

An overview of emulgels for topical application

Mina J. Jabbar*, Wedad K. Ali*

*Department of Pharmaceutics, College of Pharmacy, Mustansiriyah University, Baghdad- Iraq

Article Info:

Received Dec 2022

Accepted Mar 2023

Corresponding Author email:

pharm.dr.wedad.ali@uomustansiriyah.edu.iq

Orcid: <https://orcid.org/0000-0003-2522-5428>

DOI:

Abstract:

In recent years, gels have been preferentially used for cosmetics and topical pharmaceutical preparations due to their favorable characteristics, such as being greaseless, readily spreadable and easily removable. However, one

obstacle that faced it was the inability to enclose hydrophobic compounds. Therefore, a novel approach was developed to circumvent this limitation by mixing the gel with an emulsion, which led to creation of a new topical drug delivery system known as emulgel. Emulgel preserves all favorable features of gel and provides also dual release for drug, thus can be utilized effectively in controlling release and absorption of medication after topical application. Emulgel preparation requires coherent steps, this includes preparation of emulsion and gel and determining their mixing ratio. Finally, the prepared emulgels should be evaluated to ensure their suitability and efficacy for the topical application.

Key words: Emulgel, Extrudability, Formulation, Spreadability

نظرة عامة للمستحلب الهلامي للاستخدام الموضعي

مينا جمال جبار*، ووداد كمال علي*

*الجامعة المستنصرية / كلية الصيدلة / قسم الصيدلانيات/ العراق – بغداد

الخلاصة:

في السنوات الأخيرة ، أصبح يفضل استخدام المواد الهلامية في مستحضرات التجميل والمستحضرات الصيدلانية الموضعية نظراً لخصائصها المفضلة ، مثل كونها غير دهنية وقابلة للدهن على البشرة وقابلة للإزالة بسهولة. ومع ذلك ، هناك عقبة واحدة تواجه عدم القدرة على إحاطة المركبات الكارهة للماء. لذلك ، تم تطوير نهج جديد للتغلب على هذا القيد من خلال خلط الجل مع المستحلب ، مما يؤدي إلى إنشاء نظام توصيل دواء موضعي جديد يعرف باسم المستحلب الهلامي. يحافظ المستحلب الهلامي على جميع الميزات المفضلة للجل ويوفر أيضاً تحريراً مزدوجاً للدواء ، وبالتالي يمكن أن يستخدم بشكل فعال في التحكم في تحرير وامتصاص الدواء بعد التطبيق الموضعي. يتطلب تحضير المستحلب الهلامي خطوات متماسكة ، ويشمل ذلك تحضير المستحلب والهلام وتحديد نسبة الخلط. أخيراً ، يجب تقييم المستحلب الهلامي للتأكد من أنه مناسب وفعال للتطبيق الموضعي للأدوية.

الكلمات المفتاحية: المستحلب الهلامي ، قابلية البثق ، المستحضرات ، قابلية الانتشار

Introduction

Topical drug delivery system can be defined as the application of a drug containing formulation to the skin to treat cutaneous disorder directly¹. The topical drug delivery system is generally used where other routes (like oral, sublingual, rectal, parental) of drug administration

fails or in local skin infection like a fungal infection^[2].

In addition to oral/intravenous methods, scientists have been encouraged by advances in pharmaceutical technology to investigate alternate routes for the efficient and effective delivery of drugs to the target location. Effective pharmaceutical

administration involves the optimum delivery of drugs to the site of action within the permitted time period^[3].

Ideal formulations include patient compliance, self-administration, non-invasiveness, fewer side effects, and enhanced pharmacological efficacy. The topical preparations contain the majority of the these mentioned features^[4]. The advantages of topical administration include avoiding the hepatic first-pass impact, reducing adverse effects related to the local site of action, enhancing percutaneous absorption, and perhaps increasing bioavailability with prolonged deposition^[5]. In addition, decreased drug loss owing to metabolism or breakdown and the capacity to precisely target the drug at the intended site are further benefits^[6]. Minimizing drug breakdown and delivering the drug continuously over a longer duration increases drug transport over the stratum corneum barrier, resulting in enhanced bioavailability^[7].

Topical route of drug administration.

In this route the drug is applied on the skin and mucous membrane for the local action.

- Mucosal membranes (eye drops, antiseptic, sunscreen, callous removal, nasal, etc.)

- Skin.

A) Dermal - Rubbing in of oil or ointment (local action).

B) Transdermal - Absorption of drug through skin (systemic action)^[8]

Drug delivery across the skin.

The skin accounts for around 15% of an adult's total body weight, making it the biggest organ. It aids in thermoregulation and protects the body against external physical, chemical, and biological risks. It is continuous and consists of three structural layers: the deepest hypodermis, the middle dermis, and the outermost epidermis^[9,10]. The thickness of the epidermis varies throughout the body. It is composed of stratified, keratinized, squamous epithelium. The skin develops a

typically resistant covering that shields the deeper, more significant components. Blood vessels are widely distributed under the skin^[11]. A continuous venous plexus that receives blood from the capillaries of the skin is significant importance. In the body's most exposed areas, such as the hands, feet, and ears, the plexus gets blood directly from the small arteries through highly muscular arteriovenous anastomoses^[12]. The dermis is situated below the epidermis. It is a thick layer of collagen- and elastin-containing connective tissue that gives skin its strength and, accordingly, its flexibility^[13]. In addition to nerve endings and blood arteries, the dermis contains adnexal structures such as hair shafts, sweat glands, and sebaceous glands. Papillary dermis is the topmost layer of the dermis, whereas reticular dermis is the lowest^[14]. The hypodermis, the third and deepest layer of skin, is predominantly composed of fatty tissue. Its purpose is to connect the skin to the underlying bone and muscle. This structure is composed of connective and elastic tissue^[15]. Fibroblasts, macrophages, and adipocytes are the primary cell types, and the hypodermis contains fifty percent of the body's fat. The hypodermis is also known as the subcutaneous tissue^[14,16].

There are two major mechanisms of topical drug absorption through skin, trans epidermal and trans appendageal^[12,13]. Trans epidermal (intercellular and intracellular route), Intercellular pathway is the most prevalent route where drug molecules traverse a tortuous path around corneocyte and through the lipid bilayer to viable layers of skin. While the intracellular route is the drug's direct passage through the stratum corneum's lipid structure^[13,14]. Trans appendageal (shunt pathway) The substance enters the hair follicles, sweat glands, and sebaceous glands through the corneocytes^[17]. Appendages of the skin form a channel that continuously passes through the stratum corneum barrier. However, a number of considerations, such as the

limited area accessible for direct contact with the administered medicine owing to the tiny surface area occupied by hair follicles and sweat ducts, restrict their influence on drug penetration (typically 0.1% of the skin's surface area); thus, this pathway is restricted^[13,18].

Factors affecting topical absorption of drug

There are several factors that could affect the absorption of topically applied the drug. These factors are categories as followings:

A) Physiological Factors ^{[12, 19]:}

- 1) Stratum corneum thickness varies across races and body sections.
- 2) Age, skin care regimen, solvent exposure, health condition, and environmental variables may all alter stratum corneum integrity.
- 3) Skin pH: sweat and fatty acid released by sebum influence the pH of the skin's surface, affecting the degree of ionizable drug dissociation, thermodynamic activity, partitioning, and skin penetration.
- 4) Blood flow: cutaneous blood flow may alter the concentration level and accumulation of substances in the dermis and deeper skin layers.
- 5) Inflammation of the skin, which destroys stratum corneum consistency, increases permeability.
- 6) Temperature of the skin; As skin temperature rises, skin permeability accelerates.
- 7) Skin hydration may improve drug absorption.

B) Physiochemical Factors ^{[12, 20]:}

1) Partition coefficient (P)
In addition to its aqueous solubility, the rate of drug penetration through the skin is directly proportional to its oil/water partition coefficient. In order for a drug to permeate through the skin and enter the systemic circulation, the solubility in these two phases must be balanced. The optimal

skin absorption of drugs with a Log P between 1 and 3 was recognized.

2) Molecules with a molecular weight greater than 500 Da are incapable of penetrating the skin.

This restriction on molecule size is due to the physical arrangement of lipids between neighboring corneocytes in the stratum corneum.

3) As a result of the presence of proteins (such as keratin), the stratum corneum contains both negatively and positively charged groups, which increases the ionization amplitude. This property, in conjunction with the lipophilic properties of the stratum corneum, will create an effective barrier against the charged molecules (ions). (It is known that only unionized molecules can pass)

Classification of topical dosage forms

Conventional topical dosage form can be classified into three categories: Liquid (lotion, liniment, solution, emulsion, suspension) and semisolid dosage forms include (ointment, cream, paste, gel, emulgel) and solid dosage form like powder.

Semisolid dosage forms are used for the administration of dermatological compounds applied to the skin for medical, protective. In an acceptable base, one or more active compounds are dissolved or evenly distributed, together with any compatible excipients, such as emulsifying agent, preservatives, anti-oxidants, and stabilizing agents^[21]. Numerous considerations influence the selection of bases for semisolid dosage forms. The distribution environment, the end product's shelf life, the type of active ingredient at the site of action, and the desired therapeutic effect^[3, 22].

The base should not cause irritation, sensitization and in order to be compatible with the skin and the active substances to be incorporated, it must be smooth, inert, odorless, physically stable, and chemically inert. Generally, its consistency should be

such that it spreads and softens rapidly when subjected to stress^[23].

Semi-solid dosage forms offer several benefits and can be applied topically. Local action and possibility of adverse effects may be decreased, first pass metabolism can be avoided, improve patient acceptance, and drug therapy discontinuation in difficult instances can be easier, compared to other routes of drug administration^[13].

Conventional topical formulations such as (creams, ointments, pastes, gels, and others) have various disadvantages, including adhering to the skin, causing patient discomfort during application, being less spreadable and requiring rubbing application, and rapidly evaporating from the skin. To avoid these limitations, emulgel formulation was developed^[22].

Emulgel

Emulgel is a semisolid dosage form could be considered as a novel delivery system

for hydrophobic compounds. Emulgels are w/o or o/w emulsions that have been gelled using a gelling agent^[24]. The emulsion functions as a method for delivering controlled-release drugs, in which the particles of drugs are trapped in the interior phase and slowly absorbed by the skin through the exterior phase. The drug reaches the exterior phase of the skin via the internal phase, which serves as a drug reservoir. Small drug particles are entrapped within a gel's crosslinked network, allowing for their controlled release^[25]. It increases the length of drug interaction with the skin due to its mucoadhesive property. Emulgel acts as a dual-control release system since it possesses both gel and emulsion qualities^[26,27]. A researcher approved that emulsions can be considered as a control release delivering system when it has been prepared as a complex of tannic acid with curcumin^[28].

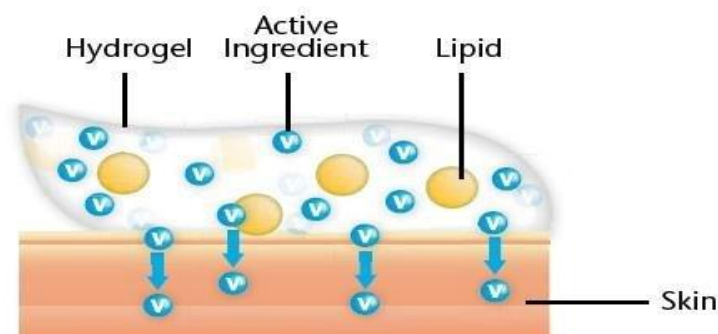


Figure (1):Schematic presentation for release of active ingredient moieties from emulgel structure and their penetration through skin ^[29].

Emulgels used for dermatological purposes provide a number of advantageous characteristics, such as emollient, non-greasy appearance, thixotropic, rapidly remove from skin and suitable for a variety of excipients^[30]. The type and concentration of polymer employed to make the gel can influence the drug's release rate and stability. Emulgel may be advantageous for the topical delivery of a drug with poor water solubility. It has been

shown to be an effective and stable carrier for drugs that are poorly water-soluble or hydrophobic^[12,26].

The easy and speedy steps needed in the development of emulgels make their production more feasible. There are no specialist instruments necessary for emulgel manufacture^[31]. Additionally, the utilized materials are generally accessible and inexpensive. All of them decrease the price of emulgel production^[25].

Emulgels have several disadvantages like poor absorption of large particle size through the skin. Some drugs have poor permeability through the skin also, skin irritation or allergic reaction may occur^[32].

Examples of drugs that prepared as emulgel to overcome some issue in other different route of administration:

Piroxicam is a non-steroidal anti-inflammatory compound with analgesic and antipyretic effects, used for the treatment of rheumatoid arthritis, osteoarthritis and traumatic contusions. It is well absorbed following oral administration however its use has been associated with a number of undesirable side effects on the stomach and kidneys in addition to gastric mucosal damage. Dermal delivery is an alternative route but requires a formulation which ensures deep skin penetration, allowing therapeutic effect at localized site^[33].

Other example is a combination of doxycycline and eugenol for oral care. Which is prepared as emulgel to avoid the GI upset as a side effect of doxycycline. Doxycycline will help in treatment of periodontitis and eugenol will act as an analgesic, anti-inflammatory, antimicrobial, and aesthetic^[34].

Other benefit for emulgel, it can be used for preparation the hydrophobic drugs (like Chloramphenicol). Chloramphenicol Palmitate was formulated as topically applied emulgel to be in systemic circulation through skin^[35].

Important constituents of emulgel preparation:

Aqueous material:

These constituents form the emulsion's aqueous phase. Water and alcohols are typical solvents^[36].

Oils:

These substances make up the emulsion's oily phase. Mineral oils are often used as the drug carrier as well as for their occlusive and sensory properties in

topically given emulsions, either alone or in combination with soft or hard paraffins^[36].

Emulsifiers:

Emulsifying agents are used to enhance emulsification during the manufacturing process and to manage stability over a shelf life that may range from days to months or years for commercially available emulsions. "Polyethylene glycol 40 stearate, Sorbitan monooleate (Span 80), Polyoxyethylene sorbitan monooleate (Tween 80), Stearic acid, and Sodium stearate" are examples^[36].

Gelling agent:

Gelling agents are used to improve the consistency of any dosage form; they may also serve as thickening agents. Examples include carbopol polymer, gellan gum, methylcellulose, and hydroxypropylmethylcellulose^[37].

Permeation enhancers:

These are substances that interact with skin cells and partition into them, causing a brief and reversible increase in skin permeability^[38].

Antioxidants:

Antioxidants are used in pharmaceutical formulations to enhance the chemical stability of drugs/components susceptible to oxidative destruction.

The choice of antioxidants is determined by the kind of vehicle employed in the manufacture of the pharmaceutical dosage form; water-soluble antioxidants are the most common^[39].

Preservatives

Formulations used topically are not sterile. However, they are manufactured under sterile conditions to reduce the risk of microbial contamination of the final product. If a product involves water, it should incorporate preservatives in its composition. Preservatives such as methyl and propyl paraben, phenol, benzoic acid,

and salt are often found in products designed for external use^[40].

Methods

Preparation of gel base:

A transparent gel is produced by dispersing the gelling agent in distilled water followed by heating to 80 °C, the dispersion is then allowed to cool overnight to 25 °C^[10]. Carbopol polymer was dispersed in purified water with continuous stirring at a moderate speed and then the pH is adjusted to (5.5) by addition drops of tri ethanol amine^[41].

Preparation of emulsion:

In order to prepare the oil phase, the lipophilic surfactant span 80 is dissolved in oil base. Also, the active ingredient is introduced to the oil phase. While preparing the aqueous phase by dissolving tween 80 in distilled water, preservatives, antioxidant and penetration enhancer are added to aqueous phase^[42]. After that the two phases of emulsion are heated separately up to 80° C until both phases became homogenous. Next, the aqueous phase is put into the oil phase while stirring continuously for two hours, followed by room-temperature cooling^[43].

Preparation of emulgel:

By combining emulsion and gel in a 1:1 weight ratio^[10].

Emulgel Evaluation

Physical examination:

Visual evaluation is done of the prepared emulgel formulations' color, phase separation, and consistency^[31].

Determination of pH:

The pH of every emulgel formulation is determined using a pH meter by introducing the electrode in the prepared formula and recording the result two minutes later^[44].

Determination of viscosity:

Using a Brookfield viscometer (Brookfield LV, spindle no. S-64), viscosity tests of prepared emulgels are performed by filling a glass container with emulgel sample and placing it in a beaker (filled with water) on a heat source to maintain $37 \pm 0.5^\circ\text{C}$ ^[45, 46].

Drug content estimation:

Determination of drug content, one gram of emulgel formulation is dissolved in an appropriate solvent then sonicated for 2 hrs. after that is filtered to produce a clear solution. A UV-visible spectrophotometer is used to measure the absorbance of the resulting solution. A drug calibration curve is used to measure the drug content ^[47].

Spreadability:

Specialized equipment was developed to examine the spreadability of formulations. Spreadability is measured in seconds by the time it takes for two slides to separate from formulations put between them when a certain force is applied; the shorter the time it takes for the separation, the greater the spreadability^{46, 48}. Each of two 6 × 2-centimeter glass slides are chosen. One of the slides for which the spreadability is to be assessed had the formulation on it. This slide is placed on top of the other slide, sandwiching the formulation between the two. Weight (100 gm) is placed on the top slide as a result of the formulation between the two slides being repeatedly pressed to produce a thin layer. Following the removal of the weight, the extra formulation that had adhered to the slides is scraped off. The length of time needed to separate the two slides is recorded³⁶.

$$\text{“Spreadability}=(M/T) *L\text{”}$$

Where, M= Weight which is put to the upper slide. L= Length taken of glass slide
T= Time (seconds) required for separated two glasses.

Extrudability:

Measuring the force necessary to extrude material from a tube is a standard empirical test. The technique for

measuring the extrudability of an emulgel formulation is based on the percentage of emulgel and it's extruded from the aluminum collapsible tube using the weight in grams necessary to extrude emulgel ribbon of at least 0.5 cm in 10 seconds. The greater the amount that can be extruded, the greater its extrudability^[49]. The extrudability is measure by this equation:

“Extrudability = Applied weight to extrude emulgel from tube (in gm) / Area (in cm²)”

***In-vitro* Drug release:**

The *in vitro* release of the active ingredient from emulgel formulations is usually carried out a modified technique using a paddle-type dissolution apparatus and a dialysis membrane (M. WT 12000)^[10]. After 24 hours of soaking in phosphate citrate buffer solution with a pH of 5.5, the membrane is opened from both sides and one end should be sealed with an elastic rubber band. One gram of emulgel is inserted into the membrane, and then the membrane's free end is sealed with another rubber band. The membrane is inserted into the dissolving jar while being linked to the paddle of dissolution apparatus. (Which filled up with 500 ml of phosphate citrate buffer) pH 5.5 at 37 ±0.5°C with stirring rate of 50 rpm). Then sample of 5 ml are taken at different time intervals and substituted with the same volume of buffer solution every time. The samples are put through (0.45 m Millipore) filter before being examined with a UV-visible spectrophotometer at the predetermined λ_{max} ¹⁰.

Stability study:

For the stability investigation a sufficient amount of emulgel formula is vacuum-sealed in 10-gram collapsible tubes and submitted to three-month stability testing at 25°C. The samples are tested for pH, physical characteristics, rheological characteristics, and drug content at regular intervals^[50].

Skin irritation Study:

Wistar rats are used for the skin irritation investigation. First, shaved the rat skin and applied emulgel to the shaved skin, observing for 24 hours for any skin changes such as color change, edema, and redness^[10, 41].

Conclusion:

Emulgel is the most modern technology utilized among topical drug delivery application. It is mostly utilized to transport both hydrophobic and hydrophilic compounds. Emulgel includes both oil and aqueous (gel) bases. Due to the fact that emulgel exhibits better spreadability, adhesion, viscosity, and extrusion. This successful drug delivery method becomes popular.

References:

- 1- Mohammed, M. M.; Hamadi, S. A.; Aljaf, A. N. Formulation of melatonin as a cream and studying the release, diffusion, and stability of the cream. Al Mustansiriyah Journal of Pharmaceutical Sciences 2009. 6 (1): 43-55.
- 2- Buhse, L.; Kolinski, R.; Westenberger, B.; Wokovich, A.; Spencer, J.; Chen, C. W.; Turujman, S.; Gautam-Basak, M.; Kang, G. J.; Kibbe, A. Topical drug classification. International journal of pharmaceutics 2005. 295 (1-2): 101-112.
- 3- Dhawas, V.; Dhabarde, D.; Patil, S. Emulgel: A comprehensive review for novel topical drug delivery system. International Journal of Recent Scientific Research 2020. 11 (4):38134-38138.
- 4- Kumar, D.; Rajni, R. S.; Rani, S.; Kumari, R. Formulation And Evaluation Of Emulgel Of An Antifungal Drug For Topical Drug Delivery. Journal of Pharmaceutical Negative Results 2023: 4087-4100.
- 5- Iqbal, M. A.; Md, S.; Sahni, J. K.; Baboota, S.; Dang, S.; Ali, J. Nanostructured lipid carriers system: recent advances in drug delivery.

- Journal of drug targeting 2012. 20 (10): 813-830.
- 6- Bhowmik, D. Recent advances in novel topical drug delivery system. *The Pharma Innovation* 2012. 1 (9).
 - 7- Gannu, R.; Palem, C. R.; Yamsani, V. V.; Yamsani, S. K.; Yamsani, M. R. Enhanced bioavailability of lacidipine via microemulsion based transdermal gels: formulation optimization, ex vivo and in vivo characterization. *International journal of pharmaceutics* 2010. 388 (1-2): 231-241.
 - 8- Verma, P.; Thakur, A.; Deshmukh, K.; Jha, A.; Verma, S. Routes of drug administration. *International Journal of Pharmaceutical Studies and Research* 2010. 1 (1): 54-59.
 - 9- Sahle, F. F.; Gebre-Mariam, T.; Dobner, B.; Wohlrab, J.; Neubert, R. H. Skin diseases associated with the depletion of stratum corneum lipids and stratum corneum lipid substitution therapy. *Skin pharmacology and physiology* 2015. 28 (1), 42-55.
 - 10- Sabri, H. S.; Alia, W. K.; Abdullah, B. H.; Al-Anic, W. Formulation design and evaluation of anti-microbial activity of emulgel containing essential oil of myrtus communis L. *Inter J Pharm Sci Rev Res* 2016. 40: 271-277.
 - 11- Abdo, J. M.; Sopko, N. A.; Milner, S. M. The applied anatomy of human skin: A model for regeneration. *Wound Medicine* 2020. 28. 100179.
 - 12- Panwar, A.; Upadhyay, N.; Bairagi, M.; Gujar, S.; Darwhekar, G.; Jain, D. Emulgel: a review. *Asian J Pharm Life Sci* 2011. 2231. 4423.
 - 13- Alkilani, A. Z.; Nasereddin, J.; Hamed, R.; Nimrawi, S.; Hussein, G.; Abo-Zour, H.; Donnelly, R. F. Beneath the Skin: A Review of Current Trends and Future Prospects of Transdermal Drug Delivery Systems. *Pharmaceutics* 2022. 14 (6). 1152.
 - 14- Agarwal, S.; Krishnamurthy, K. *Histology, skin*. 2019.
 - 15- Pappalardo, A.; Cespedes, A.; Vu, H. L.; Abaci, H. E. Advances in skin-on-a-chip and skin tissue engineering. In *Principles of Human Organs-on-Chips*, Elsevier. 2023. pp :123-166.
 - 16- Vestita, M.; Tedeschi, P.; Bonamonte, D. Anatomy and Physiology of the Skin. In *Textbook of Plastic and Reconstructive Surgery*, Springer, 2022; pp :3-13.
 - 17- Ranjan, A.; Duryodhan, V. S.; Patil, N. D. A comparative study of passive drug diffusion through human skin via intercellular and sweat duct route: effect of aging. 2023.
 - 18- Wortsman, X.; Ferreira-Wortsman, C.; Corredoira, Y.; Pizarro, K. *Comprehensive Ultrasonographic Anatomy of the Normal Skin, Nail, Hair, and Adjacent Structures. Textbook of Dermatologic Ultrasound* 2022: 89-100.
 - 19- Kolimi, P.; Narala, S.; Youssef, A. A. A.; Nyavanandi, D.; Dudhipala, N. A systemic review on development of mesoporous nanoparticles as a vehicle for transdermal drug delivery. *Nanotheranostics* 2023. 7 (1): 70-89.
 - 20- Redkar, M. R.; Patil, S. V.; Rukari, T. G. Emulgel: A modern tool for topical drug delivery. *World Journal of Pharmaceutical Research* 2019. 8 (4): 586-597.
 - 21- Maqbool, A.; Mishra, M. K.; Pathak, S.; Kesharwani, A.; Kesharwani, A. Semisolid dosage forms manufacturing: Tools, critical process parameters, strategies, optimization, and recent advances. *Ind. Am. J. Pharm. Res* 2017.7: 882-893.
 - 22- Garg, T.; Rath, G.; Goyal, A. K. Comprehensive review on additives of topical dosage forms for drug delivery. *Drug delivery* 2015. 22 (8): 969-987.
 - 23- Kumar, M. S. AN OVERVIEW OF EXCIPIENTS USED IN SEMISOLID PREPARATION. 2022.
 - 24- Arora, R.; Khan, R.; Ojha, A.; Chopra, H.; Upadhyaya, K.

- Formulation and characterization of terbinafine emulgel for superficial fungal infections. *Res. J. Pharm. Technol* 2018. 11:5029-5036.
- 25- Chauhan, S. B. Formulation and Evaluation of Emulgel for the treatment of Acne. *EVALUATION* 2020. 100 (100). 100.
- 26- Lakshmi, S. S.; Divya, R.; Rao, S. Y.; Kumari, K. P.; Deepthi, K. Emulgel-novel trend in topical drug delivery system-review article. *Research Journal of Pharmacy and Technology* 2021. 14 (5): 2903-2906.
- 27- Abdallah, M. H.; Elghamry, H. A.; Khalifa, N. E.; Khojali, W. M.; Khafagy, E.-S.; Lila, A. S. A.; El-Horany, H. E.-S.; El-Housiny, S. Ginger Extract-Loaded Sesame Oil-Based Niosomal Emulgel: Quality by Design to Ameliorate Anti-Inflammatory Activity. *Gels* 2022. 8 (11). 737.
- 28- Zou, Y.; Zhong, J.; Pan, R.; Wan, Z.; Guo, J.; Wang, J.; Yin, S.; Yang, X. Zein/tannic acid complex nanoparticles-stabilised emulsion as a novel delivery system for controlled release of curcumin. *International Journal of Food Science & Technology* 2017. 52 (5): 1221-1228.
- 29- Redkar, M. R.; Hasabe, P. S.; Jadhav, S. T.; Mane, P. S.; Kare, D. J. Review on optimization base emulgel formulation. *Asian Journal of Pharmacy and Technology* 2019. 9 (3):228-237.
- 30- Campanholi, K. d. S. S.; Junior, R. C. d. S.; Jaski, J. M.; Silva, J. B. d.; Oliveira, M. C. d.; Santos, R. S. d.; Pozza, M. S. d. S.; Castro-Hoshino, L. V. d.; Baesso, M. L.; Cardozo-Filho, L. Thermo and Photoresponsive Emulgel Loaded with *Copaifera reticulata* Ducke and Chlorophylls: Rheological, Mechanical, Photodynamic and Drug Delivery Properties in Human Skin. *Pharmaceutics* 2022. 14 (12). 2798.
- 31- Dessai, P.; Mhaskar, G. M. Formulation and Evaluation of Ginger officinale Emulgel. *Research Journal of Pharmacy and Technology* 2019. 12 (4):1559-1565.
- 32- Vishwakarma, G.; Panwar, A. S. Review on emulgel: A novel technique for drug targeting.
- 33- Khunt, D. M.; Mishra, A. D.; Shah, D. R. Formulation design & development of piroxicam emulgel. *Int J PharmTech Res* 2012. 4 (3):1332-1334.
- 34- Shelke, O.; Sharma, M. Development of sustained release hydrophobic emulgel for oral care. *Journal of Drug Delivery and Therapeutics* 2019.9 (3): 447-454.
- 35- Hafiz, Z.; Gul, S. Emulgel as Remarkable Drug Delivery System for Topical Preparations: Formulation Development of Emulgel & Quality Control Testing of Chloramphenicol Palmitate. *Current Trends in Biotechnology & Pharmacy* 2020.
- 36- Vanpariya, F.; Shiroya, M.; Malaviya, M. Emulgel: A Review. *International Journal of Science and Research (IJSR)* 2021. 10. 847.
- 37- Rowe, R. C.; Sheskey, P.; Quinn, M. Handbook of pharmaceutical excipients; Libros Digitales-Pharm-aceutical Press. 2009.
- 38- VISHWAKARMA, G.; PANWAR, A. S. EMULGEL EMERGENT SYSTEMS: AT A GLANCE FOR TOPICAL DRUG DELIVERY. *Asian J Pharm Clin Res* 2022. 15 (3):8-14.
- 39- Joshi, V.; Kumar, K.; Khairya, D.; Teotia, D. EMULGEL AS A NOVEL DRUG DELIVERY SYSTEM: A COMPREHENSIVE REVIEW. *International Journal of Indigenous Herbs and Drugs* 2022: 94-98.
- 40- Kute, S.; Saudagar, R. Emulsified gel A Novel approach for delivery of hydrophobic drugs: An overview. *Journal of Advanced Pharmacy Education & Research* Oct-Dec 2013. 3 (4).

- 41- Yadav, R.; Pandey, N. K.; Kukkar, R.; Dutta, D.; Avasthi, P.; Rana, M.; Modgil, S. Emulgel A Reliable System for Topical Delivery of Lipophilic Drugs in Present Scenario. *Research Journal of Pharmacy and Technology* 2022.15 (6): 2845-2848.
- 42- Singh, S.; Singh, I. Evolving Implementation of Emulgel as a Topical Drug Delivery System: A Systematic Review. *Current Research in Pharmaceutical Sciences* 2022: 121-131.
- 43- Kegade, P.; Sawant, R.; Parkar, S.; Gade, A. Emulgel: In treatment of periodontitis. *World Journal of Advance Healthcare Research* 2020. 4 (5): 71-75.
- 44- Mishra, A.; Mishra, A.; Chattopadhyay, P. Assessment of in vitro sun protection factor of *Calendula officinalis* L.(asteraceae) essential oil formulation. *Journal of Young Pharmacists* 2012. 4 (1): 17-21.
- 45- Rana, N.; Singh, V.; Ali, M. Formulation and Characterization of Ginger oil loaded Polyherbal Emulgels having extracts of *Nardostachys jatamansi*, *Andrographis paniculata* and *Celastrus paniculatus*. *Research Journal of Pharmacy and Technology* 2020. 13 (9): 4077-4083.
- 46- Ali, M. H. M.; Ali, W. K. Preparation and Evaluation of Emulgel as Topical Drug Delivery for Nimesulide by Using Conventional Emulsion. *Al Mustansiriyah Journal of Pharmaceutical Sciences* 2019. 19 (4):16-26.
- 47- Khan, J.; Norfarhani, S.; Sahu, R. K.; Ruhi, S.; Kaleemullah, M.; Al-Dhalli, S.; Rasny, M.; Budiasih, S.; Baber, S.; Ng, C. H. Development and Evaluation of topical Emulgel of Aspirin using different Polymeric Bases. *Research Journal of Pharmacy and Technology* 2020. 13 (12): 6300-6304.
- 48- Chandel, M.; Sharma, C.; Kashyap, V. Topical delivery of clarithromycin emulgel with biocompatible polymers. In *AIP Conference Proceedings, 2023*; AIP Publishing LLC: Vol. 2558: p 020081.
- 49- Jyothi, V.; Pullemmla, M.; Nafiroona, S.; Pujari, G.; Purama, R. Formulation and evaluation of curcumin emulgel for topical delivery. *Journal of Pharmacognosy and Phytochemistry* 2022. 11 (6): 33-41.
- 50- Saeed, A. M.; Alaayedi, M.; Alhendawi, Z. M.; Hammoodi, I. D. EMULGEL AS PHARMACEUTICAL FORMULATION: A REVIEW. *kerbala journal of pharmaceutical sciences* 2023. 1 (21).