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Research article

Solubilization of some COX-2 Inhibitors through 2-HPβCD comparison with hydrotropic solubilization

Swati S. Rawat
Shri Bhagwan College of Pharmacy, Aurangabad, Maharashtra, India

Abstract

In this study solubility of some COX-2 inhibitors (rofecoxib, celecoxib and meloxicam), was enhanced by complexing with 2-hydroxy propylene-β-cyclodextrin (2-HPβCD). HPβCD is a new derivative of β-CD, presents improved safety and solubility properties compared to the parent β-CD. The objective of this study was to prepare aqueous solution of these drugs that could be suitable for the parenteral formulations. In order to elucidate the problem of mechanism of solubilization various solution properties of hydrotropes such as viscosity, specific gravity, surface tension, refractive index, specific conductance of common hydrotropes (viz., nicotinamide, sodium salicylate and sodium benzoate) solutions were studied at 25 $\pm 2^{O}$Con the basis of earlier studies and compared with HPβCD solutions. The solubility enhancement of these drugs by HPβCD and hydrotropes was observed in decreasing order as HPβ-CD >NE>SB>SS with rofecoxib, HPβ-CD> NE>SB>SS with celecoxib but it was HPβ-CD >SB>SS>NE with meloxicam. The results indicate that the enhanced solubility of the drugs in presence of hydrotropes in low concentration is due to weak ionic interaction. At higher concentrations, the formation of molecular aggregation seems to be the possible mechanism of solubilization. When drugs are added to the HPβ-CD solution then these drugs dissolve through formation of some inclusion complexes. The stability constant (Kc) of HPβ-CD complex with the drugs was determined using solubility and spectral shift methods.

Keywords: COX-2 Inhibitors, hydrotropic solubilization, solubilization.

***Corresponding author: Swati S. Rawat,** Shri Bhagwan College of Pharmacy, Aurangabad, Maharashtra, India; E- mail: swatimonalisa@rediffmail.com