Review Article

Nanoemmigel – An Apercu

Merlin Roshma Sherin, Mohammed Irshad, Nadhiya, Naga Gouri, Fatima Grace Xavier*, Shanmuganathan Seetharaman
Dept. of Pharmaceutics, Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai, India.
***Corresponding author's E-mail:** santagracek@gmail.com

Received: 10-01-2019; **Revised:** 20-02-2019; **Accepted:** 02-03-2019.

ABSTRACT

The efficacy of drugs depends on the type of delivery system and thus newer approaches have been developed to enhance the drug efficacy. One among the newer approaches is development of nanoemmigel or nanomiemgel which comprises of two delivery systems in a single dosage from. A nanoemulsion fused with nanomicellar system by using a gelling agent. Nanomiemgel is an improvised delivery system developed to overcome the major drawbacks faced by conventional drug delivery system. It is a combination of nanoemulsion and nanomicelle which has got the advantage of both the system. The ultimate aim of the dosage form is to enhance drug delivery in an effective way which can be achieved by decreasing the particle size to nano and by achieving micellar concentration. Nanoemulsion is a solid spherical carrier in nano sizes designed to enhance site specificity. Nanomicellar system is a colloidal drug carrier composed of amphiphilic monomers. Nanoemmigel has been reported to have significant drug effect than the individual system effect on administration.

Keywords: Nanoemmigel, nanoemulsion, nanomicelle, topical delivery.

INTRODUCTION

Skin is the largest organ of the body comprising 10% of the total body mass. It has 3 main layers viz. dermis, epidermis and subcutaneous layer. The permeation rate of drugs is decided by the stratum corneum.[1] The main factors that affect skin permeation are concentration of drug, diffusion, partition coefficient, age of skin, diseases, skin condition and water content or hydration of skin. Drug delivery through the skin is safe and convenient route of drug administration and has various advantages like bypassing first pass metabolism (presystemic metabolism), long duration of action, reduction in adverse effects, increase in pharmacological and physiological action, rate, fluctuation in drug level, variation arising between patient to patient and the most important advantage is the patient compliance on drug delivery.[2]

In this present study, we have given an overview on nanoemmigel. Nanoemmigel is a novel drug delivery system which almost includes all the advantages mentioned above. It is a combination of two delivery system such as nanoemulsion and nanomicelle formulated as a single dosage form like gels, ointments, creams etc in case of topical applications which has multi absorption mechanism with several applicability.[3] This combination delivery system would have better absorption and permeability than the individual nanoemulsion gel or nanomicellar gel.

Generally combination of two different drug delivery systems offer maximum drug permeation through different paths also it enhances therapeutic effect. The globule size ranges 20-200nm for nanoemulsion and nanoemmigel ranges 10-50nm, so smaller size is the major advantage of this delivery system. Hence, the present review has been put forth to highlight the efficacy of using a new combination of two different drug delivery system.[4]

Advantages

- Faster onset of action due to increased rate of skin permeation
- Higher local drug concentration because of greater degree of skin deposition
- non-toxic and non-irritant
- effective and safe
- Skin depot effects, leading to longer drug residence time
- Improves the bioavailability of drug
- Potential reductions of total dose and frequency of application
- Avoiding both contact with the gastro intestinal tract and hepatic first-pass effects and is acceptable to many patients
- Application for the targeted drug delivery
- Transdermal delivery involves application of a pharmacologically active compound on to the skin to achieve therapeutic blood levels in order to treat diseases remote from the site of application
- Provides greater absorption of drug
- Drawback of high lipophilicity can be overcome by this dosage form

- Due to the combined system it shows maximum possible absorption pathways
- Nanoemmigel shows maximum diffusion due to different paths available for transport of drug
- Nanoemmigel have the potential for enhancing drug permeation through skin
- It is considered as a promising delivery for the development of novel drug delivery system
- Therapeutic success is achieved due to the deeper delivery of therapeutic agent into the deeper epidermal and dermal layers
- Nanoemmigel shows excellent stability and also more physically stable
- Because of their lipophilicity and nano size they were assumed to be taking advantage of transcellular route[5,6]

Besides several advantages there are few disadvantages too like Permeation through skin which has development of plague, scalling, epidermal alterations, epidermal thickening and elongation of epidermal ridges, which create barriers to the penetration of drugs through skin

Mechanism of drug delivery

The skin being a remarkably effective barrier against various therapeutic drugs, it allows the permeation of drugs that are having the capacity to permeate by multiple mechanisms. Nanoemulsions and nanomicelles individually are effective in their own ways. This topical preparation is developed to enhance the penetration by twice a combination of both the ways of delivery system.[7]

METHODS AND MATERIALS

Composition of nanoemmigel

Nanoemmigel is composed of oils, surfactants, co-surfactants, water and jelling agent.

- ❖ Oils like Isopropyl myristate, Lauroglycol, Capryol 90, Labrafac lipophil, Capyrol PGMC, Laprafac PG, natural oils such as Olive oil can be used.
- ❖ Surfactants and co-surfactants like Polysorbate 80 (Tween 80), Cremophor EL, PEG 400, Transcutol P, Propylene glycol, Isopropyl alcohol, Polyvinyl alcohol (PVA), Kolliphor TPGS, Kolliphor P 407, Kolliphor 188, Solutol HS, Polysorbate 20 can be used.
- ❖ Carbopol is the most preferably used jelling agent.[8]

Preparation of nanoemulsion

The following are the methods used for preparing nanoemulsions.[9-11]

Sonication technique

sonication mechanism is used to decrease the droplet size of conventional emulsion.

High Pressure Homogenizer

High pressure is applied over over the system having oil phase, aqueous phase and surfactant or co-surfactant with the help of homogenizer. Some problems associated with homogenizer are poor productivity, component deterioration due to generation of heat. Oil in water (O/W) liquid nanoemulsion of less than 20% oil phase can be prepared.

Microfluidizatiion

Microfluidization technology makes use of a device called micro fluidizer which uses high pressure positive displacement pump which forces the product through the interaction chamber, consisting of small channels called micro channels. The product flows through the micro channels on to an impingement area resulting in very fine particles of submicron range. The two solutions (aqueous phase and oily phase) are combined together and processed in an inline homogenizer to yield a coarse emulsion. The coarse emulsion is then run into a micro fluidizer where it is further processed to obtain a stable nano emulsion.

Production with high amplitude ultrasound

It is a viable alternative to high pressure homogenization. Intense shear forces necessary for the nano emulsification are generated by ultrasonic cavitation

Preparation of nanomicelles

The following are the methods used for preparing nanomicelles

Direct dissolution method

In this method the micelles are prepared from co-polymer with relatively high water solubility. The drug and the copolymer are dissolved directly into the aqueous media. In order to load the drug into the micelles it requires heating and sonication process.

Dialysis method

In this method the drug is dissolved in organic solvent like DMSO (dimethyl sulfoxide), DMF (N,N-dimethyl formamide), acetonitrile, tetrahydrofuran, acetone or dimethyl acetamide. Initially the drug is dissolved in suitable organic solvent inorder to stimulate the micelle formulation, the aqueous media is added to the drug copolymer mixture then the micelles are dialyzed against the water for certain period of time to eliminate the organic solvent.

Dry down evaporation method

In this method both the active agent and the copolymer are dissolved in either common solvent or mixture of two miscible solvents. Then the drug copolymer film is formed by stirring and drying the mixture and this film is reconstituted with warm water to form micelles.

Lyophilization

In this method the micelles are prepared by dissolution of both copolymer and the drug in a mixture of aqueous and organic solvent and then it is subjected to lyophilization process. After the process it is allowed to freeze dried the mixture which can be constituted to obtain drug loaded micelles.

Preparation of Nanoemmigel

Nanoemmigel is prepared by mixing nanoemulsion and nanomicelle systems together with the help of jelling agent and stirring continuously at a low rpm to get an uniform gel free from lumps and air bubbles. The pH of the preparation is maintained.[12-14]

Characterization of Nanoemmigel

1) **Physical appearance**

The colour, homogeneity, consistency, grittiness and phase separation of nanoemmigel can be visually inspected.

2) pH determination

The pH of nanoemmigel can be determined by using digital pH meter. Take required quantity of nanoemmigel in a 250ml beaker and immerse the pH meter into it and record the readings. This procedure is repeated again for two more times.

3) Rheology study of nanoemmigel

The viscosity of nanoemmigel can be determined by using the Brookfield type rotatory viscometer with spindle 63. The viscosity is measured at 10 rpm for 3 minutes at 25°C.

4) Spreadability

Spreadability is determined by using the apparatus suggested by Multimer *etal*. By this method, spreadability of nanoemmigel can be determined on the basis of 'slip' and 'drag' characteristics. The nanoemmigel is sandwiched between two glass slides which is provided with a hook. A weight of about 1 Kg is applied on the top of the two slides for 5 minutes to expel air out and to provide a uniform film of the nanoemmigel between the slides. Excess nanoemmigel is scrapped off from the edges. The top slide is subjected to pull of 80 gm, with the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5 cm is noted. A shorter interval indicates better spreadability.

5) **Extrudability**

The extrudability of nanoemmigel can be determined by using hardness tester. A 5gm of nanoemmigel is filled into an aluminium collapsible tube and a load of 1 Kg was applied for 30 seconds and the quantity of gel extruded from the tube is measured.

6) Drug content determination

The amount of drug present in specified quantity of gel is determined by using UV-Visible spectrophotometer.

7) *In-vitro* release studies

The *in-vitro* study is determined by using Franz diffusion cell.

8) Accelerated stability studies

Stability studies are carried out based on ICH guidelines. The nanoemmigel is packed in the aluminium collapsible tubes (5g) and subjected to stability studies. The formulations are stored in hot air oven at 37 ± 2◦C, 45 ± 2◦C, and 60 ± 2◦C for a period of 6 months. The drug content of the samples are analysed by measuring the absorbance using UV-Visible spectrophotometer and the pH changes are noted.

CONCLUSION

The nanoemmigel is attributed to better skin permeation because of drug being absorbed at both paracellular and transcellular layers. Nanoemmigel , a combined dosage form is a potential and promising novel drug delivery system for improving the permeation of drug through skin for targeted and local action for various ailments.

Acknowledgements: The authors are thankful to the management of Sri Ramachandra Institute of Higher education and Research for the continuous support and encouragement.

REFERENCES

1. Goel A, Ahmad FJ, Singh RM, Singh GN, 3-acetyl-11-keto-beta-boswellic acid loaded-polymeric nanomicelles for topical anti-inflammatory and anti-arthritic activity, J Pharm Pharmacol, 62, 2010, 273-78.
2. Ranade SY, Gaud RS, Current strategies in herbal drug delivery for arthritis: An overview, Int J Pharm Sci Res, 4, 2013, 3782-94.
3. Gohel M, Soni T, Hingorani L, Patel A, Patel N, Development and optimization of plant extract loaded nanoemulsion mixtures for the treatment of inflammatory disorder, Curr Res Drug Discov, 1, 2014, 29-38.
4. Goel A, Ahmad FJ, Singh RM, Singh GN, Anti-inflammatory activity of nanogel formulation of 3-acetyl-11-keto-β-boswellic acid, Pharmacology online, 3, 2009, 311-18.
5. Somagoni J, Boakye CHA, Godugu C, Patel AR, Faria HAM, Zucolotto V, Nanoemmigel- A novel drug delivery system for topical application- *In vitro* and *in vivo* evaluation, PlosONE, 9, 2014, 1-17.
6. Borhade V, Pathak S, Sharma S, Patravale V, Clotrimazole nanoemulsion for malaria chemotherapy Part I: preformulation studies, formulation design and physicochemical evaluation, Int J Pharm, 431, 2012, 138-48.

7. Pouton CW, Formulation of Poorly Water-Soluble Drugs for Oral Administration: Physicochemical and Physiological Issues and the Lipid Formulation Classification System, Eur J Pharm Sci, 2, 2006, 278-87.

8. Nawale R, Mayee R, Behaviour of natural membrane on drug permeation, Int J Pharm Innov, 3, 2013, 45-54.

9. Kumar DS, Sairam R, Anandbabu S, Karpagavalli L, Maheswaran A, Narayanan N, Formulation and evaluation of transdermal patches of salbutamol, Res J Pharm Biol Chem Sci, 3, 2012, 1482-94.

10. Singla S, Harikumar SL, Aggrawal G, Proniosomes for effective topical delivery of clotrimazole: development, characterization and performance evaluation, Asian J Pharm Sci, 7, 2012, 259-70.

11. Bachhav YG, Patravale VB. Formulation of meloxicam gel for topical application: *in vitro* and *in vivo* evaluation, Acta Pharm, 60, 2010, 153-63.

12. Fathy AI, Hamdy DM, Mansour A, Sami AM, Evaluation of the antiinflammatory and analgesic effects of piroxicam loaded microemulsion in topical formulations, Int J Pharm Pharm Sci, 3, 2011, 66-70.

13. Ammar HO, Ghorab M, El-Nahhas SA, Kamel R, Polymeric matrix system for prolonged delivery of tramadol hydrochloride, part ii: biological evaluation, AAPS Pharm Sci Tech, 10, 2009, 1065.

14. Prajapati BG, Patel MM, Cross-linked chitosan gel for local drug delivery of clotrimazole, J Sci Technol, 5, 2010, 43-52.

Source of Support: Nil, **Conflict of Interest:** None.