ABSTRACT

Development and Characterization of Efavirenz Loaded Nanoparticles
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Nanoapproach to drug delivery has widely been explored for high propensity to raise the standard of active pharmaceutical ingredients in terms of its efficacy milieu. The recent studies reveal that the vaginal route of administration was most recommended for HIV infections during pregnancy and considered as an alternative route to enhance the bioavailability. The drug administration through human vaginal cavity was known for several decades and improved therapeutic activity was achieved by vaginal mucosal absorption through various formulations, like gels, tablets, aerosol etc., The aerosol formulation is packed under pressure and contains therapeutically active ingredients that are released as foam at the site of application, upon activation of an appropriate valve. This aids to target the specific site of action and thus, eliminates the undesirable effects through out the body. Thus, this benignity of nanodrug delivery is appropriately tapped for the treatment of Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS). Efavirinz, a non-nucleoside reverse transcriptase inhibitor is a first line drug, generally prescribed for the treatment of AIDS. It possess the inherent properties such as poor solubility and variable bioavailability and consequently, a high dosage required for the treatment. Our present work is developed on this platform in the view of addressing these shortcomings. The objective of this research work is to improve the in-vivo availability of poorly aqueous soluble drug through the development of
aerosol foam formulation of Efavirenz polymeric nanoparticles for vaginal route of administration. The nanoparticles are prepared by emulsion solvent evaporation method and converted into aerosol foam formulation pressurized using 1,1,1,2 tetrafluoroethane in addition with 0.1% sodium lauryl sulphate as foaming agent. The nanoparticles containing formulation and aerosol foam formulation are characterized individually for various tests such as particle size (110 – 283 nm), zeta potential (21.6 - 33.4 mV), pH (7.1), viscosity (2 – 4 cP), entrapment efficiency (57-99%), drug release studies and release kinetics. The materials are evaluated for its compatibility using FT-IR, polymorphic changes by TGA-DSC, and also the morphological properties using Scanning Electron Microscopy. The aerosol foam formulation is evaluated for foam density (0.06-0.07g/ml), bubble size and collapsible time (1-5min), drug content per puff and finally the release studies are compared with nanoparticle formulation along with ex-vivo skin permeation studies. In-vitro cytotoxicity and anti-HIV activity studies are performed through MTT assay and syncytium inhibition process, respectively using t-lymphatic (C8166) cell lines infected with HIV_IIIB strain. Finally, the in-vivo bio distribution profile was obtained using a mice model and its deposition pertaining to major organs (heart, liver, lungs, kidney, spleen, testis and brain) and serum samples are evaluated by LC-MS technique. The method was successfully developed with solvent systems of buffer (0.3% formic acid in water): acetonitrile (30:70 v/v). The concentration of drug in blood and tissue samples is determined by using standard calibration method. The data is validated with various parameters and found to be satisfactory.
The new paradigm shift of Efaverinz to the order of nanodimensions using Eudragit E100, displayed an enhancement in the accumulation of drug to various organs, and more specifically to the brain, when compared to the free drug. Increased bioavailability implies enhanced efficacy and hence the studies reveal that formation of Efavirenz nanoparticles can serve as an effective treatment mode to curtail AIDS.