

Micro-porous membrane controlled release systems for sustained delivery of Venlafexine hydrochloride: Development and evaluation

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Motivation: Depression, a psychological disease, continues to be a serious social problem which attracts the whole scientific community. Patients are treated with antidepressants, categorized under several groups, which are given on long term basis. Venlafexine hydrochloride (VEH) is a serotonin and norepinephrine reuptake inhibitor (SNRI), widely being prescribed for broad range of depressive disorders. However, the drug has high aqueous solubility and short half life of 5 hrs.

Problem statement: VEH is mostly available as immediate release tablets which are administered thrice a day. This results into poor patient compliance and variable pharmacokinetics of the drug. Therefore, it remains a challenge to develop its sustained release formulation which could reduce its dosing frequency and maintain its effective plasma concentration for prolonged period of time. The present study is an effort to prepare once-a-day micro-porous membrane controlled release tablets for sustained delivery of VEH.

Approach: Tablet matrix was composed of HPMC K15M and guar gum mixed in various combinations. Optimized matrix was coated with a blend of ethyl cellulose (EC) and PEG 400; former maintaining the integrity of tablet whereas the latter tending to leach, thus creating micro-porous membrane in situ. EC and PEG were combined to obtain a series of membranes, having desired drug-permeation profiles. Membrane was studied for thickness, smoothness, edge coverage, uniformity and permeability. Its microstructure was analyzed using scanning electron microscopy (SEM). The formulation was evaluated for the characteristics, like, weight variation, drug content, swelling index, in-vitro drug release and stability profile under accelerated storage conditions. Drug release mechanism was investigated by applying various mathematical models to the in vitro release profiles.

Results: Weight variation and drug content and for all the batches were found to be within +5% variations. Tablet coating did not exhibit any visual imperfection or crack. Drug release was found to be regulated by the thickness of coating membrane and proportion of PEG. Results of SEM showed that in situ micro-pores were formed in the membrane in contact with dissolution medium and their number was dependent on the initial level PEG in the membrane. Besides, cumulative amount of VEH release was found to be proportional to the initial level of PEG. Overall, drug release from the formulation showed best fit in first-order model and drug release mechanism was diffusion-controlled release. No interaction between drug and excipients was revealed by DSC study. Formulations, tested for stability at $40\pm 2^\circ\text{C}$ and $75\pm 5\%$ RH for 3 months, were found to be stable.

Conclusions: The study illustrated that controlled delivery of VEH could be realized through micro-porous membrane controlled release tablets.

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