WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 13, 529-550. Review Article ISSN 2277– 7105

EMULGEL: AN ENORMOUS APPROACH FOR TOPICAL DELIVERY OF HYDROPHOBIC DRUGS

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Article Received on
01 Sept. 2020,

Revised on 21 Sept. 2020,
Accepted on 11 October 2020

DOI: 10.20959/wjpr202013-18999

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ABSTRACT

In NDDS, emulgel technology is presently of attentiveness to the pharmaceutical researchers because of their fundamental prospects and topically having property of dual controlled release i.e. gel as well as emulsion. In topical delivery system, a major constraint of gels is their incapacity to the deliver hydrophobic drugs. To control this constraint of gels and successful incorporation of hydrophobic drugs, emulsion based approach is being used. Emulsion is gelled by mixing it with a gelling agent which makes it stable and controlled release system. Due to gelling capacity of polymers can be used as thickeners and emulsifiers for a stable emulsion by increasing viscosity of aqueous phase and decreasing the surface and interfacial tension. Due to access oily bases and lack of insoluble excipients, emulgel integrate better drug release for a topical drug delivery system.

KEYWORDS: Emulgel, Gelling agent, hydrophobic drugs, Topical drug delivery.

INTRODUCTION

For local delivery of therapeutic agents, topical administration is the favorable route due to its convenience. From the past few years, topical drug delivery has been used for the treatment of local infection of vagina, nose, skin and other dermatological diseases. The drugs are mainly administered through topical route for local action includes anti-septic, anti-fungal and skin emollients for protective effect.[1] The pharmaceutical dosage form like semi-solid, gels, creams, ointments and sprays are the variety of topical drug delivery system.[2] Topically drugs administered could replace needles and vaccines, in addition to other significant such as reduce gastric degradation, frequent dosing and avoiding first pass

metabolism. In order to formulate an effective topical preparation is directly concerned with the site of action and desired effect of the preparation.[2,3] Skin is one of the main routes for the topical drug delivery system. Some drugs which are degraded in the intestinal tract and cannot be delivered orally. To overcome these problems the present study is focused to formulate emulgel. Emulgel is the combination of emulsion and gel. It shows highly effective mechanism because the permeation depth of the drug is more in emulgel. Emulsion and gel is the main component of the emulgel. It is stable and effective vehicle for the delivery of hydrophobic drugs. Emulgel are suitable to apply on hairs because of absence of greasiness and look of residue upon application.[4]

Advantages of topical drug delivery[2]

- Drug delivered more selectively to a specific site
- Avoidance of first pass metabolism and GI incompatibility
- Improve patient compliance and suitable for self-medication
- Avoidance of GI incompatibility
- Drug with short half life and potent drug are suitable for topical delivery
- Easy to apply and when needed narrow therapeutic index, has ability to easily terminate medication
- For topical delivery higher dose can be acceptable
- Better stability and loading capacity
- Provide controlled release of drug
- Low preparation cost

Disadvantages of topical drug delivery[5]

- Poor permeability of some drugs through the skin
- Skin irritation or allergic reaction may be caused
- Drugs with larger particle size / molecular weight are difficult to get absorbed through the skin
- During formulation of emulgel the occurrence of the bubble

Rational of the study

Emulgel is one of the most promising and effective drug delivery systems for the hydrophobic drugs. It is stable and better vehicle and has advantage of both emulsion as well

as gel. Emulgel shows higher aqueous release and shows more effective mechanism because the permeation depth of the drugs is more in emulgel than conventional gel formulation.

Fluconazole is belonging to a group of triazole and it inhibits important component of fungal cell by interfering with cell growth and cell wall synthesis. The problems with fluconazole is that it is poorly water soluble or hydrophobic in nature and long term therapy on higher dose causes less patient compliance. Oral delivery of fluconazole often produces gastric irritation, bloating, abdominal discomfort etc. In order to overcome these side effects, topical therapy of fluconazole can help to minimize systemic side effects and to target infection site with modifying release rate

Anatomy of skin[6]

Skin is the largest organ of the body in term of surface area and weight. It has surface area of approximately 16000cm.[2] In adults, skin represent 8% of body weight. It is the outermost layer or tissue of the living body. Skin shows a protective mechanism from external environment.

Skin can produce a favorable chemical substances named as vitamin D when skin is exposed in sunlight. The skin helps to regulate the temperature of the human body and also acts as sensory organ. Skin includes various cellular elements like melanocytes, erythrocytes, keratinocytes etc. It has multi layer structures because of different components like cells and fibers.

The skin consists of three layers

- Epidermis
- Dermis
- Subcutaneous fat tissues

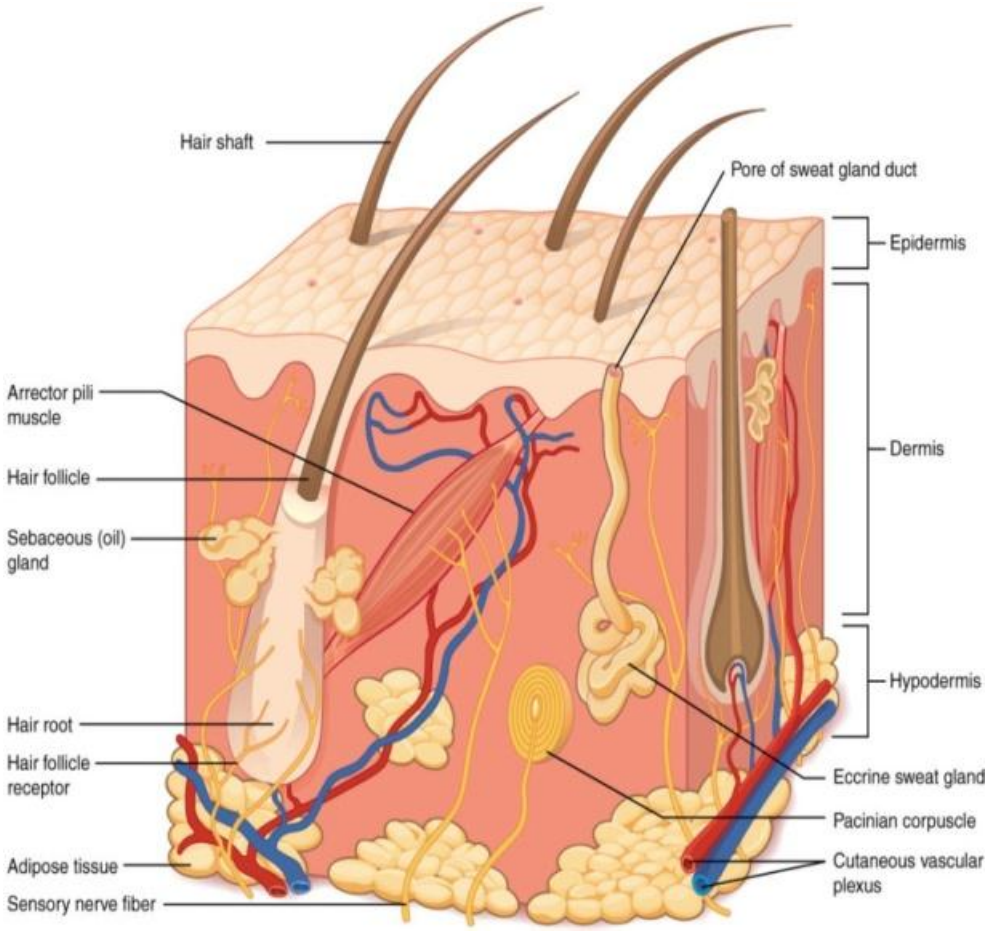

Figure 1: Anatomy of skin.

Epidermis[7]

The outermost layer of the skin is called epidermis which having thickness of about 0.2mm. No veins and capillaries are located in this layer. The thickness of epidermis is depends upon the location of the body. The epidermis mainly consist two types of cells- keratinocytes and dendritic cells. It also contains other number of cells like melanocytes, langerhans cells etc. The epidermis layer is also called as the metabolic active tissue.

The outermost layer is classified into five sub layers and these are

- Stratum corneum.
- Stratum lucidium
- Stratum granulosum
- Stratum spinosum
- Sratum basale

Stratum corneum: The exterior sublayer of the epidermis is called as stratum corneum. It is also referred as the horny cell layer having thickness of about 8-15µm. The layer is of hexagonal shaped and is helpful for prevention of skin from the large amount of dehydration. It contains main component "ceramide", which having important role in water retention.

Stratum lucidum: Stratum lucidum is composed as thin clear layer of dead skin cells. It is found only in areas of thick skin on the palms of the hands and soles of the feet.

Stratum granulosum: The layer is also called as granular cell layer having thickness of 3µm. It contains 2-4 layers of granular cell. The shape of the cells is flatter because the keratin fibers are increasingly filled up into the cells.

Stratum spinosum: It is also called prickle cell layer having thickness ranges from 50-150µm. It consists of number of cells, which may differ in shape and structure.

Stratum basale: Stratum basale is composed as single layer and is the deepest and sublayer of epidermis. In stratum basale, keratinocytes are produced and shows their movement upward to the outer surface. The process of movement of keratinocytes is known as turn-over. For one cycle of this process takes days and keratinocytes also changes their functions and structure. This is also called as basal cell layer and holds 8% of water in epidermis.

Dermis[8]: Dermis is the second layer of the skin. Its thickness is about 1-4mm. The fibrous and amorphous connective tissue and collagen are the main parts of epidermis.

In response of various stimuli, the blood-borne cells, plasma cells and leukocytes enter the dermis layer. The layer dermis gives elasticity and tensile strength to the skin. It also shows an protective mechanism for body from outer environment like thermal regulation.

The dermis layer of skin consists of two sub layers. These are:-

- Papillary layer
- Reticular layer

Papillary layer of epidermis is the upper part where as reticular layer is lower. Reticular layer is much thicker than papillary layer.

Subcutaneous layer[9]: The third layer of the skin is known as subcutaneous layer. The thickness of layer is usually 4-9mm. The subcutaneous layer has large amount of fat cells and tissues works as the store house of energy for the body. The panniculus, harmone conversion takes place like androstenedione converts into estrone by aromatase. A hormone produced by lipocytes is known as leptin which plays a role in regulation of the body weight.

Pathways of percutaneous absorption[10-13]: The following pathways are used to pass a drug molecule from stratum corneum are:

- Transfollicular route
- Transcellular route
- Intracellular route

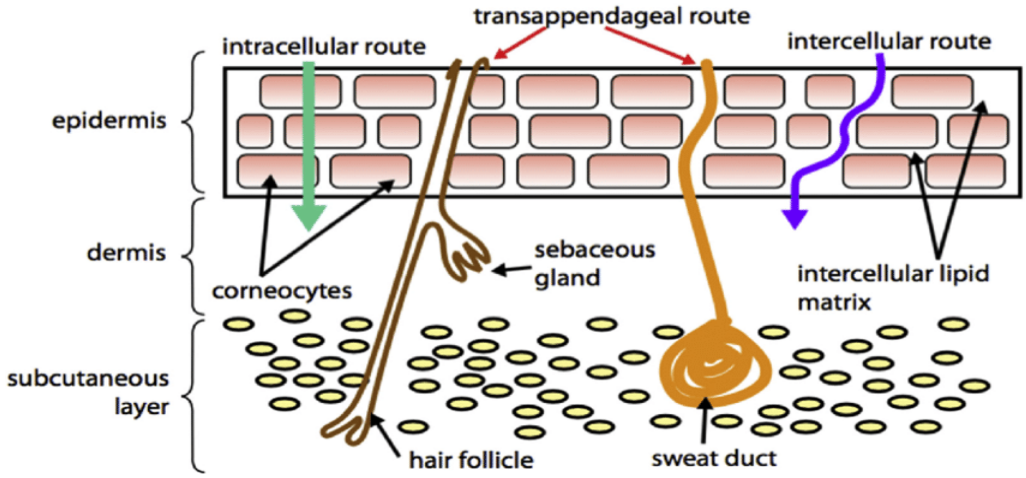

Figure 2: Absorption across the skin by intercellular and intracellular routes.[11]

The most superficial layer of the skin is epidermis and is comprises of stratified keratinized squamous epithelium which varies in thickness in different parts of body. The thickness of epidermis is approximately 100-150µm and has no blood flow. The layer of stratum corneum induces within it. Below the epidermis, dermis contains the system of capillaries and the function of capillaries is transportation of blood throughout the body. In passive diffusion, the drug can enter the blood stream after penetrate the stratum corneum. Solubility enhanced by the surfactants and co surfactants. Lipids can enhance drug flux by fluidizing the crystalline structure of the stratum corneum, partitioning the stratum corneum and dissolution of stratum corneum. To overcome the disadvantages of irritating drugs, several new active transport technologies have been developed. Most of the drugs passed through viable layers of the skin through lipid bilayer and torturous path around the corneocytes. In the outermost layer of epidermis the occupied barriers stratum corneum is indicating by equal rate of penetration of

chemical through whole skin. For delivery of pain medication and infections fighting drugs gels and creams are rubbed into the skin to infected site of the body.

Route of administration

For the desired pharmacological response, topical delivery needs direct application of the drug to the site of action onto the skin. But it has own certain limitataionns like to reach systemic circulation such as vaginal, rectal and nasal. Drug has to cross different barriers of the skin, they have been investigated. Emulgel have been investigated for various route of administration such as topical, buccal, vaginal etc.

Factors affecting topical absorption of drug[14,15]

Physiological factors

1. Thickness of skin: From epidermis to subcutaneous layer skin thickness varies and high rate of diffusion present on the palm and soles. The thickness of epidermis layer is about 100-150µm.
2. Lipid content: It is an effective water barrier. When lipid weight in stratum corneum is low, percutaneous penetration increases.
3. Hair follicles Density: Hair follicle infundibulum has a large storage capacity about 10 times more than the stratum corneum.
4. The density of sweat glands.
5. Skin pH: Sweat and fatty acid secreted from sebum influence the pH of the skin surface.
6. Blood flow.
7. Permeation of drug can enhance by skin hydration.
8. Continuity of stratum corneum disrupt by the inflammation of skin which increases permeability
9. When skin temperature increases the rate of skin permeation also increases.

Physicochemical factors

1. Partition coefficient: percutaneous absorption of the drug will be more easily when more the value of log p.
2. The molecular weight (<400 Dalton).
3. The degree of ionization (only unionized drugs gets absorbed well).
4. Vehicles effect: the most efficient absorption through the skin provided by the hydro alcoholic gel.

Formulation considerations[5]

The challenges in formulating topical emulgels are

1. Determining systems that are non-toxic, non-irritating, non-comedogenic and no sensitizing.
2. Formulating cosmetically elegant emulgel.
3. The emulgel formulation must have low allergic potential, good physiological compatibility and high biocompatibility.

Emulgel[4]

Emulgel is a combined form of emulsion and gel. It is stable and effective vehicle for the delivery of hydrophobic drugs. Emulgel shows more effective mechanism than a gel because the permeation depth of the drug is more in emulgel.

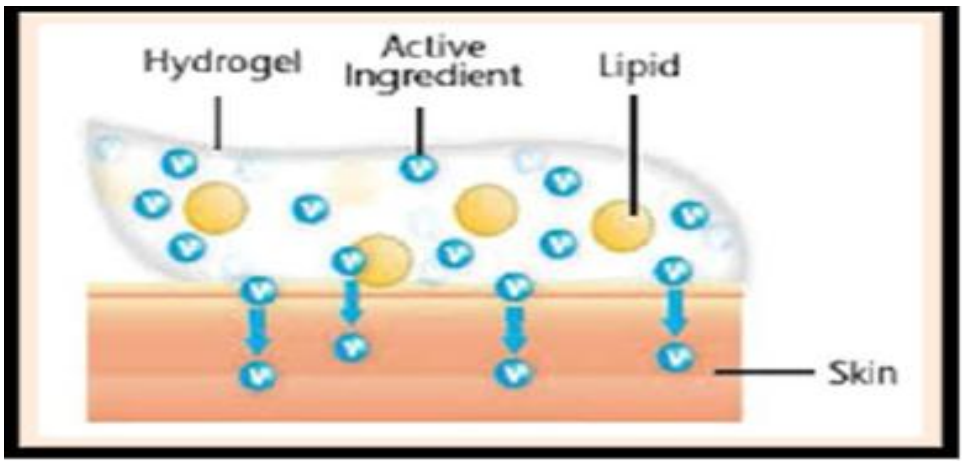

Figure 3: Emulgel.

There are two main components of emulgel and these are

- Emulsion
- Gel

The properties should be considered by a emulgel for a topical delivery are:-

- It should easily removable and should have long shelf-life.
- It should have transparent and pleasing appearance.
- It should be easily spreadable.

Advantages

- Easy method for target drug delivery on the body
- It is suitable for self medications

- It is helpful in patient acceptability
- Emulgel can be used to prolong the effect of the drug having shorter half life
- They are suitable to apply on hairs because of absence of greasiness and lack of residue upon application

Disadvantages[16]

- Skin irritation and allergic reactions
- Due to the large particle size and poor permeability of some drugs, it is not easy to absorb through the skin
- During the formulation of emulgel, there is possibility of bubble formation

Emulsion[16]

The combination of two liquids that usually don't mix and form a colloid is termed as emulsion. This colloid is called as emulsion. The colloid is referred as two phase system.

These two phases are

- Continuous phase
- Dispersed phase

The dispersed phase is dispersing into the continuous phase and forms an emulsion. Eg:- homogenized milk. The boundary between these two phases referred as "interface".

Types of emulsion

There are basically two classes of emulsion and these are

- o\w
- w\o

o\w:- in this type of emulsion, the oil phase is dispersed into aqueous phase. Eg:- homogenized milk.

w\o:- in this type of emulsion, the aqueous phase is dispersed into oil phase. Eg:- butter.

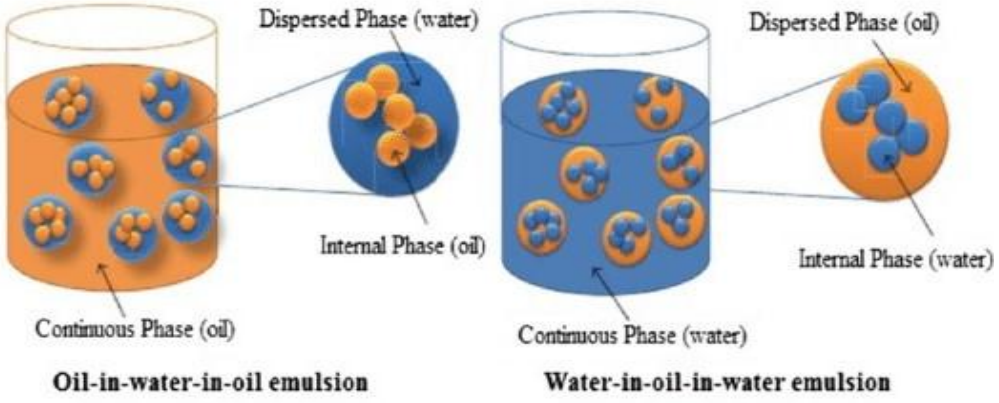

Figure 4: Types of Emulsion.[13]

Uses of emulsion

- For manufacturing of dispersion of polymer, emulsion is used
- For prevention of coagulation of product, emulsion is used
- Emulsion is a primary component for glues and paints
- Emulsion is used in pharmaceutical formulations such as creams, lotion, pastes etc.
- It plays an important role in formulation of cosmetics and its products

There are two classes of emulsion are:-

- Micro-emulsion
- Nano-emulsion

Gel[17]

It is a formulation like semi solid and having character of continuous structure. Gels have many of properties which show a better drug release than creams and other ointments. The gel having dermatological use, thus it is used in topical drug delivery system. For the treatment of skin disorder, the topical drug delivery system is mostly favorable. By this route the drug is delivered by rubbing or spraying on the surface of body. There are number of polymers are used for gel preparation and shows a 3-D polymeric matrix. Polymers like carbopol, HEC agar, guar-gum, tragancanth are used.

Advantages

- Gels are easily washed and can easily remove from application area.
- Gels have property of using for local effect and can be used as cutaneous or percutaneous drug delivery.
- Avoidance of enzyme activity and GI drug metabolism in liver.

Disadvantages

- Irritation and inflammation
- If gel containing larger particles of the drug / high molecular weight, will not absorbed properly by skin.

Types of gel[17]

Gels are classified on the basis of different system and these are

- Colloidal system e.g.:- organic and inorganic gel.
- Nature of solvent system e.g.:- organic and hydrogels.
- Rheological properties e.g.:- plastic gel-
- Physical nature e.g.:- elastic gel.

Composition of emulgel preparation[4,18]

Five important things like aqueous phase, oily phase, emulsifier, gelling agent and permeation enhancers are the formulation components of emulgel.

Aqueous material: Aqueous phase of emulsion is forms by using aqueous materials like water and alcohol, which are commonly used for this purpose.

Oils: Oily phase in the emulsion constitute by oils like liquid paraffin. Mineral oils are widely used as the vehicle for the drug as well as occlusive materials for externally applied emulsion.

Table1: Use of oil.

Chemical	Quantity (%)	Dosage form
Light liquid paraffin	7.5	emulsion and emulgel
Isopropyl myristate	7–7.5	emulsion
Isopropyl stearate	7-7.5	emulsion
Isopropyl palmitate	7-7.5	emulsion
Propylene glycol	3-5	Gel

Emulsifiers: During the self life to control the stability as well as to promote the emulsification, emulsifiers are used. Tween 20, Span 20 can be used as emulsifiers in the emulgel.

Gelling agent: As thickening agent and to promote the consistency of any dosages form, gelling agents are used. Carbopol 940, Guar-gum are used as gelling agent in emulgel.

Table 2: **Various gelling agent used for formulation of Emulgel & MBG.**

Gelling agent	Advantages	Concentration (%w/w)	Dosage form
Carbopol-934	Form gel at very low concentration and provide control release of incorporated drugs	1% ,1.78%	Emulgel
Carbopol-940	Form highly viscous gels and provide controlled release of incorporated drugs	1%	Emulgel
HPMC-2910	Produce natural gel of very stable viscosity	2.5%, 5%	Emulgel
HPMC	It shows better drug release rate	3.5%	Gel
NaCMI	Suitable for sterile gels as it can be stand autoclaving without serious deterioration	3-4%	Gel
Natural gelling agents			
Chitosan	More controlled gel stability	2-3%	Gel
Guar gum	It shows better drug release	1%, 2.5%	Emulgel
Gelatin	It produce natural gel of very stable viscosity	2-3%	Gel

Permeation enhancers: To induce a temporary and reversible increase in skin permeability, permeation enhancers partitions into and interact with skin constituents. Permeation enhancer may acts by temporary disrupts the skin barrier and improve partitioning of the drug. Propylene glycol, methanol, clove oil can be used as penetration enhancer in emulgel.

Table 3: List of penetration enhancers.

Penetration Enhancer	Concentration used (%w/w)	Dosage form
Oleic acid	1%	Emulgel
Lecithine	5%	Gel
Urea	10%	Gel
Isopropyl myristate	5%	Gel
Linoleic acid	5%	Gel
Clove oil	8%	Emulgel

Major components of emulgel and their role

Table 4: Components and their functions.[4,18]

Components	Function
Guar-gum	Natural gelling agent
Carbopol-940	Synthetic gelling agent
Light liquid paraffin	Oily phase
Tween 20	Emulsifier
Span 20	Emulsifier
Methyl parabren	Preservative

Propyl paraben	Preservative
TEA	pH adjuster
Propylene glycol	Penetration enhancer
Ethanol	Solvent

Natural polymer as gelling agent in emulgel: Natural polymers are produced by living organism and result from only raw materials that are found in nature. Most of the natural polymers build by condensation polymerization. These natural polymers are readly bio-degradable and biocompatible with the human being. Some natural gelling agent are used in preparation of emulgel are Tragacanth, Chitosan, Guar-gum, Albumin etc.

Synthetic polymers as gelling agent in emulgel[5]: Synthetic Polymers are made by chemical processes in laboratories. Many of raw materials for synthetic polymers are obtained from petroleum, after the refining and cracking processes. Examples are: - Carbomers, Nylon, Teflon etc.

Method of preparation of emulgel[19]

Step 1:- Preparation of gel base

A gel base will be prepared by the addition of polymer such as natural or synthetic into the calculated amount of water. The pH of the gel base will be maintained by the TEA.

Step 2:-Preparation of aqueous phase

Aqueous phase will be prepared by dispersing the emulsifier to purified water and heat it separately 70ºC.

Step 3:-Preparation of oil base

Oil base will be prepared by dispersing any mineral oil in hard or soft paraffin and heat it separately at 70ºC.

Step 4:-Emulsification

After heating both the phase, the oil phase is added to the aqueous phase with continuous stirring until it cool. The preparation emulsion is either of o\w or w/o.

Step 5:-Formation of emulgel

The prepared emulsion will be incorporated to the gel base with appropriate ratio. The formulation prepared is results as emulgel and will be packed in wide mouth glass jar covered with screw capped plastic lid.

Figure 5: Flow chart of Emulgel formulation.

Evaluation parameter

Visual examination: In the visual examination, we inspected for the color, phase separation, and homogenecity of emulgel and also examine the color, appearance and odor of fluconazole.[20]

Spreadability test: From each formulation, a sample of 0.5gm was taken. The sample was pressed between the two slides for 5 minutes or the time where spreading stops. The diameter of the spread circle was taken in cm and shows the comparative value for spreadability.[21]

pH determination: By using a digital pH meter, the pH of each formulation is calculated. The readings of pH will be taken an average of 3 times.[22,23]

Drug content: A calculated amount of emulgel formulation was taken and was dissolved in phosphate buffer of pH 7.4 in a volumetric flask. The flask is shaken for about 2 hours and kept for 24 hours aside. After 24 hours, the solution was filtered out. The appropriate number of dilutions was made and analyzed in the UV at λmax.260nm with the use of phosphate buffer.[23]

Swelling Index: In order to determine the swelling index of formulated emulgel, on porous aluminium foil 1gm of gel is taken and than in a 50 ml beaker containing 10ml 0.1N NaOH

placed separately. Than at different time intervals samples were removed from beakers. Than on a dry plate put it for some times after it reweighted.[24]

Microbiological assay: for performing microbiological assay, ditch plate was used. For evaluation of fungi static or bacteriostatic activity of compound, this technique is used. Sobouraud's agar dried plates which is previously prepared were used. In a ditch cut in a plate, 3gm of emulgel are placed. From the ditch to the edge of plate at a right angle freshly prepared culture loops are streaked cross the agar.[25]

Skin irritation test- on two sites per rabbit area of skin approximately 1" x 1"(2.54 x 2.54cm^2). Attach sample of 0.5gm under a double gauge layer was applied to each side. Emulgel was applied on the rabbit skin and animas were return to their cages. Emulgel is removed after exposure of 24 hours. To remove any remaining test sample residue the test sides were wipe with tap water.[26,27]

Stability studies: For more satisfactory formulation, the stability study was performed. The formulation was packed in collapse tubes and stored for three months at room temperature. The formulations were analyzed after every one month for physical properties, spreadability, pH, and drug content.[22,23]

FTIR analysis: In FTIR analysis compatibility of drugs with other components was identified. All the formulations of the emulgel were checked out in the wave number range of 1000-4000cm^{-1}. FTIR spectrum of all the formulations of emulgel was compared with the standard spectrum of the drug.[20]

***In-vitro* permeation study:** By using an eggshell membrane with a receptor compartment (80ml capacity) *in-vitro* permeation studies were performed. With the help of a thread, the eggshell membrane was fixed at the end of the hollow tube as a donor compartment and beaker present as a receptor compartment. a specified quantity of prepared emulgel was applied on to the surface of the eggshell membrane and eggshell membrane clamped between the donor and receptor chamber. Receptor compartment filled with phosphate buffer solution pH 7.4 to solubilize the drug. On the magnetic stirrer, the whole assembly was placed and the solution was continuously stirred with the help of a magnetic bead. The temperature was maintained at 37±0.5ºC. at a suitable interval, a 1ml sample was withdrawn and analyzed for drug content spectrophotometrically at 260nm.[28,29]

Packaging of emulgel: An aluminium laminated tubes closed by a moulds seal with a propylene screw cap or membrane sealed lacquesed aluminium tubes with inner coating of phenoxy-epoxy are generally used for the packaging of emulgel.

Material for laminate tubes

- For light, air and moisture barrier foil laminates are used.
- For chemical resistant barrier all plastic laminates are used.

Marketed Preparations: The various preparations of emulgels available in market are shown in table:

Table 5: Marketed products.

Product	Drug	Manufacture
Voltaren emulgel	Diclofenac-diethyl-ammonium	Novartis pharma
Miconaz-H-Emulgel	Miconazole nitrate, hydrocortisone	Medical union pharmaceuticals
Excel gel	Clindamycin, adapalene	Zee laboratories
Pernox gel	Benzoyl peroxide	Cosme remedies Ltd
Lupigyl gel	Metronidazole, clindamycin	Lupin pharma
Clinagel	Clindamycin phosphate, allantonin	Stiefel pharma
Topinate gel	Clobetasol propionate	Systopic pharma
Kojivit gel	Kojic acid, dipalmitate acid	Micro gratia pharma
Accent gel	Aceclofenac	Intra labs India Pvt. Ltd
Avindo gel	Azithromycin	Cosme pharma lab
Cloben gel	Clotrimazole, betamethasone	Indoco remedies
Nadicin cream	Nadifloxacin	Psycho remedies

3 Current elevations in development of emulgel for various drugs.

Drug	Aim	Use	References
Amphotericin B	Evaluation of the *in vivo* leishmanicidal activity of amphotericin B emulgel: An alternative for the treatment of skin leishmaniasis	Leishmaniasis therapy	[30]
Metronidazole and ciprofloxacin	Groundnut oil based emulsion gels for passive and iontophoretic delivery of therapeutics	Passive and iontophoretic delivery of therapeutics	[31]
Amlodipine besylate	Preparation of amlodipine besylate emulgels for transdermal administration and its	Transdermal delivery	[32]

	percutaneous permeability *in vitro*		
Acyclovir and ketoconazole	Topical delivery of acyclovir and ketoconazole	Viral and fungal cutaneous manifestations	[33]
Lacidipine	Novel non-ionic surfactant proniosomes for transdermal delivery of lacidipine: optimization using 23 factorial design and in vivo evaluation in rabbits	Antihypertensive	[34]
Pravastatin	Optimised transdermal delivery of pravastatin		[35]
Ciprofloxacin	Genipin-Crosslinked Gelatin-Based Emulgels: an Insight into the Thermal, Mechanical, and Electrical Studies		[36]
Diclofenac sodium	Evaluation of skin penetration of diclofenac from a novel topical non aqueous solution: A comparative bioavailability study	Pain relief	[37]
Diclofenac sodium	Nanoemulsion-based gel formulation of diclofenac diethylamine: design, optimization, rheological behavior and in vitro diffusion studies	Management of pain	[38]
Pinhão starch	Pinhão starch and coat extract as new natural cosmetic ingredients: Topical formulation stability and sensory analysis	Antioxidant activity	[39]
Terpinen-4-ol	The effect of rheological behavior and microstructure of the emulgels on the release and permeation profiles of Terpinen-4-ol	Antimicrobial properties	[40]
Betamethasone dipropionate	Development of a topical ointment of betamethasone dipropionate loaded nanostructured lipid carrier	For the treatment of atopic dermatitis	[41]
LEVORAG® Emulgel : Hibiscus esculentus extract, Carboxymethyl beta-glucan Dimethicone,	Prospective multicenter observational trial on the safety and efficacy of LEVORAG® Emulgel in	For treatment of acute and chronic anal fissure	[42]

glycerine, prunus amygdalus dulcis oil, borago officinalis seed oil Malva sylvestris extract, calendula officinalis extract, glycyrrhiza glabra extract	the treatment of acute and chronic anal fissure		
Cyclosporin A	Formulation and evaluation of Cyclosporin A emulgel for ocular delivery	Topical ocular delivery	[43]
Meloxicam	Formulation and characterisation of Meloxicam loaded emulgel for topical application	Anti-inflammatory	[44]
Nimorazole	Preparation and evaluation of Radiosensitizing agent Nimorazole in topical emulgel	hypoxic cell radiosensitizing agent	[45]
Ketoprofen	Formulation development, *in vitro* and *in vivo* evaluation of microemulsion-based gel loaded with ketoprofen	Anti-inflammatory	[46]
Calcipotriol	Calcipotriol delivery into the skin as emulgel for effective permeation	In treatment of Psoriasis.	[47]
Allopurinol	Design and development of allopurinol emulgel	[48]	
Terbinafine hydrochloride	Formulation, development and *in-vitro* evaluation of Terbinafine hydrochloride emulgel for topical	In treatment of fungal infection	[49]

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