Indian Journal of Novel Drug Delivery

IJNDD

An Official Publication of Karnataka Education and Scientific Society

Review Article

An Overview: Emulgel as a Novel Topical Drug Delivery

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ARTICLE DETAILS

Article history:
Received on 1 June 2023
Modified on 23 June 2023
Accepted on 26 June 2023

Keywords:
Emulgels,
Topical Drug Delivery,
Emulsion,
Gel,
Gelling Agent.

ABSTRACT

Topical drug delivery refers to the administration of medications through cutaneous, vaginal, ophthalmic, and rectal channels to any part of the body. Drugs may be administered for systemic or local effects. It is possible to create topical preparations through different physicochemical characteristics like solid, semisolid and liquid. Emulgel is a topical remedy. Prepared using an emulsion as well as gel mixture. Emulgel is regarded as one of the most significant topical delivery systems since it contains both an emulsion and a gel release control system. Emulgels often don't have any harmful side effects. This novel drug delivery system's main goal is to use the skin to introduce hydrophobic medications into the bloodstream. Typically, emulsion is mixed with gel basis to create emulgel. In comparison to other topical drug delivery systems, it exhibits improved drug release due to the absence of insoluble excipients and excessive oily bases. Due to non-greasy due to the gel phase's existence, this encourages good patient compliance. Studies on emulgel indicate that it will be possible to give more topical medications in the future due to its advantages over other methods.

INTRODUCTION

Topical drug delivery refers to the application of a medication-containing formulation to the skin for the treatment of cutaneous illnesses. When other drug delivery methods like oral, sublingual, rectal, or parental are ineffective or when a local skin infection such a fungal infection occurs, the topical drug delivery technique is typically used [1]. Topical delivery system's primary benefit is avoiding first pass metabolism. Another benefit of using oral medication is avoiding the risks and hassles of IV healing and the numerous circumstances of absorption like pH fluctuations, the presence of enzymes, and gastric emptying time. The topical medication delivery mechanism is typically utilized when other drug administration methods are ineffective. The skin is one of the body sections, that is, easiest to administer substances topically. Molecules enter the skin primarily through the intact stratum corneum, sweat ducts, and sebaceous follicle.

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Topical channels such as the skin, rectal, vaginal, and ophthalmic are utilised to deliver drugs for localised action on the body. Emulgel (gellified emulsion), a topical drug delivery mechanism, is frequently utilised when other drug administration methods are ineffective in treating cutaneous problems like fungal infections, acne, psoriasis, and other conditions [2, 3].

Emulgel

By combining w/o or o/w emulsions with a gelling agent, emulgel can be created [4]. The emulsion serves as a controlled release drug delivery method as well, permitting the delayed absorption of drug particles that have been retained in the internal phase by the skin after passing through the external phase. The medicine is carefully administered to the skin's surface phase through the internal phases of the skin, which act as a drug reservoir. The cross-linked network of gel enables it to store minute medicine particles and release them gradually. It increases the amount of time a medicine is in contact with the skin due to its mucoadhesive property [5]. Emulgel serves as a dual control release mechanism since it possesses both the

characteristics of a gel and an emulsion [6]. Water-in-oil emulsions are more usually employed for emollient activities, the treatment of dry skin, and emollient applications [7, 8], whereas oil-in-water emulsions are better used in general cosmetic functions as a water washable medicine foundation. When an emulsion has the thixotropic property, the processes of penetration into the skin are facilitated. In order to improve emulsion penetration and stability, it is added to the gel. Gels for dermatological use further benefit from being emollient, greaseless, thixotropic, simple to remove, nonstaining, and compatible with a range of excipients [9, 10]. Emulgels might be a better choice if one is worried about the topical distribution of a medicine that isn't particularly water soluble. It has also demonstrated to be an improved and stable delivery system for hydrophobic or poorly water-soluble drugs [11–12].

Types of Emulgel:

Macroemulsions Gel

These are the most prevalent types of emulgel when the emulsion droplet size is more than 400 nm. Though they are seemingly opaque, a microscope makes the individual droplets plainly visible. Although macroemulsions are thermodynamically unstable, surface active compounds can stabilise them. In the case of mefenamic acid emulgel, Carbopol 940 was used as a gelling agent. The oil phase was liquid paraffin. Clove and mentha oil were used to increase penetration. Following that, it was assessed for rheological tests, spreading coefficient investigations, a skin irritancy test, *in-vitro* release, etc [13].

Nanoemulgel

Nanoemulgel is the name for a nanoemulsion that has been put into a gel. Nanoemulsions are transparent (translucent) dispersions of oil and water that are thermodynamically stable, and they are held together by an interfacial coating of surfactant and cosurfactant molecules with droplet sizes of less than 100 nm. *In vitro* and *in vivo*, nanoemulsion formulations have better transdermal and dermal delivery qualities. In comparison to more traditional topical formulations like emulsions and gels, nanoemulsions have enhanced the transdermal penetration of numerous medications. E.g. Oleic acid and isopropyl myristate were used in a 3:1 ratio as the oil phase to create the carvingilol nanoemulgel. As a surfactant and cosurfactant, Tween 20 and carbitol were utilised. As a gelling agent, carbopol 934 was utilized [14].

Microemulsion

Since the size of the droplets in microemulsions ranges from 10 to 100 nm and they do not coalesce, they are transparent and thermodynamically stable. Specific ratios of water, surfactant, cosurfactant, and oil make up microemulsions. By lowering the stratum corneum's diffusion barrier, the components of the microemulsion may increase the pace at which the drug permeates the body. However, because microemulsions have a low viscosity, they have a limited ability to adhere to skin, which limits their use in the pharmaceutical sector. To circumvent this drawback, the microemulsion has been combined with gelling agents such carbopol 940, xanthan gum, and carrageenan to create a microemulsion-based gel with a higher viscosity that may be appropriate for topical administration. Additionally, microemulsion-based gel promotes greater medication accumulation in the skin for effective action by preventing drug absorption into the bloodstream. For instance, clotrimazole microemulsion-based vaginal gel was created utilising Cremophor EL as the surfactant and Capryol 90 as the oil phase. As a gelling agent, carbopol ETD 2020 is employed [15].

Advantages of Emulgel

- ✓ Hydrophobic medications can be swiftly incorporated into the gel foundation using water/oil/water emulsions.
- ✓ Increased load capacity and stability.
- ✓ Simple to produce and inexpensive mechanism.
- ✓ Avoid sonication.
- ✓ The first metabolism is avoided.
- ✓ Avoid gastrointestinal incompatibility.
- ✓ Target drug delivery on the body.
- ✓ Improved patient compliance.
- ✓ Improved appropriateness and patient acceptance for self-medication.
- ✓ The ability to quickly stop taking drugs [16].

Disadvantages of Emulgel

- ✓ People with contact dermatitis may have skin irritation as a result of the medication and/or excipients.
- ✓ Some medicines pass through the skin with little permeability.
- ✓ The potential for allergic responses.
- ✓ Drugs with larger particle sizes do not readily penetrate the skin [17].

Rational

Topical medications including ointments, creams, and lotions are frequently used yet have significant drawbacks. When administered, they are extremely sticky and make the patient uncomfortable. Additionally, they have a lower spreading coefficient, require rubbing when applying, and also have a stability issue. All these factors within the primary group of semisolid preparations have led to an increase in the use of transparent gels in medicinal and cosmetic preparations. The surface tension between a colloid, which is normally 99% by weight liquid, and a macromolecular network of fibres constructed from a little quantity of a gelating material present immobilises the colloid. Despite the fact that gels have many benefits, hydrophobic medication delivery is a significant drawback. A method based on emulsions is therefore being employed to get around this restriction, allowing even a hydrophobic medicinal moiety to be successfully integrated and given through gels [18].

Physiology of Skin [19-20]:

The majority of topical medications are meant to be used topically. Therefore, while developing a topical dose form, it is essential to have a fundamental understanding of how the skin functions physiologically. The surface area of an average adult's skin is around 2 m^2, and it receives about one-third of the blood that flows through the body. The number of sweat ducts and hair follicles per square centimetre of human skin is between 200 and 300. The pH of the skin varies from 4 to 5.6. Sweat and fatty acids generated by sebum have an impact on the pH of the skin's surface. The skin is composed of four distinct layers of tissue.

Non-viable Epidermis

Most substances that come into contact with skin are physically separated from it by the stratum corneum, the skin's top layer. The stratum corneum covers the majority of the body and is 10 to 20 cell layers thick. Each cell is a flat, plate-like structure with dimensions of 34–44 mm in length, 25–36 mm in width, and 0.5–0.20 mm in thickness, with a surface area of 750–1200 mm stacked up to one another in a brick-like pattern. The stratum corneum is composed of protein (75-85%), which is primarily keratin, a neutral lipid (5-15%), and phospholipids, glycosphingolipids, and cholesterol sulphate.

Viable Epidermis

This layer of skin lies between the stratum corneum and the dermis and ranges in thickness from 50 to 100 m. The architecture of the cells of the living epidermis resembles those of other living tissues physicochemically. Tonofibrils serve to bind cells together. This area's density is very similar to that of water. About 90% of it is water.

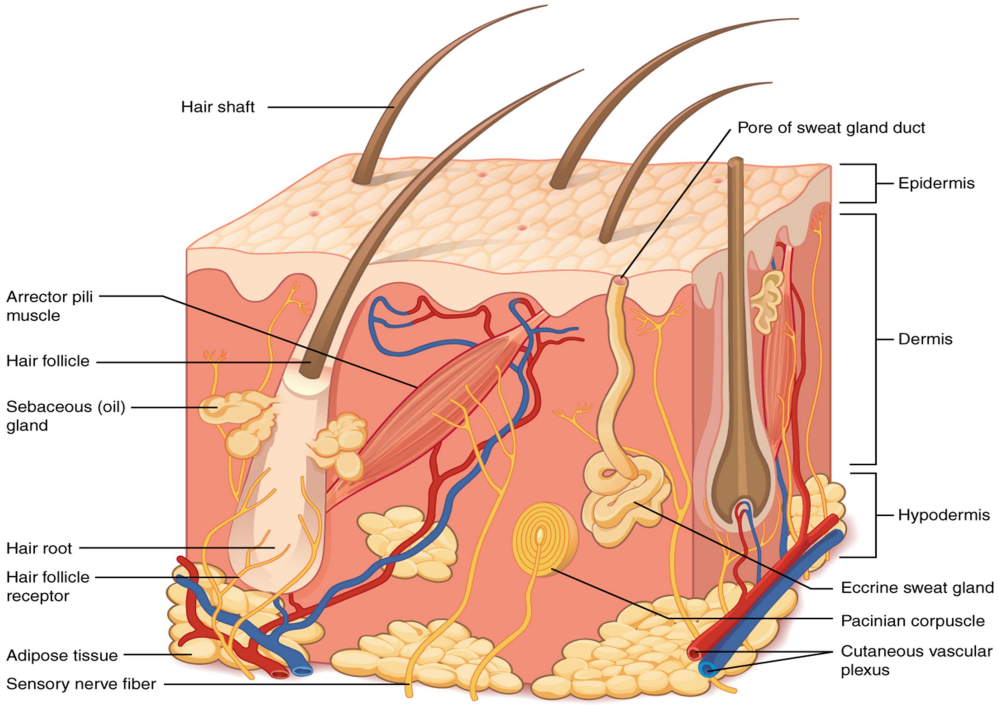

Figure 1: Anatomy of Skin

Dermis

The viable epidermis is immediately below the dermis. Few cells in healthy tissue histologically resemble this structural fibrin; it is one. The dermis ranges in thickness from 2000 to 3000 m and is composed of a matrix of loose connective tissue formed of fibrous protein embedded in an amphorphose base substance.

Subcutaneous Connective Tissue

Although it contains blood and lymphatic arteries, sweat gland secretary pores, and cutaneous nerves, the subcutaneous tissue, also known as the hypodermis, is not actually thought of as a true component of the organised connective tissue. Although adipose tissue may act as a drug depot, the majority of researchers believe that drugs enter the circulatory system through the skin before they reach the hypodermis.

Drug Delivery across the Skin:

The outermost layer of the skin i.e. epidermis; is made up of stratified keratinized squamous epithelium, the thickness of which varies across the body. Dermatological problems are diagnosed and treated using the skin as the target organ. There are two-way barrier functions of skin to stop the absorption and loss of electrolytes and water. Three main pathways for topical medication absorption:

1) Transcellular
2) Intercellular
3) Follicular

Most medications travel over the tortuous route that skirts corneocytes and through the lipid bilayer to reach the skin's viable layers. Since many years ago, antimicrobial medications and painkillers have been delivered to an affected place of the body via creams and gels that are rubbed into the skin. These include, among others, topical creams for skin infections, gels and creams to treat vaginal yeast infections, and creams to relieve arthritis pain. Due to more current technologies, other drugs can now be absorbed transdermally (through the skin). These can be utilised to treat the entire body (systemic), not simply the areas that are damaged (such, for example, the skin) [21–22].

Factors Affecting Topical Absorption of Drug [23]:

Physiological Factors

- Skin thickness
- Lipid content
- Density of hair follicles
- Density of sweat glands
- Skin pH
- Blood flow
- Hydration of skin
- Inflammation of skin.

Physiochemical Factors

- Partition coefficient
- Molecular weight (<400 dalton)
- Degree of ionization (only unionized drugs gets absorbed well)
- Effect of vehicles.

Important Constituents of Emulgel Preparation [24-27]:

Aqueous Material

The emulsion's aqueous phase is formed by this. Alcohols and water are often used agents.

Oils

The emulsion's oily phase is made up of these components. Because of their occlusive and sensory qualities as well as their utility as a medicine delivery method, mineral oils are commonly used for topically administered emulsions, either alone or in conjunction with soft or hard paraffin. Oral formulations frequently use fixed oils of vegetable origin, such as arachis, cottonseed, and maize oils, as well as non-biodegradable mineral and castor oils that have a local laxative effect.

Emulsifiers

Emulsifiers are used to control the emulsification and stability processes. Because emulsions are thermodynamically unstable, adding the proper emulsifying agent can increase their stability. Water in oil emulsions are created with mineral oils, such as liquid paraffin, with HLB values less than 8, whereas o/w emulsions are created using surfactants with HLB values bigger than 8, such as nonionic surfactants (spans, tweens). When span 20 and tween 20 are used together rather than individually, the emulsion is more stable.

Penetration Enhancers

Vehicles for pharmaceuticals frequently contain penetration-enhancing components that temporarily disrupt the skin barrier, fluidize the lipid channels between corneocytes, change how the drug is partitioned into skin structures, or improve transport into the skin in other ways.

Properties of Penetration Enhancers

- They ought to be non-irritating, non-toxic, and non-allergenic.
- They should preferably act quickly, with predictable and repeatable activity and duration of impact.
- They shouldn't interact with the body's pharmacological systems or bind to receptor locations.
- In order to allow therapeutic drugs to enter the body while avoiding the loss of endogenous material from the body, the penetration enhancers must function unidirectional.
- The penetration enhancers must to be suitable for incorporation into different topical treatments, making them compatible with excipients and medications alike.
- Their appearance should be respectable, and their skin should have the right "feel."

Gelling Agents

In order to make gel bases, gelling agents are combined with emulsion to form emulgel. By expanding in the aqueous phase and forming structures that resemble gel, these chemicals, also known as thickening agents, improve the consistency of any dosage form. A system becomes thixotropic when a gelling agent is added. It was decided that the HPMC-based Emulgel was superior since it released drugs more quickly than the Carbopol-based Emulgel. Emulgels made from NaCMC have the best *in-vitro* and *in-vivo* performance and have higher mucoadhesivity, which increases the duration of the medication's residence time, making them perfect for vaginal use. Using HEC-based Emulgel, low mucoadhesion but good drug release profiles and rheological features were demonstrated. Pemulen-based emulgel is meant for buccal administration.

Table 2: Various Gelling Agents Used In Pharmaceutical Dosage Forms [28]

Sr.No	Gelling Agents	Concentration (%w/w)	Pharmaceutical Adaptability	API
1	Sodium CMC	3-4%	stand autoclaving hence suitable for sterile gels	Benzydamine
2	Carbopol-934	1%	Provide controlled release of API incorporated	Chlorphenesin
3	Carbopol-940	1%	Because of high viscous gel, provide controlled release of API incorporated	Mefenamic acid
4	HPMC	2.5%	Having good stability, microbial resistance,	Clorphenesin
5	Combination of HPMC & Carbopol	1.2%	Combination improve stability	Ketorolac, Clotrimazole
6	Pluronic® F127	1-3%	Good clarity and better solubility in cold water	Piroxicam
7	Pemulen	0.1-0.4%	Provide rapid release of oil phase, excellent stability	Flurbiprofen

Preparation of Emulgel [29-30]

Step 1: Formulation of gel base

By combining DDW and a known amount of polymer at reasonable speed with a magnetic stirrer while maintaining a pH range of 5-6.5, the gel base is created.

Step 2: Preparation of oil in water or water in oil form of emulsion

Smix is made in the right proportions utilizing a magnetic stirrer. Drop by drop, while swirling continuously, add the Smix to oil phase to create a transparent emulsion.

Step 3: Formulation of emulgel

To create emulgel, drop wise add the produced emulsion into the gel basis while stirring continuously with a homogenizer.

CONCLUSION

Topical medicine delivery will be widely employed in the upcoming years to improve patient compliance. Emulgel will become a well-

liked drug delivery method since Spreadability, adhesion, viscosity, and extrusions are their strong points. They will also be used as a way to incorporate hydrophobic medications into water-soluble gel bases.

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