International Journal of Research in Engineering and Science (IJRES)
ISSN (Online): 2320-9364, ISSN (Print): 2320-9356
www.ijres.org Volume 10 Issue 12 ǁ December 2022 ǁ PP. 401-406

Formulation and evaluation of emulgel for topical drug delivery system

[1.] Asmit kamble
[2.] sejal kamble
[3.] Amol patil

Date of Submission: 09-12-2022 Date of acceptance: 23-12-2022

I. INTRODUCTION

Emulgel are emulsions, either of the oil-in-water or water in oil type, which are gelled by mixing with a gelling agent. Emulsified gel is stable one and better vehicle for hydrophobic or poorly water soluble drugs. They have a high patient acceptability since they possess the advantages Topical drug delivery and antifungal activity of both emulsions and gels.Direct (oil-in-water) systems are used to entrap lipophilic drugs,whereas hydrophilic drugs are encapsulated in the reverse (water-in-oil) systems. Therefore they have been recently used as vehicles to deliver various hydrophobic drugs to the skin. In the local market,Emulgel are available: Voltarenemulgel (Novartis Pharma, Switzerland), containing diclofenacdiethylamine and Miconaz-H emulgel (Medical Union Pharmaceuticals, Egypt), containing miconazole nitrate and hydrocortisone.

Topical drug administration is a localized drug deliver Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. Skin is one of the most readilyaccessibleorgans on human body for topical administration and is main route of topical drug delivery system. The emulsion gels are hydrogels containing randomly distributed oil microdroplets.Topical drug delivery systems have been used for centuries for the treatment of local skin disorders, one side the topical applications of the drug offer the potential advantages of delivering the drug directly to the site of action and delivering the drug for extended period of time at the effected site that mainly acts at the related regions. On the other hand, topical delivery system increases the contact time and mean resident time of drug at the applied site leading to an increase in local drug concentration while the pharmacological activity of Emulgelformulations may not change as rapidly as the solution form. Several antifungal agents are available on the market in different topical preparations (e.g. creams, ointments, and powders for the purpose of local dermatological therapy).One of these antifungal agents is Itraconazole, which has both antifungal and antibacterial properties. It is applied locally in mild uncomplicated dermatophyte and other cutaneous infections.

Both oil-in-water and water-in-oil emulsions are extensively used for their therapeutic properties and as vehicles to deliver various drugs to the skin. Emulsions possess a certain degree of elegance and are easily washed off whenever desired. They also have a high ability to penetrate the skin. In addition, the formulator can control the viscosity, appearance, and degree of greasiness of cosmetic or dermatological emulsions. Oil-in-water emulsions are most useful as water washable drug bases and for general cosmetic purposes, while water-in-oil emulsions are employed more widely for the treatment of dry skin and emollient applications. Gels for dermatological use have several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, nonstaining, compatible with several excipients, and water-soluble or miscible. The rheological properties and the breakdown behaviour of gels filled with emulsions droplets can be varied by changing the interactions between oil droplets and gel matrix, the oil content and the oil droplet size.

Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. These are apply a wide spectrum of preparations for both cosmetic and dermatological, to their healthy or diseased skin.

1)These formulations range in physicochemical nature from solid through semisolid to liquid. Drug substances are seldom administered alone,but rather as part of a formulation, in combination with one or more non medicated agents that serve varied and specialized pharmaceutical function. Drugs are administered topically for their action at the site of application or for systemic effects.

2) Drug absorption through the skin is enhanced if the drug substance is in solution, if it has a favourable lipid/water partition coefficient and if it is a nonelectrolyte. For the most part, pharmaceutical

preparations applied to the skin are intended to serve some local action and as such are formulated to provide prolonged local contact with minimal systemic drug absorption. Drug applied to the skin for their local action include antiseptics, antifungal agent, skin emollients and protectant.

3) The main advantages of topical delivery system are to bypass first pass metabolism. Avoidance of the risks and inconveniences of intravenous therapy and of the varied conditions of absorption like pH changes,presence of enzymes, gastric emptying time are other advantages of topical preparations. The topical drug delivery system is generally used where the others system of drug administration fails or it is mainly used in fungal infection.

4) Human skin is a uniquely engineered organ that permits terrestrial life by regulating heat and water loss from the body whilst preventing the ingress of noxious chemicals or microorganisms. It is also the largest organ of the human body, providing around 10% of the body mass of an average person, and it covers an average area of 1.7 m2.Whilist such a large and easily accessible organ apparently offers ideal and multiple sites to administer therapeutic agents for both local and systemic actions, human skin is a highly efficient self repairing barrier designed to keep the insides in and the outside out.

5) Gels are a relatively newer class of dosage form created by entrapment of large amounts of aqueous or hydroalcoholic liquid in anetwork of colloidal solid particles, which may consist of inorganic substances, such as aluminum salts or organic polymers of natural or synthetic origin.

6) They have a higher aqueous component that permits greater dissolution of drugs, and also permit easy migration of the drug through a vehicle that is essentially a liquid, compared with the ointment or cream base.

7) These are superior in terms of use and patient acceptability. In spite of many advantages of gels a major limitation is in the delivery of hydrophobic drugs. So to overcome this limitation, emulgels are prepared and used so that even a hydrophobic therapeutic moiety can enjoy the unique properties of gels. In fact, the presence of a gelling agent in the water phase converts a classical emulsion into an emulgel. Both oil-inwater and water-in-oil emulsions are used as vehicles to deliver various drugs to the skin. Emulgels for dermatological use have several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, nonstaining, long shelf life, bio-friendly, transparent & pleasing appearance.

8) Use of topical agents requires an appreciation of the factors that influence percutaneous absorption.Molecules canpenetrate the skin by three routes: through intact stratum corneum, through sweat ducts, or through sebaceous follicle. The surface of the stratum corneum presents more than 99% of the total skin surface available for percutaneous drug absorption

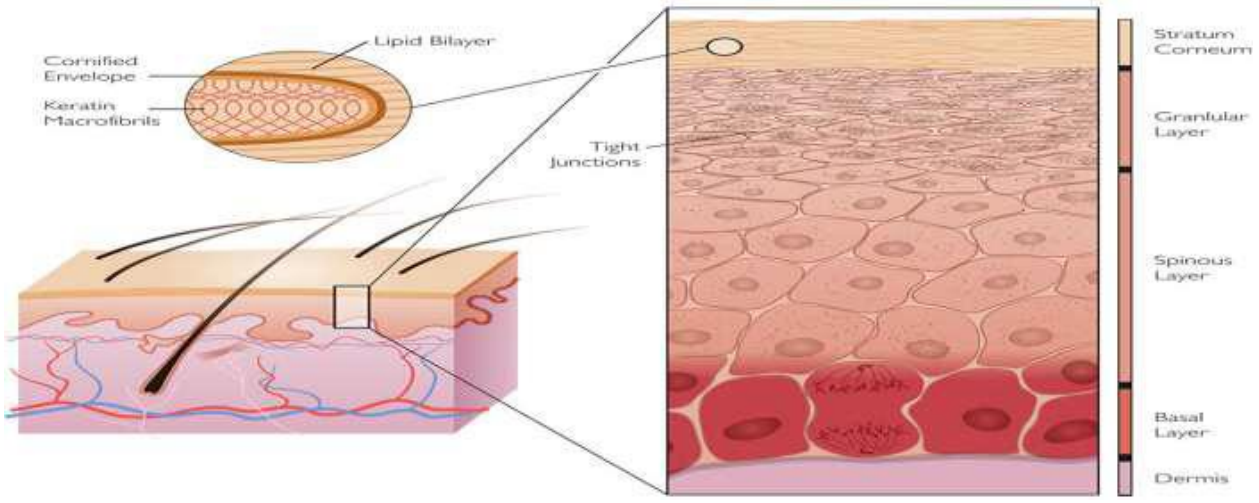

Figure 1: Layer of human skin2

Human skin(Fig. 1 & 2) is a uniquely engineerorgan that permits terrestrial life by regulating heat andwater loss from the body whilst preventing the ingress ofnoxious chemicals or microorganisms. It is also the largestorgan of the human body, providing around 10% of thebody mass of an average person, and it covers an averagearea of 1.7 m2. Whilst such a large and easily accessibleorgan apparently offers ideal and multiple sites to administer therapeutic agents for both local and systemicactions, human skin is a highly efficient self-repairingbarrier designed to keep the insides in and the outside out.

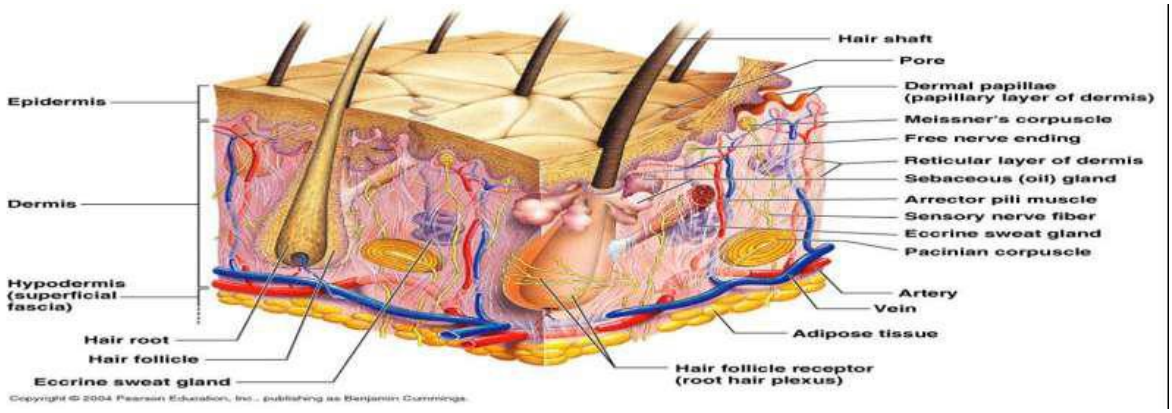

Figure 2: Anatomy of human skin2

Many widely used topical agents like ointments,creams, lotions have numerous disadvantages. They are usually very sticky causing uneasiness to the patient whenapplied. Moreover they also have less spreading coefficientand need to apply with rubbing. They also exhibit theproblem of stability1, 4.Due to all these factors, within the major group ofsemisolid preparations, the use of transparent gels hasincreased both in cosmetics and in pharmaceutical preparations. A gel is colloid that is typically 99% by weightand a macromolecular network of fibers built from a smallamount of a gelatin substance present. Gels are a relativelynewer class of dosage form created by entrapment of largeamounts of aqueous or hydro alcoholic liquid in a networkof colloidal solid particles. Gel formulations generallyprovide faster drug release compared with ointments andcreams1, 5.In spite of many advantages of gels a majorlimitation is their inability to delivery hydrophobic drugs.

To overcome this limitation an emulsion based approach is being used so that a hydrophobic therapeutic moiety can be successfully incorporated and delivered through gels.When gels and emulsions are used in combined form thedosag forms are referred as emulgels6.In fact, the presence of a gelling agent in the waterphase converts a classical emulsion into an emulgel. Direct(oil-in-water) system is used to entrap lipophilic drugs where as hydrophilic drugs are encapsulated in the reverse(Water-in-oil) system. Emulsions possess a certain degreeof elegance and are easily washed off whenever desired.They also have a high ability to penetrate the skin.

Drug Delivery across the Skin

The epidermis is the most superficial layer of the skin and is composed of stratified keratinised squamous epithelium which varies in thickness in different parts of the body. It is thickest on with elastic fibers. The skin forms a relatively waterproof layer that protects the deeper and more delicate structures. Blood vessels are distributed profusely beneath the skin. Especially important is a continuous venous plexus that is supplied by inflow of blood from the skin capillaries. In the most exposed areas of the body—the hands, feet, and ears blood is also supplied to the plexus directly from the small arteries through highly muscular arteriovenous anastomoses. A unique aspect of dermatological pharmacology is the direct accessibility of the skin as a target organ for diagnosis and treatment. The skin acts as a two-way barrier to prevent absorption or loss of water and electrolytes. There are three primary mechanisms of topical drug absorption: transcellular,intercellular, and follicular.Most drugs pass through the torturous path around corneocytes and through the lipidbilayer to viable layers of theskin. The next most common (and potentially under-recognized in the clinical setting) route of delivery is via the pilosebaceous route. The barrier resides in the outermost layer of the epidermis,the stratum corneum, as evidenced by approximately equal rates of penetration of chemicals through isolated stratum corneum or whole skin. Creams and gels that are rubbed into the skin have been used for years to deliver pain medication and infection fighting drugs to an affected site of the body. These include, among others, gels and creams for vaginal yeast infections, topical creams for skin infections and creams to soothe arthritis pain. New technologies now allow other drugs to be absorbed through the skin (transdermal). These can be used to treat not just the affected areas (for example, the skin) but the whole body (systemic) .

FACTORS AFFECTING TOPICAL ABSORPTION OF DRUG -
Physiological Factors
1. Skin thickness.

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

Physiochemical Factors
1. Partition coefficient.
2. Molecular weight (<400 dalton).
3. Degree of ionization (only unionized drugs gets absorbed well).
4. Effect of vehicles

FACTORS TO BE CONSIDERED WHEN CHOOSING A TOPICAL PREPARATION
1) Effect of the vehicle e.g. an occlusive vehicle enhances penetration of the active ingredient and improves efficacy. The vehicle itself may have a cooling, drying, emollient or protective action.
2) Match the type of preparation with the type of lesions. For example, avoid 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, ointments and w/o creams are less irritating, while gels are irritating. Ointments no contain preservatives or emulsifiers if allergy to these agents is a concern.

METHOD TO ENHANCE DRUG PENETRATION AND ABSORPTION
1. Chemical enhancement
2. Physical enhancement
3. Biochemical enhancement
4. Supersaturation enhancement

ADVANTAGES
A) Hydrophobic drugs can be easily incorporated into gels using d/o/w emulsions.
B) Hydrophobic drugs cannot be incorporated directly into gel base because solubility act as a barrier and problem arises during the release of the drug. Emulgel helps in the incorporation of hydrophobic drugs into the oil phase and then oily globules are dispersed in aqueous phase resulting in o/w emulsion. And this emulsion can be mixed into gel base. This may be proving better stability and release of drug than simply incorporating drugs into gel base.
c) Better stability: Other transdermal preparations are comparatively less stable than emulgels. Like powders are hygroscopic, creams shows phaseinversion or breaking and ointment shows rancidity due to oily base.
d) Better loading capacity: Other novel approaches like niosomes and liposomes are of nano size and due to vesicular structures may result in leakage and result in lesser entrapment efficiency. But gels due to vast network have comparatively better loading capacity.
e) Production feasibility and low preparation cost: Preparation of emulgels comprises of simpler and short steps which increases the feasibility of the production. There are no specialized instruments needed for the production of emulgels. Moreover materials used are easily available and cheaper. Hence, decreases the production cost of emulgels.
f) No intensive sonication: Production of vesicular molecules need intensive sonication which may result in drug degradation and leakage. But this problem is not seen during the production of
g) emulgelsas no sonication is needed.
h) Controlled release: Emulgels can be used to prolong the effect of drugs having shorter t1/2

IMPORTANT CONSTITUENTS OF EMULGEL PREPARATION
1) Aqueous Material: This forms the aqueous phase of the emulsion. Commonly used agents are water, alcohol
2) Emulsifiers: Emulsifying agents are used both to promote emulsification at the time of manufacture and to control stability during a shelf life that can vary from days for extemporaneously prepared emulsions to months or years for commercial preparations.eg Polyethylene glycol 4027 stearate, Sorbitan monooleate28 (Span 80), Polyoxyethylenesorbitanmonooleate (Tween 80)29, Stearic acid30, Sodium stearate.

3) OIL-These agents form the oily phase if the emulsion. For externally applied ol emulsions, mineral oils, either alone or combined with soft or hard paraffins, are widely used both as the vehicle for the drug and for their occlusive and sensory characteristics. Widely used oils in oral preparations are non biodegradable mineral and castor oils that provide a local laxative effect, and fish liver oils or various fixed oils of vegetable origin (e.g., arachis, cottonseed, and maize oils) as nutritional supplements.

4) Gelling Agent: These are the agents used to increase the consistency of any dosage form can also be used as thickening agent.
5) Permeation Enhancers: These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability.Until cooled to room temperature. And add Glutarald.Ehyde in during of mixing of gel and emulsion in ratio 1:1 to obtain the emulgel

Itraconazole

Itraconazole is a orally or topically active antifungal agent with a broad spectrum of activity. In addition, the drug has an interesting tissue distribution, which has made possible effective and rapid treatments of candidiasis, when the drug is administered topically. A topical itraconazole-containing formulation may be of use for several reasons including the opportunity to generatehigh local tissue levels and lower systemic exposure. Most pharmaceutical drug substances are lipophilic compounds, which are practically insoluble in water. For skin care and thetopical treatment of dermatological disease, a wide choice of vehicles ranging from solids tosemisolids.Itraconazole is effective against severalfungal strains such as Candida albicansandCandida topicalic, which are responsible for topical candidiasis inmore than 25% of patients sufferingfrom this condition.Candida-relatedfungal infection is a common skindisease affecting two thirds of allpersons at least once during their lifetimeTopical drug administration is alocalized drug delivery system any where in the body throughophthalmic, rectal, vaginal and skin astopical routes. Topical formulationsupplies a wide spectrum of preparations,both cosmetic and dermatological, totheir healthy or diseased skin. Theseformulations range in physicochemical nature from solid through semisolid toliquid. Drug substances are seldomadministered alone, but rather as part formulation, in combination with oneor more nonmedical agents that servevaried and specialized pharmaceuticalfunctions. Drugs are administeredtopically for their action at the site ofapplication, or for systemic effects2.Drug absorption through the skin isenhanced if the drug substance is insolution, if it has a favorable lipid/water partition coefficient, and if it is anonelectrolyte. For the most part,pharmaceutical preparations applied tothe skin are intended to serve somelocal action and, as such, are formulatedto provide prolonged local contact, with minimal systemic drug absorption.Drugs applied to the skin for their localaction include antiseptics, antifungalagents, skin emollients, and protectants.The main advantage of topical deliverysystem is to bypass first passmetabolism. Avoidance of the risks and inconveniences of intravenous therapy and of the varied conditions ofabsorption, like pH changes, presence ofenzymes, gastric emptying time areother advantage of topicalpreparations. The topical drug delivery system is generally used wherethe others system of drugadministration fails or it is mainly usedin fungal infection. Human skin is auniquely engineered organ that permits

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REFERENCES

[1]. Kshirsagar N A. Drug Delivery Systems. Ind. J. Pharmacol. 2000; 32:S54- S61.
[2]. Rashmi M. Topical gel: A review august vol. 2008; available from http://www.pharmainfo.com
[3]. Sharma S. Topical preparations are used for the localized effects at the site of their application by virtue of drug penetration into the underlying layers of skin or mucous membranes. Pharmaceutical reviews 2008; 6:1

[4]. Laithy HM. and El shaboury KMF. The development of CutinaLipogels and gel microemulsion for topical administration of fluconazole. Ame Pharm Sci. PharmSciTech. 2003; 3:10 25.
[5]. McGrath JA, Eady R & Pope Fm.chapter 3 anatomy and organization of human skin, p 3.1 3.15
[6]. Kumar L, Verma R. *In vitro* evaluation of topical gel prepared using natural polymer International Journal of Drug Delivery 2010; 2:58-63.
[7]. Gennaro AR, ed. Remington: the Science and Practice of Pharmacy. Easton, Mack Publishing Company19th ed.; 1995.
[8]. Ansel HC, Allen LV Jr., Popovich NG. Pharmaceutical Dosage Forms and Drug Delivery Systems.New York Lippincott Williams and Wilkins 7th ed.; 1999.
[9]. Topical Emulsion- Gel Composition Comprising Diclofenac Sodium. Patent no. WO/2004/017998).
[10]. Mohamed MI. Optimization of ChlorphenesinEmulgel Formulation. AAPS J. 2004; 6 (3).*Kailashet. Al.* ,Volume 1 – Issue 4 Vol: 1(4) March 2013 27 www.ijopils.com
[11]. Gupta A, Mishra AK, Singh AK, Gupta V, Bansal P. Formulation and evaluation of topical gel of diclofenac sodium using different polymers. Drug Invention Today 2010; 2:250-253.
[12]. Rieger MM, Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy.3rd ed., PA Lea and Febiger, Philadelphia; 1986. pp. 502-533
[13]. Stanos SP. Topical Agents for the Management of Musculoskeletal Pain. J Pain Symptom Manage 2007; 33.
[14]. Stanos SP. Topical Agents for the Management of Musculoskeletal Pain .J Pain Symptom Manage March 2007; 33.
[15]. Jain A, Deveda P, Vyas N, Chauhan J et al. Development Of Antifungal Emulsion Based Gel For Topical Fungal Infection(S). IJPRD 2011;