Effect of Permeation Enhancers on Transdermal Delivery of Venlafaxine Hydrochloride from Carbopol Gel

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ABSTRACT

In this study, we investigated the effect of different permeation enhancers at different concentrations viz. oleic acid, olive oil and castor oil from transdermal gel for transdermal delivery of venlafaxine, a newer antidepressant. It is a first line drug in the treatment of depression and inhibits brain serotonin and norepinephrine neuronal uptake. It is also used in the treatment of anxiety disorders. Transdermal delivery of venlafaxine hydrochloride may result in enhanced patient compliance by reducing the incidence of the undesirable GI problems associated with its multiple oral dosing. The differential scanning colorimetry study was used to investigate the drug-polymer interaction. The prepared gels were evaluated for several physico-chemical parameters such as drug content, spreadability, pH, viscosity and physical appearance to justify their suitability for topical use. The in vitro permeation studies were performed by using Franz diffusion cell and rat skin as a semi permeable membrane. This indicate that penetration enhancers in 5% v/w concentration enhance the permeation of venlafaxine hydrochloride but oleic acid show maximum permeation rate was 197 µg/cm²/hr as compared to olive oil (154.69µg/cm²/hr) and castor oil (175.8µg/cm²/hr). It is further optimized by increasing the concentration of permeation enhancer at levels as high as 10% v/w and 15% v/w. The result indicates that increase in the concentration of enhancer enhances the percutaneous permeation of venlafaxine. Oleic acid was found to be superior to olive oil and castor oil implying the ability of oleic acid to increase the drug diffusion by SC lipid disruption and increase partition coefficient into SC. The permeation rate of venlafaxine hydrochloride with 15% v/w oleic acid was higher (rat abdominal skin flux = 8.507 µg/cm²/hr) than with 15% v/w olive oil and castor oil. These studies show promising potential of transdermal patches of venlafaxine.

KEYWORDS: Venlafaxine; permeation enhancers; carbopol 934P; transdermal.

Introduction

Depression is the most common mental illnesses worldwide. It is associated with a high mortality rate because a large fraction of the depressive patients suffer from suicidal tendency. Medication noncompliance is a major factor resulting in failure of antidepressant therapy. Therefore, oral administration is thought to be non-ideal for most anti-depressant medications and there is a recent focus on alternative drug delivery for optimizing the ideal antidepressant treatment.

Venlafaxine hydrochloride (VH) is a first line drug in the treatment of depression. It inhibits central serotonin and norepinephrine neuronal reuptake and has proven efficacy in the treatment of depression and anxiety disorders (Yardley et al., 1990; Bymaste, 2001). The drug is effective in the treatment resistant depression and thought to be superior to selective serotonin reuptake inhibitors in preventing the recurrence of depression (Nemeroff and Entsuah, 2008). VH had proved that it also has analgesic efficacy against neuropathic pain as well as premenstrual dysphoric disorders (Sindrup et al., 2001; 2003). However, a drug of low half-life (4.9 h), VH, needs frequent administration to maintain a blood level of effective therapeutic concentration. Its oral bioavailability is 10-45%. After oral administration, rapid dissolution result in rapid increase in plasma levels of active compounds followed by a decrease in blood plasma levels over a several hours as active compound undergoes extensive metabolism in liver and gets converted into the active metabolite, O-desmethyl venlafaxine., until sub-therapeutic levels are approached after about 12h following administration, thus require additional dosing with drug. The oral use of VH is associated with a number of predictable adverse effects like nausea, vomiting, tachycardia, increased blood pressure, fatigue, headache, dizziness, sexual dysfunction, and dry mouth etc (Stahl, 2005).

These adverse effects which may hinder the proper compliance of VH can be reduced if adequate therapeutic levels are maintained in blood without significant fluctuations. Hence, maintaining plasma concentration within an acceptable range would lower the incidence of nausea and vomiting (Sherman et al., 2001; Evangelos et al., 2006). Several companies have launched the extended release oral formulations claim control blood plasma level and lower incidence of nausea and vomiting. However, such once-daily extended release oral