INTRODUCTION

Successful treatment for herpes simplex virus (HSV) infections has already been achieved by oral, intravenous and topical route of antiviral drug administration. When infection is limited to the skin, topical therapy should be considered because of convenience in application and reduced drugs systemic side effects. Human herpes simplex virus infections where topical treatment of antiviral agents should be beneficial include herpes genitalis, herpes labialis and herpetic keratitis.

Antiviral drug treatment of primary HSV infections and topical treatment has been effective in immunocompromised patients with mucocutaneous HSV infections and in primary genital herpes. However systemic antiviral treatment is preferred to treat cervical or intraoral lesions.

Recurrent labial and perioral HSV type 1 infection in normal hosts, common fever blisters or cold sores, is most frequently encountered cutaneous viral infections. Topical treatment is hence desirable. The lips are accessible for frequent antiviral drug application.

There is no cure of these herpes virus infections. However there are antiviral drugs that can relieve the symptoms of these infections. They work best when used as early in infection as possible. These drugs may also prevent future outbreak of HSV infections.¹

Topical drug delivery has been used as a route of medicinal delivery for many thousands of years and there have been considerable advances in our mechanistic understanding of the process in past many years.² The transdermal drug delivery has gained importance in recent years. It has potential advantages in avoiding hepatic first pass metabolism, maintaining constant blood levels for prolonged period of time resulting in a reduction in dosing frequency, improved bioavailability, decreased gastrointestinal irritation that occur due to local contact of drug with gastric mucosa and improved patient compliances.³
However skin irritation, high manufacturing costs and less cosmetic appearance are the major disadvantages of transdermal drug delivery systems. The main focus of recent advances with traditional passive transdermal drug delivery is reducing skin irritation and making product more aesthetically acceptable for patients. Other alternative systems are also in developing stage like physical enhancement which are more focused on delivery of large molecules like peptides and hydrophilic compounds.\(^4\)

An approach commonly researched for promoting permeation through skin of poorly penetrating drug molecule is the formulation of a suitable delivery vehicle, or incorporation of a chemical enhancer into transdermal delivery systems. Physical mechanisms like iontophoresis can be used for promoting the diffusion of certain classes of drug. Understanding of constitution and function of stratum corneum facilitate improved permeation of drugs through it. The biochemical order of the intercellular lipid matrices of the stratum corneum or keratinized environment of the corneocytes must be altered to allow the penetration of compounds at a suitable rate to the desired site of activity. Ideal chemical penetration enhancers should specifically promote the penetration of compounds across the skin barrier without exhibiting irreversible effects on its properties.

Diffusion of drugs across the skin is a passive process. Compounds with low solubility and affinity for the hydrophilic and lipophilic components of stratum corneum would partition at slow rate. These difficulties may be overcome by addition of a chemical adjunct to delivery system that would promote drug partitioning into the stratum corneum. Chemical permeation enhancers added to topical vehicles also partition into stratum corneum and affect the intrinsic diffusional barrier properties of this structure. Chemical enhancers may act by spatial disruption of the normally ordered arrangement of the intercellular lipid molecules.\(^5\)

Different chemical permeation enhancers are as following:

- Sulphoxides and similar chemicals – e.g. dimethylsulphoxide (DMSO), DMA, DMF
- Azone
Pyrrolidones – e.g. N-methyl-2-pyrrolidone (NMP)
- Fatty acids
- Alcohols, fatty alcohols and glycols – e.g. ethanol, propylene glycol
- Surfactants – e.g. sodium lauryl sulphate (SLS), Tweens
- Terpenes – e.g. limonene, cineole, menthol

Iontophoresis, by definition, facilitates the movement of charged molecules across the transdermal membrane under the influence of externally applied potential difference. A very minute current (0.5 mA/cm²) is applied through a reservoir containing drug by two electrodes placed at a distance on the skin. Iontophoresis has been particularly effective in treatment of palmoplantar hyperhidrosis. Today the treatment of hyperhidrosis is most successful and popular application of iontophoresis in dermatological medication. In addition to local indication, the approach of iontophoresis research is more focused towards exploiting this technique for systemic delivery of drugs. Apart from ionized molecules, unionized molecules can also be delivered by electroosmotic flow of solvent created in this technique.

An iontophoretic device comprises a power source and two electrode compartments. The drug formulation (D⁺A⁻) containing the ionized molecule (D⁺) is placed in the electrode compartment bearing the same positive charge. The indifferent electrode compartment is placed at a distal site on the skin. Ag/AgCl electrode is preferred over platinum electrode. The anodal compartment contains an ionizable drug D⁺ with its counter-ion A⁻ and Na⁺Cl⁻. Application of an electrical potential causes a current to flow through the circuit. At the electrode solution interface Ag⁺ and Cl⁻ react to form insoluble AgCl which is deposited on the electrode surface. Electromigration transports the cations, including the drug molecule, from the anodal compartment and into the skin. At the same time, endogenous anions, primarily Cl⁻, move into the anodal compartment. In the cathodal chamber, Cl⁻ ions are released from the electrode and electroneutrality requires that either an anion is lost from the cathodal chamber or that a cation enters the chamber from the skin.
There are two types of technique: anodal iontophoresis and cathodal iontophoresis.

Advantages of iontophoresis:

- It is a non-invasive technique.
- Overcome the disadvantages of parenteral therapy.
- Self-administration is possible.
- Hydrophilic drug can be transported across the skin.
- Charged drug molecules permeate across the skin by the repulsion force of electrode.
- Uncharged compounds permeate by the process of electroosmosis.
- Allows the permeation of drugs having higher molecular weight.
- Lower doses of drug can be delivered compared to transdermal drug delivery system.
- Onset of action is fast.