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Comparison of Hydrophilic and Lipophilic Surfactants for the Improvement of Solubility of BCS Class II Drug by First Generation Solid Dispersion Method

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***SUMMARY*. Limitation of BCS class-II drugs like diclofenac sodium (DS) can be overcome by using solid dispersion technique. The purpose of the study was to calculate the effect of molecular weight of different surfactants on solubility and dissolution behavior of DS. For this purpose, two different types of surfactants *i.e.*, lipophilic (propylene glycol and span 60) and hydrophilic (polyvinyl pyrrolidone and polyethylene glycol) were used. Solidly dispersed diclofenac sodium was prepared by simple mixing of different ratios of surfactant. Pure DS and their 1:5 SD-DS were further analyzed by phase solubility studies, FTIR analysis, while Gibbs free energy was calculated for the confirmation of electrostatic attraction between the surfactant and DS. Solubility of DS was increased from 12 to 85%, 8 to 53%, 12 to 78% and, 16 to 111% by using PVP, Span 60, PEG and PG, respectively, showing direct relation of molecular weight of surfactant with solubility. Dissolution studies showed DS-span 60-5 and DS-PG-5 follow zero order kinetics with 0.456 and 0.953 rate constants and lowest AIC value of 21.80 and 29.35%, respectively, while DS-PVP-5 and DS-PEG-5 follow Hixon-Crowell model. FTIR peaks confirmed that all spectra of DS were equivalent to spectra obtained by the addition of surfactant with peaks at 3260-3265 cm^{-1}, 1640- 1660 cm^{-1}, 1400-1600 cm^{-1} and 700-800 cm^{-1}. Stability studies calculations confirmed the stability of DS-PG-5 with 14-month shelf life. Prepared solidly dispersed DS can be used as an alternative to less soluble DS in the treatment of osteoarthritis and various inflammatory conditions.**

RESUMEN. La limitación de los medicamentos BCS de clase II como el diclofenaco sódico (DS) se puede superar mediante el uso de la técnica de dispersión sólida. El propósito del estudio fue calcular el efecto del peso molecular de diferentes tensioactivos sobre la solubilidad y el comportamiento de disolución del DS. Para ello, se utilizaron dos tipos diferentes de tensioactivos, es decir, lipófilos (propilenglicol y span 60) e hidrófilos (polivinilpirrolidona y polietilenglicol). Se preparó diclofenaco sódico sólidamente disperso mediante mezcla simple de diferentes proporciones de tensioactivo. El DS puro y su SD-DS 1:5 se analizaron más mediante estudios de solubilidad de fase, análisis FTIR, mientras que se calculó la energía libre de Gibbs para confirmar la atracción electrostática entre el tensioactivo y el DS. La solubilidad de DS se incrementó de 12 a 85%, 8 a 53%, 12 a 78% y 16 a 111% usando PVP, Span 60, PEG y PG, respectivamente, mostrando una relación directa del peso molecular del surfactante con la solubilidad. Los estudios de disolución mostraron que DS-span 60-5 y DS-PG-5 siguen una cinética de orden cero con constantes de velocidad de 0,456 y 0,953 y el valor AIC más bajo de 21,80 y 29,35 %, respectivamente, mientras que DS-PVP-5 y DS-PEG-5 siguen Modelo de Hixon-Crowell. Los picos de FTIR confirmaron que todos los espectros de DS eran equivalentes a los espectros obtenidos mediante la adición de surfactante con picos en 3260-3265 cm^{-1}, 1640-1660 cm^{-1}, 1400-1600 cm^{-1} y 700-800 cm^{-1}. Los cálculos de los estudios de estabilidad confirmaron la estabilidad de DS-PG-5 con una vida útil de 14 meses. El DS preparado sólidamente disperso se puede utilizar como una alternativa al DS menos soluble en el tratamiento de la osteoartritis y diversas afecciones inflamatorias.

KEY WORDS: diclofenac sodium, Gibb's energy, polyethylene glycol, solid dispersion,, solubility, surfactant's molecular weight.

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