of their little size, drugs are able to effectively penetrate the skin.

Emulgel offers a dual control release effect and is created by mixing an emulsion with a gel basis. Creaming, phase separation, and improved stability are just a few of the issues that the emulgel process helps to resolve. Emulgel allows for the delivery of hydrophobic medicines by combining them with the oil phase of an emulsion. This method enhances localised medication bioavailability and patient compliance.

ACKNOWLEDGEMENT

The authors acknowledge the support received from college management.

CONFLICT OF INTEREST

Declared none.

SOURCE OF FUNDING

No agency provided any funding.

AUTHORS' CONTRIBUTION

Eisha Ganju: Concept, Analysis, Checking

Susheel Deshmukh: Literature Review, Writing manuscript

Bhaskar Kumar Gupta: Revision, Correction, Illustrations

REFERENCES

1. Ghosh PK, Majithiya RJ, Umrethia ML, Murthy RS. Design and development of microemulsion drug delivery system of acyclovir for improvement of oral bioavailability. *AAPS PharmSci Tech.* 2006;7(3): E172-E177
2. Kute S, Saudagar R. Emulsified gel: A novel approach for delivery of hydrophobic drugs: An overview. *J Adv Pharm Educ Res.* 2013;3(4):368-76.
3. Jain A, Deveda P, Vyas N, Chauhan J, Khambete H, Jain S. Development of antifungal emulsion based gel for topical fungal infection(s). *Int J Pharm Res Dev.* 2011;3(2):18-25.
4. Hussain A, Singh SK, Baboota S, Ali J, Kumar R, Prasad B. Formulation and optimization of nanoemulsion using antifungal lipid for topical delivery. *Int J Biol Macromol.* 2012;50(5):439-49.
5. Emami J, Rezazadeh M, Sadeghi H, Varshosaz J. Formulation of a topical antifungal emulgel containing sertaconazole nitrate. *Drug Dev Ind Pharm.* 2016;42(4):544-51.
6. Bonacucina G, Martelli S, Palmieri GF. Rheological, mechanical and functional properties of topical preparations containing the synthetic polymeric emulsifier Pemulen™ TR-2. *AAPS PharmSciTech.* 2004;5(1):48-59.
7. Prajapati ST, Patel CG, Patel CN. Formulation and evaluation of topical aceclofenac gel using different gelling agent. *Int J Pharm Pharm Sci.* 2011;3(1):110-2.
8. Patel V, Patel RP, Bakshi V. Formulation development and evaluation of diclofenac sodium gel using aqueous microemulsion. *Bull Pharm Res.* 2012;2(3):122-8.
9. Bharadwaj S, Jain S, Choudhury A, Jha A, Dey A. Emulgel: A topical preparation for hydrophobic drugs. *Pharm Innov J.* 2015;4(5):13-6.

10. Pathan IB, Setty CM. Chemical penetration enhancers for transdermal drug delivery systems. *Trop J Pharm Res.* 2009;8(2):173-9.
11. Agrawal SS, Munjal P. Permeation studies of atenolol and metoprolol tartrate from three different polymer matrices for transdermal delivery. *Indian J Pharm Sci.* 2007;69(4):535-9.
12. Attia MA, El-Gibaly I, Shaltout SE, Fetih GN. Transdermal permeation and anti-inflammatory effect of piroxicam formulated in different formulae. *Drug Dev Ind Pharm.* 2004;30(2):245-56.
13. Chouksey R, Jain AK, Pandey H, Maithil A. Enhancement of bioavailability of aceclofenac by preparing microemulsion gel. *Asian J Pharm Life Sci.* 2012;2(2):151-60.
14. Mortazavi SA, Moghimi HR, Khosravi M, Aninaghi A, Farzaneh A. Preparation and evaluation of an emulgel containing propranolol hydrochloride for skin administration. *Iran J Pharm Res.* 2014;13:21-7.
15. Panchal JH, Patel PB, Patel RB, Bhimani BV. Formulation and evaluation of topical emulgel of mefenamic acid. *J Pharm Sci Biosci Res.* 2011;1(1):1-9.
16. Sintov AC, Botner S. Transdermal drug delivery using microemulsion and aqueous systems: influence of skin storage conditions on the in vitro permeability of diclofenac from aqueous vehicle systems. *Int J Pharm.* 2006;311(1-2):55-62.
17. Abdel-Mottaleb MM, Mortada ND, El Shamy AA, Awad GA. Preparation and evaluation of fluconazole topical gel. *Int J Pharm Pharm Sci.* 2012;4(5):176-83.
18. Vyas A, Kumar Sonker A, Pahwa R. Emulgel: A new approach to topical drug delivery. *Int J Pharm Erudition.* 2013;3(1):1-6.
19. Parmar VK, Patel HR, Bhimani BV, Bhatt NM, Patel CN. Emulgel: A topical preparation for hydrophobic drugs. *Pharm Innov.* 2013;2(4):50-63.
20. Khullar R, Kumar D, Seth N, Saini S. Formulation and evaluation of mefenamic acid emulgel for topical delivery. *Saudi Pharm J.* 2012;20(1):63-7.
21. Rachakonda VB, Basu B, Rao GY, Kumar AS, Sastry TP. Preparation and evaluation of diclofenac sodium emulgel for topical application. *Indian J Pharm Educ Res.* 2012;46(1):65-70.
22. Mohammad TK, Zakir MA, Riyaz AM. Formulation and evaluation of novel topical emulgel of clotrimazole for antifungal activity. *Int J Pharm Biol Sci.* 2013;4(1):33-43.
23. Dubey A, Prabhu P, Kamath JV. Formulation and evaluation of topical gel containing miconazole nitrate microsponges. *Asian J Pharm Clin Res.* 2013;6(4):168-72.
24. Sheth NS, Mistry RB. Formulation and evaluation of miconazole nitrate emulgel by quality by design approach. *Int J Pharm Investig.* 2013;3(3):164-71.
25. Khalil Y, Sakr A, Abd El-Razik A. Formulation and evaluation of silver sulfadiazine emulgel. *Int J Pharm Pharm Sci.* 2013;5(4):307-13.
26. Jain A, Gautam SP, Gupta Y, Khambete H, Jain S. Development and characterization of ketoconazole emulgel for topical drug delivery. *Der Pharmacia Lettre.* 2010;2(5):415-27.
27. Mirani AN, Patil MS. Formulation and evaluation of an emulgel of ibuprofen. *Int J Pharm Life Sci.* 2013;4(6):2698-705.
28. Singh M, Sharma S, Khokra SL, Saini V. Formulation and evaluation of topical emulgel of rofecoxib. *Int J Pharm Pharm Sci.* 2011;3(1):210-3.
29. Sahu GK, Nayak N, Mishra L. Formulation and in-vitro evaluation of carbopol 934 based modified emulgel of ketoprofen. *Int J Pharm Res Bio Sci.* 2012;1(5):65-76.
30. Osmani RA, Aloorkar NH, Kulkarni AS, Harkare BR, Bhosale RR. A novel approach for topical delivery of hydrophobic drugs: Emulgel. *J Adv Pharm Sci.* 2013;3(3):17-24.
31. Bhardwaj V, Tripathi P, Verma A. Topical emulgel: A review on various pharmaceutical approaches for improving its performance. *J Pharm Sci Innov.* 2013;2(5):1-6.
32. Pandey S, Goswami L, Rath B, Kumar A. Formulation and characterization of diclofenac sodium loaded nanoemulsion based emulgel. *J Pharm Res.* 2012;5(10):4898-904.
33. Shakeel F, Baboota S, Ahuja A, Ali J, Faisal MS, Shafiq S. Nanoemulsions as vehicles for transdermal delivery of aceclofenac. *AAPS PharmSciTech.* 2007;8(4).
34. Mate A, Ade P, Pise A, More S, Pise S, Kharwade R. Formulation and evaluation of polyherbal gel for the management of acne. *Int J Curr Res Rev.* 2021;13(4):117-22.
35. Baboota S, Shakeel F, Ahuja A, Ali J, Faisal MS, Shafiq S. Design, development and evaluation of novel nanoemulsion formulations for transdermal potential of celecoxib. *Acta Pharm.* 2007;57(3):315-32.
36. Kalia YN, Naik A, Garrison J, Guy RH. Iontophoretic drug delivery. *Adv Drug Deliv Rev.* 2004;56(5):619-58.