Design and in vitro/in vivo evaluation of novel nicorandil extended release matrix tablets based on hydrophilic interpolymer complexes and a hydrophobic waxy polymer.

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Abstract

The purpose of this work was to develop an extended release matrix tablet of nicorandil; a freely water soluble drug used in cardiovascular diseases. Chitosan (CH) / hyaluronate sodium (HA), pectin (PE) or alginate sodium (AL) interpolymer complexes (IPCs) were prepared. The optimum IPCs (CH: HA, 40: 60), (CH: PE, 30: 70) and (CH: AL, 20: 80) were characterized by Fourier transform infrared spectroscopy. The IPCs were based on electrostatic interactions between protonated amine groups of CH and carboxylate groups of HA, PE or AL. Nicorandil matrix tablets were prepared using the optimum IPCs, alone or in combination with Imwitor® 900 K. Evaluations such as weight variation, thickness, content uniformity, friability, disintegration and in vitro release studies were performed. The tablets showed acceptable pharmacotechnical properties and complied with compendial requirements. Results of the dissolution studies revealed that formula F11 (CH: AL, 20: 80) IPC: Imwitor® 900 K, 3: 1) could extend drug release > 8h. Most formulae exhibited non-Fickian diffusion drug release profiles. When compared to the immediate release Ikorel® tablet, the duration of effective nicorandil therapeutic concentration from formula F11, in healthy human volunteers, was significantly ($P<0.05$) extended from 4 to 8h with expected lowering in side effects potential.

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