

Nano-Formulations for Transdermal Drug Delivery

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ABSTRACT

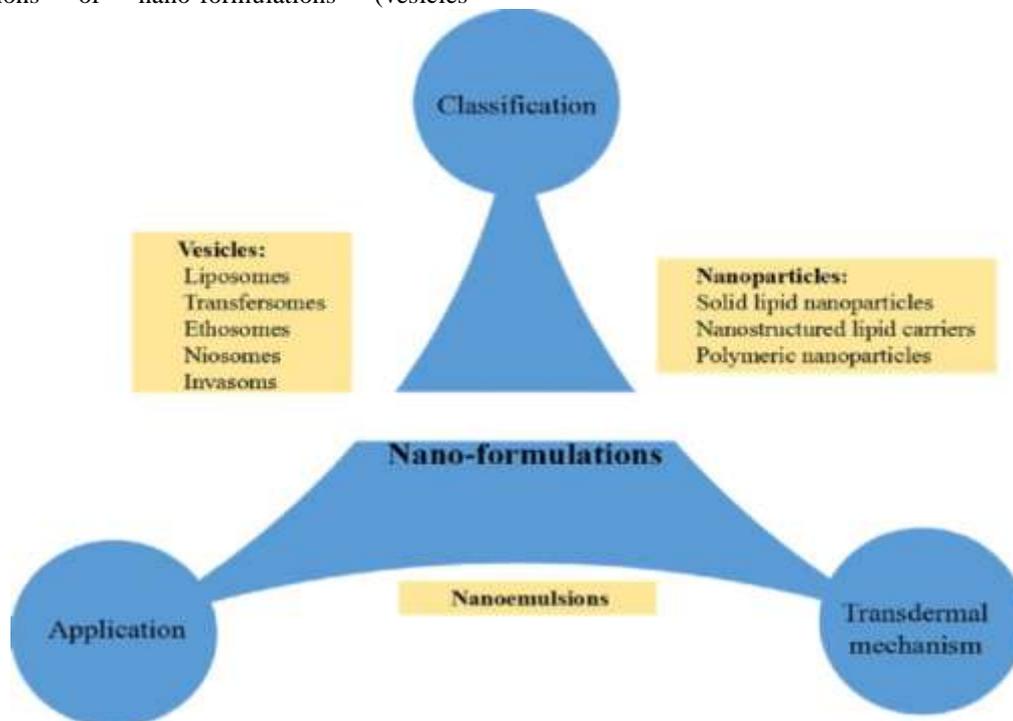
Transdermal drug delivery refers to a means of delivering drugs through the surface of the skin for local or systemic treatment. The drug functions after absorption through the skin into the systemic circulation via capillary action at a certain rate. Use of traditional physical and chemical enhancers to improve the transdermal permeation rate by increasing drug solubility, diffusion coefficient, and reservoir effect is not feasible owing to the toxic side effects of the overuse of chemical penetration enhancers. Nano-formulations generally vary in size and range from 10 nm to 100 nm. The smaller particle size leads to increased drug permeability, stability, retention, and targeting, making nano-formulations suitable for transdermal drug delivery. The different applications of nano-formulations (vesicles

or nanoparticles and nanoemulsions) have been widely studied. Here, the classification, characteristics, transdermal mechanism, and application of the most popular nano-formulations in transdermal drug delivery system are review.

Key Words: Transdermal Drug Delivery , Nanoformulation, Skin permeation, Stratum corneum barrier, Controlled release, Bioavailability enhancement.

Graphical Abstract

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I. INTRODUCTION

The skin is the largest and most visible organ of the body. The skin covers a total surface area of approximately 1.5–2 m² and is the barrier

between human body and the external environment [1]. Many of its functions include temperature regulation, immunity from microorganisms, maintaining electrolyte balance, as well as

protection from physical injuries, chemical agents, and ultraviolet radiation [2,3]. In addition, skin is also an important avenue for absorption of drugs and exerting their efficacy. The skin is composed of epidermis, dermis, and subcutaneous tissue, and contains appendages (such as hair follicles, sebaceous glands, sweat glands), blood vessels, lymphatic vessels, nerves, etc. The epidermis can be divided into five layers from the inside to the outside, namely the stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum (SC) (Fig. 1) [3,4]. The properties of SC are quite different from those of the other layers, with the overall structure composed of inactive keratinocytes and intercellular lipids that form a 'brick and mortar' model, in which, the protein-rich keratinocytes serve as the bricks and the intercellular lipids serve as the mortar [5,6]. SC is the main factor determining the skin barrier, and also the major obstacle limiting the rate of percutaneous absorption even though the thickness is only 10–20 μm [7,8]. There are two routes of transdermal permeation of drugs. One is through the natural channel of skin appendages. These channels are hydrophilic and have a diameter of few microns. Owing to the fact that the average follicular orifice area on the human skin surface is only about 0.1% of the total surface area [9], it is not the primary pathway of percutaneous absorption. The second route is through the penetration of the epidermis, to enter the dermis through the SC and the deeper epidermis, being absorbed in the body circulation by the capillaries. As for the penetration of drugs and passing through the SC, two pathways exist, namely, the transcellular route, through which substances infiltrate the keratinocytes and intercellular lipids, and subsequently pass through and are transported. The drug needs to diffuse through hydrophilic and hydrophobic areas, and therefore, it may not be applicable to most drugs. The second and most likely route taken by drugs when penetrating the SC is via a tortuous pathway through the lipids surrounding the keratinocytes, known as the intercellular route (Fig. 2) [10].

Transdermal drug delivery system (TDDS) refers to a route of drug delivery through the skin to achieve local or systemic therapeutic action. It is one of the focus areas of research for the third-generation pharmaceutical preparations, next only to oral medication and injection [11]. The reasons lie in the administration route of the drug, which is convenient, easy to use, non-invasive, and also improves patient compliance [12]. It also reduces the fluctuation of the drug concentration in

the blood, provides steady plasma levels and fewer chances of overdose and easy detection of the drug [13,14]. At the same time, it evades the gastrointestinal environment, such as pH, enzymatic activity, and the interference of drug and food interaction on the drug efficacy and the 'first pass effect' (where active drug molecules can be converted to inactive molecules or even to molecules responsible for side effects) by liver. These conditions lengthen the therapeutic effect of drugs with shorter half-life and enhance their long-term stability of drug [15]. Administration of drugs can be stopped at any point after removal of the stimulation from the site [16].

Although TDDS has many advantages, the use of drugs in TDDS is currently limited. As mentioned above, the most resistance during the percutaneous permeation of the drugs comes from the SC of the skin [17]. When many drugs are delivered through the skin, adequate permeability rate is difficult to achieve as per therapeutic requirements. To overcome these difficulties, nanotechnology may be a good choice. Nanotechnology refers to the technology of using a single atom or molecule to produce or process macromolecular matter into a material with a particle size of 1–100 nm. One of the important areas of nanotechnology is nano-formulations [18]. Given their small particle size, nano-formulations have a better effect on drug retention, specificity and targeting (Fig. 3) [19], which makes an ideal TDDS. They have many advantages, such as being painless, minimal skin injury (does not change the general structure of SC of the skin and does not destroy the skin barrier function), and promotes permeation of macromolecular drugs, which has become a very popular field of research on TDDS [20]. Nano-formulations can be divided into vesicles including liposomes, transfersomes, ethosomes, niosomes, invasomes, and nanoparticles including lipid nanoparticles, polymeric nanoparticles and nano-emulsions (Fig. 4). As for active transdermal administration, microneedles are not involved, instead, ultrasonic, electroporation, hot perforation and comprehensive application of other methods enhancing penetration are used. This review is based on the advances in research on nano-formulations of passive TDDS, and focuses on the classification, components, characteristics, transdermal mechanism and application of nano-formulations (Table 1). We hope to present a foundation for future research in nano-formulations for TDDS, and to enhance our understanding for clinical and therapeutic applications.

Section snippets

Vesicles

Vesicles are water-filled colloidal particles. The walls of these capsules consist of amphiphilic molecules in a bilayer conformation [21]. In conditions of excess water, these amphiphilic molecules form one (unilamellar vesicles) or more (multilamellar vesicles) concentric bilayers [22]. With the goal of increasing the penetration function of the components, vesicles can carry water-soluble and liposoluble drugs to achieve transdermal absorption. When applied to topical application, vesicles.

Transdermal mechanism of nano-formulations

Depending on the physical characteristics of their inherent small particle size and large specific surface area, nano-formulations can react fully with the skin surface and promote drug transdermal absorption. However, different nano-formulations interact with the skin through different mechanisms. For example, lipid-based nano-formulations have structural similarities with those comprising the epidermis and in particular the SC. So, they could attach onto the skin surface and increase skin.

II. CONCLUSION

In this review, we systematically summarized the components, characteristics, and transdermal mechanisms, as well as the application of liposomes, transfersomes, ethosomes, niosomes, invasomes, solid lipid nanoparticles, nanostructured lipid carriers, polymeric nanoparticles and nano-emulsions for TDDS. This review offers a complete picture of TDDS and aims to improve the understanding of the nano-formulations used in TDDS. Furthermore, it lays a foundation for future research and promotes the.

REFERENCES

- [1]. C.Y.Zhao et al acta pharm.sin.b(2016).
- [2]. G.Cevc et al J Control release (2010).
- [3]. M.Armengot-Carbo et al Actas Dermosifiliogr(2015).
- [4]. B.Illel et al J.Pharm.Sci(1991).
- [5]. F.Erdo et al J.Control .Release(2016).
- [6]. S.Meng et al Eur.J.Pharm.Sci(2016).
- [7]. Y.H.Weng et al Acta Phaem Sin.B (2017).
- [8]. J.Liu et al Chin.Chem .Lett(2017).
- [9]. P.L.Honeywell Nguyen et al Drug Discov.Today (2005) .
- [10]. Z.Li et al Acta Pharm .Sin B(2016).
- [11]. Li Xuanhuan, Lyu Huixia & Zhu Lyufeng (2023).
- [12]. Research Progress in the Application of Nanoformulations in Transdermal Drug Delivery Systems. Progress in Pharmaceutical Sciences, 47(7): 504-518.
- [13]. Detailed review of nanoemulsions, lipid vesicles, nanoparticles, polymer nanoparticles and more in TDDS
- [14]. Li Xuanhuan, Lyu Huixia & Zhu Lyufeng (2023)
- [15]. Research Progress in the Application of Nanoformulations in Transdermal Drug Delivery Systems. Progress in Pharmaceutical Sciences, 47(7): 504-518.
- [16]. Detailed review of nanoemulsions, lipid vesicles, nanoparticles, polymer nanoparticles and more in TDDS.
- [17]. Pps.cpu.edu.cn
- [18]. Praveen Kolimi, Sagar Narala, Ahmed Adel Ali Youssef, Dinesh Nyavanandi & Narendar Dudhipala (2023)
- [19]. A systemic review on development of mesoporous nanoparticles as a vehicle for transdermal drug delivery. Nanotheranostics 7(1):70-89.
- [20]. Focuses on mesoporous nanoparticles and their potential as controlled transdermal carriers.
- [21]. Yunxiang Kang, Sunxin Zhang, Guoqi Wang, Ziwei Yan, Guyuan Wu, Lu Tang & Wei Wang (2024)
- [22]. Nanocarrier-Based Transdermal Drug Delivery Systems for Dermatological Therapy. Pharmaceutics 16(11):1384.
- [23]. Covers a wide range of nanocarrier types for transdermal delivery in dermatology.