Available online on 30.08.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Review Article

Microemulsions: Transdermal Drug Delivery Systems with Enhanced Bioavailability

R Santosh Kumar* and T V Sai Pravallika

GITAM Institute of Pharmacy, GITAM (Deemed To Be University) Rushikonda, Visakhapatnam-530045, Andhra Pradesh, India.

ABSTRACT

Microemulsions are preferred because of its advantages like low cost of preparation and enhanced bioavailability due to increased absorption of drug through skin which is achieved by adding penetration enhancers. Most frequently used permeation enhancers are saturated and unsaturated fatty acids like oleic acid . Microemulsions are the systems which can be used as a carrier to enhance the solubility of the drug and they protect the drug from oxidation, degradation and hydrolysis. As this system is directly applied on the skin, there is lesser risk of side effects like toxicity. Thus, microemulsions can be used as safe and effective dosage form to enhance the bioavailability of drugs in the transdermal drug delivery system. This article summarizes the structure of microemulsions, its components, merits and demerits of microemulsion system.

Keywords: Microemulsion, transdermal drug delivery, bioavailability.

Article Info: Received 14 July 2019; Review Completed 13 Aug 2019; Accepted 20 Aug 2019; Available online 30 Aug 2019

Cite this article as:

Santosh Kumar R, Sai Pravallika TV, Microemulsions –Transdermal Drug Delivery Systems with Enhanced Bioavailability, Journal of Drug Delivery and Therapeutics. 2019; 9(4-A):835-837 http://dx.doi.org/10.22270/jddt.v9i4-A.3671

***Address for Correspondence:**

R. Santosh Kumar, GITAM Institute of Pharmacy, GITAM (Deemed to be University), Gandhinagar, Visakhapatnam-530045, Andhra Pradesh, INDIA.

Introduction

Microemulsion system composed of water, oil and amphiphile are optically isotropic systems. They are thermodynamically stable system and a new approach to transdermal drug delivery system. Microemulsions are clear systems having higher absorption and diffusion rates due to its penetration property. Microemulsions are widely studied dosage forms as they enhance the bioavailability of poorly soluble drugs. They have low surface tension, small droplet size which enhances the absorption and permeability of the drugs . Due to its thermodynamic stability and solubilisation properties it is used as a vehicle in the novel drug delivery system. In the year 1943, Hoar and Schulman coined the term "Microemulsion" to define a solution obtained on titrating an oil in water emulsion with an alcohol.

The skin is the largest organ of the body and it is a very suitable site for administration of drugs. In this aspect, the field of transdermal drug delivery has been developing safe and beneficial means for the delivery of drugs through the skin. [1-5]

Skin

Structure and Functions of the skin

The skin acts a protective barrier between the body and external environment against microbes, U.V radiations, chemical , allergens etc. The skin is also responsible for the maintenance of thermoregulation by fluid transpiration (sweating) and the exchange of gases and toxins with the external environment.

The skin consists of three layers namely, the outer most layer called the epidermis, middle layer that is the dermis and the inner most layer hypodermis.

Epidermis is the outer most layer and forms a waterproof barrier over the body surface .It is made up of keratinocytes (95%) , melanocytes, Langerhans cells and merkel cells . It has multi-layered regions of epithelial cells and is further subdivided into stratum corneum, stratum lucidum, stratum granulosum , stratum spinosum , stratum basale . Dermis which is the middle layer of the skin consists of blood vessels, lymph vessels, hair follicles, sweat glands, collagen bundles, fibroblasts, nerves and sebaceous glands. Dermis is bound together by a protein called collagen. This layer provides flexibility and strength to the skin. It also has pain and touch receptors. Hypodermis the inner most layer of the skin is also called as the sub cutaneous fat layer. It has a network of collagen and fat cells. It is responsible for the conservation of body's heat and acts as a shock absorber.[3-5]

Skin permeation pathways

The three main skin permeation pathways are intracellular (transcellular) , intercellular and appendageal. Appendageal permeation is less significant in normal conditions as it occupies lesser surface area. Intracellular route is found to be more complex as the movement of molecules involves crossing of lipid bilayers for which the molecules should have sufficient lipid-water partitioning properties. In case of intercellular route the molecules pass through spaces that consist of free fatty acids, their esters, cholesterol and its sulphates which are arranged in a bilayer . [3-5]

Microemulsion structure

Microemulsion is a composition of water, oil, mixture of surfactant and co-surfactant. Microemulsion's structure is in the form of droplets dispersed in the continuous phase with the help of a surfactant.

There three types of microemulsion structures are as follows –

1. Oil in water phase
2. Water in oil phase
3. Bi-continuous phase

There are four types of microemulsion systems which exist in equilibrium as stated by Winsor.

- Winsor-I; has two phases o/w, the lower water phase is in equilibrium with the upper oil phase.
- Winsor-II; has two phases w/o, the upper water phase is in equilibrium with the lower oil phase.
- Winsor-III; has three phases (o/w + w/o), middle microemulsion phase is in equilibrium with upper oil phase and lower water phase.
- Winsor-IV; it has a single phase; homogenous mixture of oil, water and surfactant. [1]

Components of microemulsion components

Oil phase

The oil phase solubilizes the required dose of lipophilic drug and increases the fraction of lipophilic drug transported via intestinal lymphatic system thus enhancing the absorption of the drug. Oil phase influences the curvature and has the ability to penetrate through the tail area thus causing the swelling of the tail group region. Oils with long chain alkanes have lesser penetrating ability while the short chain alkanes have higher penetrating ability thus causing the swelling of the tail group region.

Examples

- Saturated fatty acids- lauric acid, capric acid
- Unsaturated fatty acids- linoleic acid , linolenic acid
- Fatty acid ester ethyl or methyl esters of oleic acid, lauric acid

Aqueous phase

The water phase is made up of active hydrophilic agents. Water is the most widely used aqueous phase . Preserved buffers are also used by some researchers.

Surfactants

Surfactants decrease the interfacial tension thus facilitating dispersion during the preparation of microemulsion. It forms a flexible film giving a correct curvature to the interfacial region.

Types of surfactants

- Nonionic
- Zwitterion
- Cationic
- Anionic

Nonionic surfactants show low toxicity and low irritancy so commonly used in the preparation of microemulsion. Examples polysorbates , propylene glycol caprylate.

- ✓ Low HLB (3-6) W/O microemulsion
- ✓ High HLB (8-18) O/W microemulsion
- ✓ HLB >20 needs cosurfactants to decrease effective.

Cosurfactants

The flexibility required by interfacial film to form different curvatures of a microemulsion is provided by a cosurfactant. Short to medium chain alcohols are used as cosurfactants to decrease the interfacial tension and increase fluidity. Examples; short chain alcohols - ethanol to butanol and medium chain alcohols like glycols. [8-10]

Advantages of microemulsions

- ➢ Rapid drug release due to large interfacial area
- ➢ Better thermodynamic stability
- ➢ Low viscosity
- ➢ Improves efficacy of the drug
- ➢ Can solubilize both hydrophilic and lipophilic drugs

Disadvantages of microemulsions

- ➢ High amounts of surfactants are needed for the stabilization of droplets
- ➢ Limited solubilizing capacity for high melting point substances
- ➢ Surfactants should be non toxic
- ➢ Temperature and pH influences the stability
- ➢ Phase separation usually occurs [11-12]

Transdermal drug delivery (TDD)

It is a painless method of drug delivery into the systemic circulation . It avoids hepatic first pass metabolism and acts as a substitute for patients incapable of taking drugs orally.

Firstly the drug penetrates through the stratum corneum and then enters the deeper epidermis and dermis layers.

Factors affecting TDD

Skin hydration

On contact with water the permeability of the skin is improved. Hydration is an important factor in increasing the permeability of the skin .So humectants are used in transdermal drug delivery.

Temperature and pH

Permeability increases ten folds with the difference in temperature . As the temperature falls the diffusion coefficient also decreases.

Diffusion coefficient

It depends on the properties of the drug , diffusion medium and interaction between them .

Drug concentration

The concentration gradient is higher if the drug concentration is more across the skin barrier .

Partition coefficient (K)

The drugs with lower K value have lesser permeability. The K value required for optimal transdermal permeability is 1 or greater. [13-15]

Advantages of TDD

- Improves bioavailability, shows longer duration of action thus decreasing the dosing interval.
- It is a steady infusion over longer periods and has lesser side effects so acts as a goal of therapy.
- It is advantageous in patients who are unconscious.
- It has a simple dosing regimen, usually weekly once.
- It is a painless means of drug administration
- It avoids first pass metabolism

Disadvantages of TDD

- Drugs with hydrophilic structures show less penetrating capability.
- It cannot reach high drug levels in plasma.
- Drugs having large molecule size cannot be used in transdermal drug delivery.
- Some people tend to be sensitive which results in discontinuation of therapy.
- It cannot be delivered in large doses.
- Drugs only with relative potency are suitable for TDD. [13-15]

Conclusion

The permeation rate of drugs is found to be increased by the use of microemulsions in the transdermal drug delivery. Permeation enhancers like the saturated and unsaturated fatty acids play a vital role in making the microemulsions a carrier in transdermal drug delivery. In conclusion, microemulsions increase the solubilisation of drugs as well as protect from oxidation, hydrolysis and degradation.

References

1. Hoar TP, Schulman JH. Transparent water-in-oil dispersions: The oleopathic hydro-micelle. Nature 1943;152:102-3
2. Menon GK. New insights into skin structure: Scratching the surface. Adv Drug Deliv Rev 2002;54:S3-17
3. Freinkel RK, Woodley DT. The Biology of the Skin. Boca Raton: CRC Press; 2001.
4. Igarashi T, Nishino K, Nayar SK. The appearance of human skin: A survey. Found Trends Comput Graph Vis 2007;3:1-95
5. Bolzinger MA, Briancon S, Pelletier J, Chevalier Y. Penetration of drugs through skin, a complex rate-controlling membrane. Curr Opin Colloid Interface Sci 2012;17:156-65.
6. Patzelt A, Lademann J. The increasing importance of the hair follicle route in dermal and transdermal drug delivery. In: Percutaneous Penetration Enhancers Chemical Methods in Penetration Enhancement. Berlin; Heidelberg: Springer; 2015. p. 43-53
7. Sarkhejiya Naimish A, Nakum Mayur A, Patel Vipul P, AtaraSamir A, Desai Thusarbindu R; Emerging Trend Of Microemulsion In Formulation and Reserach; International Bulletin of Drug Research., 1(1) 54-83
8. Y. Srinivasa Rao, K. Sree Deepthi and K.P.R. Chowdary; Microemulsions: A Novel Drug Carrier System; International Journal of Drug Delivery Technology.,1(2) (2009) 39-41
9. Maurya S., Arya R., Rajpal G., Dhakar R. Self-Micro Emulsifying Drug Delivery Systems (SMEDDS): A Review On Physico-Chemical And Biopharmaceutical Aspects. *Journal of Drug Delivery and Therapeutics*, 2017; *7*(3):55-65. https://doi.org/10.22270/jddt.v7i3.1453
10. Prince L. M; A theory of aqueous emulsions I. Negativeinterfacial tension at the oil/water interface; J. Colloid Interface Sci., 23 (1976)165-173
11. Sushama Talegaonkar, Adnan Azeem, Farhan Ahmad J, Roop Khar K, Shadab Pathan A, Zeenat Khan I; Microemulsions :A Novel approach to enhanced drug delivery; Recent patents on drug delivery and formulation; 2, 2008; 238-257
12. Syeda Ayesha Fathima, Shireen Begum, Syeda Saniya Fatima. Transdermal Drug Delivery System. International Journal of Pharmaceutical and Clinical Research. 2017; 9(1): 35-43.
13. Nikhil Sharma, Bharat Parashar, Shalini Sharma, Uday Mahajan, "Blooming Pharma Industry with Transdermal Drug Delivery System. Indo Global Journal of Pharmaceutical Sciences. 2012; 2(3): 262-278.
14. Ita, K. Transdermal Drug Delivery: Progress and Challenges. J. Drug Deliv. Sci. Technol. 2014, 24, 245–250.
15. Schoellhammer, C.M.; Blankschtein, D.; Langer, R. Skin Permeabilization for Transdermal Drug Delivery: Recent Advances and Future Prospects. Expert Opin. Drug Deliv. 2014, 11, 393–407