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Recent development on drug entrapped Nanogel for effective topical application

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Abstract

Nanoparticle research is currently an area of intense scientific interest due to a wide variety of potential applications in biomedical, optical and electronic fields. Solid lipid nanoparticles are at the forefront of the rapidly developing field of nanotechnology with several potential applications in drug delivery, clinical medicine and research, as well as in other varied sciences. Due to their unique size-dependent properties, lipid nanoparticles offer the possibility to develop new therapeutics. The ability to incorporate drugs into nanocarriers offers a new prototype in drug delivery that could be used for secondary and tertiary levels of drug targeting. Hence, solid lipid nanoparticles hold great promise for reaching the goal of controlled and site specific drug delivery and hence have attracted wide attention of researchers. This review presents a broad treatment of solid lipid nanoparticles as a potential carrier for enhanced dermal/topical delivery of ACV discussing it's method of preparation, advantages, use. The present investigation was enthused by the possibility to develop solid lipid nanoparticles (SLNs) of hydrophilic drug acyclovir (ACV) and evaluate their potential as the carrier for dermal delivery. ACV-loaded SLNs (ACV-SLNs) were prepared by the optimized double emulsion process. Overall, it was concluded that ACV-loaded SLNs might be beneficial in improving dermal delivery of antiviral agent(s) for the treatment of topical herpes simplex infection.

Keywords: Solid Lipid Nanoparticle (SLP), HSV infection, Acyclovir, Topical application.

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1. Introduction:

The present investigation was enthused by the possibility to develop solid lipid nanoparticles (SLNs) of hydrophilic drug acyclovir (ACV) and evaluate their potential as the carrier for dermal delivery. Herpes simplex virus (HSV) infection has been a global health problem affecting around 21 million people every year. According to a recent survey in US population, approximately 50% to 80% of adults suffer from oral herpes infection while at least one in every five is infected with genital herpes. HSV infection primarily affects the dermal or basal epidermal layer of the skin, mucous membranes, and occasionally oesophagus and brain. Among the various antiviral drugs used for the alleviation of HSV infection, acyclovir (ACV) is the most commonly prescribed treatment. Like Herpes simplex there are different kinds of diseases that can be well treated with topically administered drug. Compared with oral administration, topical administered drug leads to tenfold higher concentration over the entire epidermis. However, this concentration fails to produce desired therapeutic effect at the site of infection. Although stratum corneum (SC) barrier can be overcome by chemical (penetration enhancers) and physical techniques, these practices induce either irritation or damage, resulting in the disruption of skin barrier function. Hence, it is crucial to enhance the penetration of topically administered drug upto dermis while maintaining the normal skin barrier Function. Solid Lipid Nanoparticles (SLNs) are solid, that are compatible with inflamed and damaged skin. By virtue of their unique capability to load lipophilic as well as hydrophilic agents, SLNs stands attractive for use in dermal/topical delivery of various cosmetics and pharmaceutical agents, with enhanced penetration through skin. The present study, therefore, examines the feasibility of using SLNs as a potential carrier for enhanced dermal/topical delivery of ACV.

1.1. Nanoparticle:

In nanotechnology, a particle is defined as a small object that behaves as a whole unit in terms of its transport and properties. Particles are further classified according to size: in terms of diameter, coarse particles cover a range between 10,000 and 2,500 nanometers. Fine particles are sized between 2,500 and 100 nanometers. Ultrafine particles or nanoparticles are sized between 100 and 1 nanometers[1]. There are several methods for creating nanoparticles, including both attrition and pyrolysis by using ball mill, a planetary ball mill, or other size reducing mechanism.

1.2. Functionalization:

The surface coating of nanoparticles is crucial to determining their properties. In particular, the surface coating can regulate stability, solubility and targeting. A coating that is multivalent or polymeric confers high stability.

1.2.1. Surface coating for biological applications:

For biological applications, the surface coating should be polar to give high aqueous solubility and prevent nanoparticle aggregation. In serum or on the cell surface, highly charged coatings promote non-specific binding, while polyethylene glycol linked to terminal hydroxyl or methoxy groups repel non-specific interactions.[2][3] Nanoparticles can be linked to biological molecules which can act as address tags, to direct the nanoparticles to specific sites within the body,[4] specific organelles within the cell,[5] or to follow specifically the movement of individual protein or RNA molecules in living cells.[6]Common address tags are monoclonal antibodies, aptamers, streptavidin or peptides. These targeting agents should ideally be covalently linked to the nanoparticle and should be present in a controlled number per nanoparticle. .

1.2.2. Solid lipid nanoparticle:

A solid lipid nanoparticle (SLN) is typically spherical with an average diameter between 10 to 1000 nanometers. Solid lipid nanoparticles possess a solid lipid core matrix that can solubilize lipophilic molecules. The lipid core is stabilized by surfactants (emulsifiers). The term lipid is used here in a broader sense and includes triglycerides (e.g. tristearin),

diglycerides (e.g. glycerol bahenate), monoglycerides (e.g. glycerol monostearate), fatty acids (e.g. stearic acid), steroids (e.g. cholesterol), and waxes (e.g. cetyl palmitate).

1.2.3. Advantages of SLNs:

Control and/or target drug release.

Improve stability of pharmaceuticals.

High and enhanced drug content (compared to other carriers).

Feasibilities of carrying both lipophilic and hydrophilic drugs.

Most lipids being biodegradable, SLNs have excellent biocompatibility. Water based technology (avoid organic solvents).

Easy to scale-up and sterilize.

More affordable (less expensive than polymeric/surfactant based carriers). Easier to validate and gain regulatory approval.

1.2.4. Methods of preparation of SLN:

High shear homogenization:

Hot homogenization

Cold homogenization

Ultrasonication/high speed homogenization: Probe ultrasonication

Bath ultrasonication

Solvent emulsification/evaporation

Micro emulsion based SLN preparations

SLN preparation by using supercritical fluid Spray drying method

1.2.5. Transdermal application Acyclovir Nanogel:

By virtue of their unique capability to load lipophilic as well as hydrophilic agents, SLNs stands attractive for use in dermal/topical delivery of various cosmetics and pharmaceutical agents [7][8] with enhanced penetration through skin [9][10]. However, their utility in achieving an efficient dermal delivery of antiviral agents has been seldom explored. The present study, therefore, examines the feasibility of using SLNs as a potential carrier for enhanced dermal/topical delivery of ACV.

2.0. HERPES SIMPLEX DISEASES:

Herpes simplex virus 1 and 2 (HSV-1 and HSV-2), also known as Human herpes virus 1 and 2 (HHV-1 and -2), are two members of the herpes virus family, Herpesviridae, that infect humans Both HSV-1 (which produces most cold sores) and HSV-2 (which produces most genital herpes) are ubiquitous and contagious. They can be spread when an infected person is producing and shedding the virus. Symptoms of herpes simplex virus infection include watery blisters in the skin or mucous membranes of the mouth, lips or genitals[11]. Lesions heal with a scab characteristic of herpetic disease. Sometimes, the viruses cause very mild or atypical symptoms during outbreaks. However, as neurotropic and neuroinvasive viruses, HSV-1 and -2 persist in the body by becoming latent and hiding from the immune system in the cell bodies of neurons. After the initial or primary infection, some infected people experience sporadic episodes of viral reactivation or outbreaks.

2.1. Etiology of herpes simplex virus:

There are two different strains of herpes simplex viruses:

Herpes simplex virus type 1 (HSV-1) is usually associated with infections of the lips, mouth, and face. It is the most common herpes simplex virus and most people develop it in childhood. HSV-1 often causes lesions inside the mouth, such as cold sores (fever blisters), or infection of the eye (especially the conjunctiva and cornea). Herpes simplex virus 2 (HSV-2) is sexually transmitted. Symptoms include genital ulcers or sores. In addition to oral and genital sores, the virus can also lead to complications such as infection of the lining of the brain and the brain itself (meningoencephalitis) in neonatal infants due to infection during birth.

2.2. Treatment of the diseases:

Acyclovir, a synthetic analogue of 2-deoxiguanosin, is one of the most effective and selective against the virus of the herpes groups. ACV is active against herpes simplex virus type-1 (HSV-1). Herpes simplex virus -2 (HSV-2), varicella zoster virus. The mechanism of action of this drug has been extensively studied and it's anti-viral activity has been shown to result from the inhibition of the DNA replication of herpes virus. ACV is effective against cutaneous infection due to HSV-1, whose target side is the basal epidermis. However it has been suggested that ACV topical therapy has a low efficacy due to lack of penetration of enough amount of drug to the target site.

3. Conclusion:

The SLNs have the potential to achieve, at least partially, these broad objectives. SLNs of ACV (a hydrophilic drug) were prepared by an optimized double emulsion process. Although the developed system showed a high potential for the treatment of dermatological disorders, e.g. HSV infection. The incorporation of prepared SLNs in some cream or gel formulation for potential application purpose is also desirable.

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