www.pharmaerudition.org

ISSN: 2249-3875

International Journal of Pharmaceutical Erudition

Research for Present and Next Generation

AUG 2021

Vol: 11 Issue:02

(74-84)

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

Review Article

COMPREHENSIVE REVIEW ON EMULGEL – NOVEL TOPICAL DRUG DELIVERY SYSTEM

Durgesh Ray*, Abadhesh Niranjan, Lalit kumar and Ritesh kumar Diwedi

Department of pharmaceutics, Hygia Institute of Pharmaceutical Education & Research,

Ghaila Road, Gazipur Balram road, Lucknow, Uttar Pradesh 226020

Emulgel could also be a topical drug Delivery System that's used to treat pains and aches caused by colds, headaches, muscle aches, backaches, arthritis, and other conditions and injuries. Topical application of therapeutic agents offers various advantages over the other route of administration The patient's adherence to topical formulations is significant in relation to chronic skin diseases, like fungal infections, acne, psoriasis. Emulgel is one of the recent technologies in NDDS used topically having characteristics of dual control release i.e., emulsion also as a gel. Emulgel has emerged together of the foremost interesting topical delivery systems because it features a dual release system i.e., gel and emulsion. When gel and emulsion are utilized in combined form, the dosage form is referred to as Emulgel.

Key Words: Emulsion, Gel, Topical drug delivery, Epidermal Skin diseases.

INTRODUCTION

A topical drug delivery system is defined as the application of a drug-containing formulation to the skin or mucous membrane, to treat a specific cutaneous disorder (e.g., acne) or cutaneous manifestation of a generalized disease directly. The topical drug delivery system is beneficial where other routes (like oral, sublingual, rectal, parental) of drug administration fails or in local skin infection sort of a mycosis.[1] Topical drug administration may be a localized drug delivery system anywhere within the body through ophthalmic, rectal, vaginal, and skin as topical routes.[2] These are applying a good spectrum of preparations for cosmetic and dermatological, to their healthy or diseased skin. The main advantage of the topical delivery system is to avoidance of the first-pass metabolism. Easy applications. Avoidance of the risks and inconveniences of intravenous therapy and of the numerous conditions of absorption, like pH changes, the presence of enzymes, gastric emptying time [3,4] are another advantage of the topical drug delivery system is usually used where the other system of drug administration fails. The formulations are available in several forms like from solid through semisolid to liquid. Drugs are administered topically for his or her action at the location of the application or for systemic

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

effects. Drug absorption is enhanced through the skin if the drug substance is in solution, if it's a positive lipid/water partition coefficient and if it's a non-electrolyte.

The Skin is the most important part of the human body for topical administration and molecules penetrate the skin mainly by three routes: through intact stratum corneum, through sweat ducts, and through the sebaceous follicle [5]. The cause for a topical drug delivery system is to heighten the skin permeability and retain in the dermis. Topical drug delivery is employed for localized action on the body through ophthalmic, rectal, vaginal, and skin as topical routes.

The topical drug delivery system such as Emulgel (jellified emulsion) is generally used where the other systems of drug administration fail to directly treat cutaneous disorders such as fungal infections, acne, psoriasis, etc. [5]

Fig. 1: An Emulgel marketed product

Advantages [5,6]

1. The hydrophobic drug are often easily incorporated into the gel using emulsions.2
2. Avoidance of the first-pass metabolism.
3. Avoidance of gastrointestinal incompatibility
4. More selective to a selected site.
5. Improve patient compliance.
6. Suitability for self-medication.
7. Ability to simply terminate medication when needed.
8. Convenient and straightforward to use.
9. Incorporation of hydrophobic drugs
10. Better loading capacity
11. Better stability
12. Production feasibility and low preparation cost
13. Controlled release
14. Controlled release, medication is often terminated when needed

Disadvantages

1. Drug of huge particle size tough to soak up through the skin
2. Skin irritation or allergy on dermatitis.
3. the likelihood of allergenic reactions.
4. The poor permeability of some drugs through the skin.
5. Drug of huge particle size tough to soak up through the skin.
6. The presence of the bubble during the formation of Emulgel.

Rationale of Emulgel of topical drug delivery system:

There are many widely used topical agents like ointment, cream, lotion that have many disadvantages. they need very sticky causing uneasiness to the patient when applied. Moreover, they need also a lesser spreading coefficient and wish to use with rubbing. and

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

that they exhibit the matter of stability also., the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparation. A gel may be a colloid that's typically 99% wt. liquid, which is immobilized by natural phenomenon between it and a macromolecular network of fibers built from a touch amount of a gelatin substance present. In spite of the various advantages of gels, a serious limitation is within the delivery of hydrophobic drugs. So, to beat this limitation an emulsion-based approach is getting utilized so as that even a hydrophobic therapeutic moiety is typically successfully incorporated and deliver through gels.[9] Numbers of medicated products are applied to the skin or mucosal membrane that heighten a fundamental function of the skin or pharmacologically alters an action within the underlined tissues.

Drug Delivery Across Through the skin

Three primary mechanisms of topical drug absorption ie. transcellular, intercellular, and follicular. The barrier resides within the outermost layer of the epidermis, the corneum, as evidenced by approximately equal rates of penetration of chemicals through isolated corneum or whole skin [10]. in the surface of the corneum occur quite 99% of the whole skin surface is available for percutaneous drug absorption. .[11] Emulgel can provide a local concentration of drugs within the affected area. It is used as a vehicle to deliver various drugs to the skin. The permeation of the drug and its absorption is enhanced by utilizing chemical enhancement physical enhancement, biochemical enhancement, and supersaturation enhancement [12]

Physiology of skin

The skin is that the largest organ of the body, with a complete area of about 20 square feet. The skin protects us from microbes and therefore the elements help regulate blood heat and permit the sensations of touch, heat, and cold. there are the following topical preparations that are meant to be applied to the skin. So, a basic knowledge of the skin and its physiology function is vital for designing topical dosage forms. The skin covers an area of roughly 2m2 and receives about one-third of the blood circulating through the body. the average human skin surface contains on the standard 40-70 hair follicles and 200-300 sweat ducts on every square centimeter of the skin.

The pH of the skin varies from 4 to five .6. Sweat and carboxylic acid secreted from sebum influence the pH of the skin surface.

The skin consists of three layers.

1. Epidermis –
2. Dermis
3.Subcutaneous

1. Epidermis -

it is the outermost layer of skin, The epidermis is composed of layers, the layers are -

• Stratum corneum (horny layer);

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

• Stratum lucidum

• Stratum granulosum (granular layer);

• Stratum spinosum (prickle cell layer);

• Stratum Basale (germinative layer).

2. Dermis –

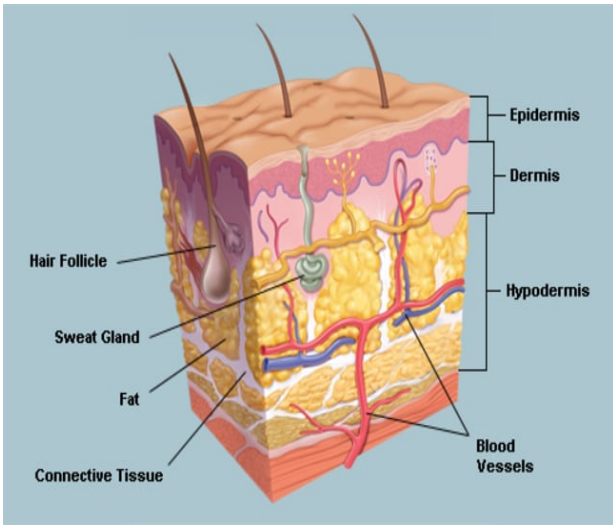
The dermis, beneath the epidermis, contains tough animal tissue, hair follicles, and sweat glands.

It is composed of two layers:

Lamina Lucida;

Lamina densa.

3. Subcutaneous - The deeper subcutaneous tissue (hypodermis) is formed of fat and animal tissue.[13]



Factors affecting topical absorption of drug

Physiological factors [14,15]

1. Skin thickness.
2. Lipid content.
3. The density of hair follicles.
4. The density of sweat glands.
5. Skin pH.
6. Blood flow.
7. Hydration of skin.
8. Inflammation of skin.

Physicochemical factors

1. Partition coefficient.
2. The molecular weight (<400Dalton).
3. The degree of ionization (only unionized drugs gets absorbed well).
4. Effect of vehicles.

Followings Factors to be Considered When Choosing a Topical Preparation [16,17]

1. Development of the vehicle e.g., an occlusive vehicle enhances penetration of the active ingredient and improves efficacy. The vehicle has a cooling, drying, emollient or protective action.

2. Match the sort of preparation with the sort of lesions. For example, they prevent greasy ointments for acute weepy dermatitis

3. Match the type of preparation with the site. (e.g., gel or lotion for hairy areas)

4. Irritation or sensitization potential. Generally, w/o creams are less irritating, while gels are more irritating. Ointments don't contain preservatives or emulsifiers if allergies to those agents may be a concern.

Various ingredients of Emulgel formulation:

1. **Aqueous material**: They make the aqueous phase of the emulsion. Generally, Rosewater and sterile water is used

2. Oils: they're liable for the oily phase of the

emulsion. The oil phase has great importance within the formulation of emulsion / microemulsion / nano emulsion as physicochemical properties of the oil (e.g., molecular volume, polarity, and viscosity). Widely used oils in oral preparations are non-biodegradable mineral and castor oils that provide a local laxative effect, Oil phrases that are used in the development of Emulgel are balsam oil, birch oil[18], castor oil, [19,20] isopropyl myristate, myrrh oil, rosehip oil, wheat germ oil.[21]

2. **Emulsifiers**: Emulsifying agents are used both to market emulsification at the time of manufacture and to regulate stability during a time period which will vary from days for extemporaneously formulated emulsions to months or years for commercial preparations. Emulsifiers are wont to control the emulsification process and stability E.g., Polyethylene glycol 40stearate,[22] Sorbian monooleate (Span 80) [23], Polyoxymethylene sorbitol monooleate (Tween80) [24], Stearic acid and Sodium stearate,[25] wheat germ oil.

3. **Penetration enhancer:** Penetration enhancers are the substances which are used to increase permeation of skin mucosa. that Ideally, these materials should be pharmacologically inert, nonirritating, nontoxic, and compatible with the excipients and drugs, colorless, odorless, tasteless, and inexpensive, and have good solvent properties. E.g. – Sulfoxide, linalool propylene glycol, clove oil,[26] isopropyl myristate, olive oil., Urea, oleic acid, [27] etc.

TABLE 1: VARIOUS GELLING AGENTS UTILIZED IN PHARMACEUTICAL DOSAGE FORMS

S.no	Various Gelling agents	(%w/w) Conc.. Used	Pharmaceutical adaptability	Active pharmaceutical ingredient
1.	Sodium CMC	3-4%	stand autoclaving hence suitable for sterile gels	Benzydamine [30]
2.	Carbopol-934	4%	Provide controlled release of API incorporated	Chlorphenesin[31]
3.	Carbopol – 940	1 %	provide controlled release of API incorporated	Mefenamic acid [32]
4.	HPMC	2.5%	Having good stability, microbial resistance	Chlorphenesin [33]
5.	Combination of HPMC &Carbopol	1.2%	Combination improves stability Ketorolac	Clotrimazole [34,35]
6.	Pluronic® F127	1-3%	Good clarity and better solubility in cold water	Piroxicam[36]
7.	Pemulen	0.1-0.4%	Provide rapid release of the oil phase,	Flurbiprofen [37]

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

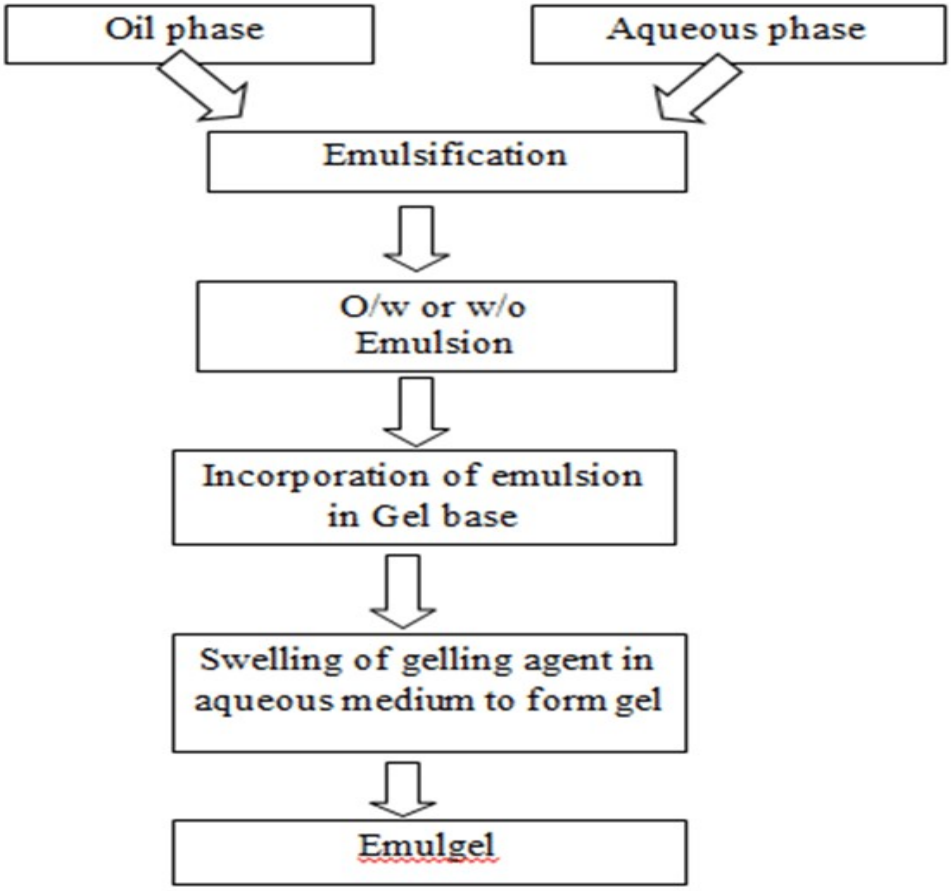


Fig. 2: (Basic steps involved in preparation of Emulgel)

4. Gelling agents: are wont to forming gel base by incorporating emulsion make Emulgel. These are also known as thickening agents which expand the consistency of any dosage form by swelling in the aqueous phase and forming a jelly-like structure.[28] The Incorporation of gelling agent the system makes it thixotropic [29]

5. pH adjusting agent: NaOH, triethylamine.

Emulgel Preparation

Step 1: Preparation of emulsion each of two O/W or W/O

Step 2: Preparation of gel base Step

Step 3: merged an emulsion into a gel base with continuous stirring

The formulations were prepared by dispersing Carbopol 934 in purified water with constant stirring at a moderate speed and Carbopol 940 in purified water with constant stirring at a moderate speed then the pH is adjusted to six .5 using triethanolamine (TEA). The oil phase of the emulsion was manufactured by dissolving Span 80 in light liquid paraffin having the drug in ethanol solution while the aqueous phase was prepared by dissolving Tween 80 in purified water. Methyl and Propylparaben were dissolved in propanediol and were mixed with the aqueous

phase. the oil phase and aqueous phases both were separately heated to 70 ° to 80 °C; then the oily phase was added to the aqueous phase with continuous stirring until cooled to temperature. And add glutaraldehyde during of blending of gel and emulsion in ratio 1:1 to get the Emulgel.[38]

Evaluation of Emulgel [39,40]

Fourier transforms infrared spectroscopy (FTIR)

The primary objective of this investigation was to spot a stable storage condition for the drug in solid-state and identification of compatible excipients for formulation.

Physical examination

The Prepared Emulgel formulations were examined visually for his or her color, homogeneity& consistency.

Determination of pH

the formulation decided by using a digital pH meter. The pH meter electrode was washed by water then dipped into the formulation to live pH and this process was repeated 3 times.

Measurement of viscosity

The viscosity of the formulated batches decided to employ a Brookfield Viscometer (RVDV-I Prime, Brookfield Engineering Laboratories, USA) with spindle 63. The formulation whose viscosity was to be determined was added to the beaker and was allowed to calm down for 30 min at the assay temperature (25±1 °C) before the measurement was taken. The spindle was lowered perpendicularly into the middle of Emulgel taking care that -spindle doesn't touch the rock bottom of the jar and rotated at a speed of fifty rpm for 10 min. The viscosity reading was noted.

Spreadability

To determine the spreadability of the gel formulations, two glass slides of ordinary dimensions were selected. Formulation whose spreadability was to be determined was placed over one slide and therefore the other slide was placed over its top such the gel is sandwiched between the 2 slides. The slides were pressed upon one another so on displace any air present and therefore the adhering gel was wiped off. the 2 slides were placed onto a stand such only the lower slide is held firm by the other fangs of the clamp allowing the upper slide to slide off freely by the force of weight tied The time taken by the upper slide to completely detach from the lower slide was noted.

Globule size and its distribution in Emulgel

Globule size and distribution are decided by Malvern zeta sizer. A 1.0 g sample is dissolved in purified water and agitated to urge homogeneous dispersion. The sample was injected into a photocell of the zeta sizer. Mean globule diameter and distribution are obtained.

Swelling index

To determine the swelling index of prepared topical Emulgel, 1 g of gel is taken on porous aluminum foil then placed separately during a 50 ml beaker containing 10 ml 0.1 N NaOH. Then

samples were faraway from beakers at different time intervals and put it on a dry place for a few time after it reweighed.

In vitro drug release study

The in vitro drug release studies of the Emulgel were administered on Diffusion cells using egg membrane. This was clamped carefully to at least one end of the hollow glass tube of dial y sis cell. prepared emulgel (1g) was applied to the surface of the egg membrane dialysis membrane. The receptor chamber was crammed with freshly prepared PBS (pH 7.4) solution to solubilize the drug. The receptor chamber was stirred by a magnetic stirrer. The samples (1 ml aliquots) were collected at suitable interval sample were analyzed for drug content by UV-visible spectrophotometer after appropriate dilutions. Cumulative corrections were made to get the entire amount of drug released at the whenever interval. The cumulative amount of drug release across the egg membrane decided as a function of your time. The cumulative % Drug release was calculated using the standard calibration curve.

Microbiological assay

Ditch plate technique was used. it's a way used for the evaluation of the bacteriostatic or fungistatic activity of a compound. it's mainly applied for semisolid formulations. Previously prepared Sabouraud's agar dried plates were used. Three grams of the Gellified emulsion are placed during a ditch cut within the plate. Freshly prepared culture loops are streaked across the agar at a right angle from the ditch to the sting of the plate.

Skin irritation test

A 0.5 g sample of the test article was then applied to every site (two sites per rabbit) by introduction under a double gauze layer to a neighborhood of skin near about 1" x 1" (2.54 x 2.54 cm2). The Gellified Emulsion was applied to the skin of a rabbit. Animals were returned to their cages. After 24 hours, the Gellified emulsion is removed. The test sites were wiped with water to get rid of any remaining test article residue . [41]

Stability studies

The prepared Emulgels were packed in aluminium collapsible tubes (5 g) and subjected to stability studies at 5 °C, 25 °C/60% RH, 30 °C/65% RH, and 40 °C/75% RH for a period of three mo. the prepared Samples were withdrawn at 15-day time intervals and evaluated for physical appearance, pH, rheological properties, drug content, and drug release profiles.[42]

CONCLUSION

Emulgel is alternative approach of hydrophobic drugs to delivery topically with advantages of emulsion and gel to improve patient acceptability. Emulgel helps in enhancing spread ability, adhesion, viscosity, and extrusion. It is used both pharmaceutical and cosmetical applications as well as it allows to

incorporate herbal formulations. The topical drug delivery system are going to be used extensively thanks to better patient compliance. Since Emulgel possesses an edge in terms of Spreadability, adhesion, viscosity and extrusion, they will become a popular drug delivery system. Moreover, they're going to become an answer for loading hydrophobic drugs during a water-soluble gel. Bases

REFERENCE

1. Kullar R, Saini S, Steth N, Rana AC. Emulgel a surrogate approach for topical used hydrophobic drugs. Int J Pharm Biol Sci 2011; 1:117-28.

2. Single V, Saini S, Joshi B, Rana AC. Emulgel: a new platform for topical drug delivery. Int J Pharm Biol Sci2012; 3:485-98.

3. Haneefa KPM, Mohanta GP, Nayar C. Emugel: An Advanced Review. J Pharm Sci Res. 2013;5(12):254-258.

4. El Laithy HM, El-shaboury KM. The development of Cutina lipogels and gel microemulsion for topical administration of fluconazole. AAPS Pharm SciTech. 2002;3(4): E35.

5. Stan-Posthuma JJ, Vink J, Le Cessie S, Bruijn JA, Bergman W, Pavel S. Topical tretinoin under occlusion on a typical navei. Asian J Pharm Clin Res1998; 8:539-48.

6. Mohamed MI. Optimization of chlorphenesin emugel formulation. AAPS J2004; 6:81-7.

7. Mishra AN. Controlled and novel drug delivery. 4th ed. CBS Publisher and Distributers, Delhi; 1997. p.107-9.

8. Swarbrick J. Encyclopedia of pharmaceutical technology. 3rd ed. Vol. 1. Informa Healthcare; 2007. p.1311-23.

9. Cecv G, Mazgareanu S, Rother M. Preclinical characterization of NSAIDs in ultra-deformable carriers or conventional topical gels. Int J Pharm2008; 360:29-39.

10.Kumar S, Singh N, Satish, Arora SC. Emulgel: An Insight. European J Pharm Med Res.2015;2(4):1168-1186.

11.Upadhyaya S, Chauhan B, Kothiyal P. Emulgel: A Novel Approach for Topical Delivery of Hydrophobic Drugs. Int J Univ Pharm Biosci.2014;**3(2)**:176-189.

12.Pathan IB, Shetty CM. Chemical penetration enhancers for transdermal drug delivery systems. Trop J Pharm Res. 2009;8(2):173-179.

13.Nursingtimes.net/clinical- archive /dermato - logy skin -1-the structure-and-function-of-the-skin-25-11-2019

14.Kalia YN, Guy RH. Modeling transdermal drug release. Adv Drug Delivery Rev2001; 48:159-72.

15.Ayub AC, Gomes AD, Lima MV, Vianna-Soares CD, Ferreira LA. Topical delivery of fluconazole: *in vitro* skin penetration and permeation using emulsions as dosage forms. Drug Dev Ind Pharm 2007; 33:273-80.

16.Gaur PK, Mishra S, Purohit S, Dave K.

Transdermal drug delivery system: a review. Asian J Pharm Clin Res2009; 2:14-20.

17.Subramanian N, Ghosal SK, Moulik SP. Enhanced *in vitro* percutaneous absorption and *in vivo* anti-inflammatory effect of a selective cyclooxygenase inhibitor using microemulsion. Drug Dev Ind Pharm2005; 31:405-16.

18.Jager S, Laszczyk MN, Scheffler A: A preliminary pharmacokinetic study of Betulin, the main pentacyclic triterpene from extract of outer bark of birch. Molecules 2008; 13:3224–3235.

19.Maissa C, Guillon P, Simmons P, Vehige J: Effect of castor oil emulsion eye drops on tear film composition and stability. Contact Lens Anterior Eye 2010; 2:76–82.

20.Lawrence MJ, Rees GD: Microemulsion based media as novel drug delivery systems. Adv. Drug Deliv. Rev2000; 45:89–121.

21.Karabacak M, Kanbur M, Eraslan G, Sanca ZS: The antioxidant effect of wheat germ oil on subchronic comaphos exposure in mice. Ecotoxicol. Environ. Saf. 2011; 74:2119–2125.

22.Benson HA. Transdermal drug delivery: penetration enhancement techniques. Curr Drug Delivery2005; 2:23-33.

23.Rutter N. Drug absorption through the skin: a mixed blessing. Arch Dis Child1987; 62:220-1.

24.Zhang X, Zhao R, Qian W. Preparation of an Emulgel for the treatment of aphthous ulcer on the basis of carbomers. Chin Pharm J1995; 30:417-8.

25.Swarbrick J. Encyclopedia of Pharmaceutical Technology. 3rd ed.; 2006. p.1551.

26.Baibhav J, Singh G, Rana AC, Saini S: Development and Characterization of Clarithromycin Emulgel for topical delivery. IJDDR, 2012; 4(3):310-323.

27.Khullar R, Kumar D, Seth N, SainiSeema: Formulation and evaluation of mefenamic acid emulgel for topical delivery. Saudi Pharmaceutical Journal, 2012; 20:63–67.

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

29.Baibhav J, Singh G, Rana A. C., Saini S, Singla V: Emulgel: A Comprehensive Review on The Recent Advances in Topical Drug Delivery, International Research Journal of Pharmacy.2011; 2(11);66-70.

30.Perioli L, Ambrogi V, Venezi L, Giovangoli S, Panago C: Formulation studies of benzydamine mucoadhesive formulations for vaginal administration. Drug Dev. Ind. Pharm2009;35:769–779.

31.Deveda P, Jain A, Vyas N, Khambete H, Jain S: Gellified emulsion for sustained delivery of itraconazole for topical fungal diseases. Int. J. Pharm. Pharm. Sci. 2010; 2: 104– 112.

32.Khullar R, Kumar D, Seth N, Saini S: Formulation and evaluation of mefenamic acid Emulgel for topical delivery. Saudi Pharm. J. 2011:63–67

33.Mohamed MI: Optimization of chlorphenesin Emulgel formulation. AAPS Pharm. Sci.

Technol.2004; 6:534–542.

34.El-Setouhy DA, El-Ashmony SM: Ketorolac trometamol topical formulations: release behavior, physical characterization, skin penetration, efficacy and gastric safety. J. Pharm. Pharmacol.2010; 62:25–34.

35.Shahin M, Hady SA, Hammad M, Mortada N: Novel jojoba oil-based emulsion gel formulations for clotrimazole delivery. AAPS Pharm. Sci. Technol.2011; 12:239–247.

36.Shokri J, Azarmi S, Fasihi Z: Effect of various penetration enhancers on percutaneous absorption of piroxicam from Emulgel.Res. Pharm. Sci.2012;7:225–2234.

37.Perioli L, Panago C, Mazzitelli S: Rheological and functional characterization of new anti-inflammatory delivery system designed for buccal administration. Int. J. Pharm. 2008; 356:19–28.

38.Williams AC, Barry BW. Terpenes and the lipid-protein partitioning theory of skin penetration enhancement. Pharm Res1997; 8:17-24.

39.Ranga PM, Sellakumar V, Natarajan R, Mohan KK. Formulation and *In-vitro* evaluation of ciprofloxacin-loaded topical Emulgel. Int J Pharm Chem Sci2012; 1:237-42.

40.Narendran H, Koorapati S, Mamidibathula L. Formulation and evaluation of aceclofenac-lycopene transemulgel. World J Pharm Res2013; 2:1036-45.

41.Chaudhari P, Ajab A, Malpure P, Kolsure P, Sanap D. Development and *in vitro* evaluation of thermoreversible nasal gel formulations of rizatriptan benzoate. Indian J Pharm Educ Res2009; 43:55-62.

42.Jones DS, Woolfson AD, Brown AF., viscoelastic and mucoadhesive properties of pharmaceutical gels composed of cellulose polymers. Int J Pharm1997; 151:223-33.