DESIGN OF AN ORAL IONIC NANOEMULSION FORMULATION FOR TARGETED TREATMENT OF MIGRAINES:

ABSTRACT

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ABSTRACT

Migraine is the third most prevalent disorder and is regarded as the seventh-highest cause of disability worldwide. It is prevalent globally and significantly affects quality of life. Current strategies to treat migraine include the use of analgesics such as aspirin and non-steroidal anti-inflammatory Ibuprofen commonly formulated in conventional drug systems. The oral drug delivery system is the most popular and convenient route to administer various dosage forms for systemic therapy. However, several molecules have poor stability in gastrointestinal fluid and possess limited ability to cross the Blood Brain Barrier (BBB). To overcome the BBB in order to allow central nervous system delivery, several strategies have been explored. The nanotechnology based drug delivery system approach can results in improved bioavailability, increased drug solubility and improved permeability. A nanoemulsion is an advanced mode of drug delivery system that can be developed to overcome the major drawbacks associated with conventional drug delivery systems. They are designed to address some of the problems associated with conventional drug delivery systems such as low availability and noncompliance. Stability, solubility, absorption, bioavailability and site targeting are often challenges experienced by therapeutic agents orally administered. An oral drug formulation in a nanoemulsion system can improve the bioavailability, rapid absorption and effective relief compared to a conventional oral solid dosage and therefore there is an urgent need to design an ionic nanoemulsion for fast effective relief of migraine pain. Nanoemulsions can be characterised using various methods such as zeta potential, zeta size and particle size/size distribution by dynamic light scattering.

The purpose of this study was to synthesize and characterize Ibuprofen (IBU) loaded PLGAPVA nanoparticles in an oral ionic nanoemulsion formulation, and to evaluate their potential for transport of Ibuprofen to the CNS via oral delivery path for improved efficacy with reduced side effects. IBU-loaded PLGA-PVA nanoparticles was prepared by the solvent emulsion evaporation method and synthesis was confirmed by analyzing the physicochemical properties including Scanning Electron Microscopy (SEM), Fourier Transformation Infrared Spectroscopy (FTIR), zetasizer, Ultraviolet (UV) spectroscopy and Thermogravimetric Analysis (TGA). SEM of the nanoparticles explored the morphology in terms of shape and pore distribution of the nanoparticles. The size, charge and polydispersity index (PDI) of the synthesized nanoparticles were evaluated utilizing the zeta-sizer and the nanoparticles were found to be in the size range of 140 ± 23, 50 nm, with polydispersity index (PDI) of 0.190 and with a zeta potential of -53.01 (±10) mV. A drug loading efficacy of 78% was attained by the nanoparticulate formulation. IBU release studies showed a constant release over a 24-hour period. The synthesized IBU-PLGA-PVA nanoparticles were dissolved in two pH environments simulating the stomach pH 1, 2 and intestinal pH 6, 8. At pH of 6.8 26% of IBU was released from the copolymeric nanoparticles, whereas only 25% was released at pH 1.2. This illustrates the shielding effects of the PLGA-PVA nanoparticulate formulation on the IBU in an acidic environment of the stomach. FTIR results exhibited the formation of nanoparticulate structure with comparable peaks between the polymers, IBU and the PLGAPVA nanoparticles. IBU compared to PLGA-PVA nanoparticles showed peaks at 3320 attributed to -C-O vibration, at 3328 attributed to -N-H stretching and -CH_2 bending at 2950. TGA thermal studies indicated that the PLGA-PVA nanoparticulate structure increased the stability of IBU. In addition, HEK 293 neural cells were treated with IBU loaded PLGA-PVA

copolymeric nanoparticles and evaluated for cytotoxicity utilising a 3-(4, 5-dimethylthiazole-2yl)-2, 5-diphenyltetrazolium bromide dye (MTT) assay and absorbance measured at 570 nm employing a multimode microplate reader. From the MTT assay analysis conducted, the results indicated that the IBU-PLGA-PVA- nanoparticles were less toxic to the HEK-293 cells compared to free Ibuprofen. The combined trials and results from the synthesis of IBU-PLGAPVA nanoparticles, showed evidence that these nanoparticles can be utilized as potential invaluable formulation for oral drug delivery of Ibuprofen with improved bioavailability and rapid relief of migraine at a low dose for a longer period of time.