분류번호	Ⅳ-P-2

Effects of Sulfobutyl Ether β-Cyclodextrin on Physicochemical Properties of Dexamethasone Dipropionate

Jee Hyun Moon°, Ik Sang Oh and In Koo Chun
College of Pharmacy, Dongduk Women's University, Seoul 136-714, Korea

Complex formation of practically insoluble dexamethasone dipropionate (DDP) with β-cyclodextrin (β-CD), dimethyl-β-cyclodextrin (DMCD), trimethyl-β-cyclodextrin (TMCD), 2-hydroxypropyl-β-cyclodextrin (HPCD) and sulfobutyl ether β-cyclodextrin (SBCD) in water was investigated by solubility method at various temperatures. Water solubility of DDP was found to be 1.78 μg/ml at 37°C. Propylene glycol (PG)-water cosolvent increased the solubility of DDP, but the solubilization was not sufficient (8.93 μg/ml in 20% PG). The addition of CD markedly increased the solubility of DDP in water, and A_L type phase solubility diagrams were obtained with β-CD, TMCD, HPCD and SBCD, where the apparent stability constants of the soluble complexes at 25°C were determined to be 1388, 216, 1054, and 1992 M^{-1}, respectively. However, DMCD remarkably increased the solubility of DDP, and showed an A_P type diagram, suggesting that DMCD forms a soluble complex of high order with DDP. The stability constant for the DDP-DMCD complex at 25°C was determined to be 19132 M^{-1}. The thermodynamic parameters were calculated for the inclusion complex formation in aqueous solution. CD (1×10^{-2}M) remarkably decreased the partition coefficients of DDP between isopropyl myristate/water in the order of TMCD < β-CD < HPCD < SBCD < DMCD, and in squalane/water system in the order of HPCD < TMCD < β-CD < DMCD < DMCD ≤ SBCD. This finding represents that, in a o/w type cream, cyclodextrin complexation with DDP may result in high concentration of DDP in aqueous phase. The permeation of DDP through a cellophane membrane was highly suppressed by the addition of CD, and the degree of suppression was different among CDs, indicating that CD may control the skin permeation of DDP. The dissolution rates of solid dispersions with CDs were much faster than those of drugs alone and corresponding physical mixtures. All DDP-CD solid dispersions exceeded the equilibrium solubility. Consequently these results suggest that complex formation of DDP with CDs may provide useful means to markedly enhance the solubility, and CDs are useful in the semi-solid preparations such as creams and gels for topical application.