Study of Phase Behavior of Poly(ethylene glycol)–Polysorbate 80 and Poly(ethylene glycol)–Polysorbate 80–Water Mixtures

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ABSTRACT: Mixtures of poly(ethylene glycols) (PEGs) with polysorbate 80 are often used to dissolve poorly water-soluble drugs in dosage forms, where polysorbate 80 helps either in enhancing dispersion or in inhibiting precipitation of drugs once the solution is mixed with water. Binary phase diagrams of polysorbate 80 with several low molecular weight PEGs and a ternary phase diagram of polysorbate 80 with PEG 400 and water are presented. Two phases were observed in the binary mixtures when the concentration of PEG 200, PEG 300, PEG 400, or PEG 600 was >55%(w/w). The miscibility of the binary mixtures increases with an increase in temperature; the upper consolute temperatures of PEG 200–polysorbate 80, PEG 300–polysorbate 80, PEG 400–polysorbate 80, and PEG 600–polysorbate 80 mixtures were 100, 85, 75, and 40 °C, respectively. The upper consolute temperature of PEG 1000–polysorbate 80 could not be determined because the melting temperature of the mixtures is ~40 °C and the consolute temperature appeared to be less than this temperature. The decrease in upper consolute temperature with an increase in PEG molecular weight indicated a greater miscibility of the two components. In the ternary system, phase separation of polysorbate 80 was observed when the concentration of PEG 400 was >50–60 % (w/w), possibly because of the high exclusion volume of PEG 400. © 2000 Wiley-Liss, Inc. and the American Pharmaceutical Association J Pharm Sci 89:946–950, 2000

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INTRODUCTION

Poly(ethylene glycols) (PEGs) enjoy wide application in pharmaceutical dosage forms because of their high solubilization capacities for poorly water-soluble drugs and a relatively low toxicity. Depending on their molecular weights (MWs), they exist either as liquid or solid at room temperature. Liquid forms of PEG are commonly used as solvents or cosolvents for drugs in preclinical and clinical studies.[1] PEG 400, which exists as a liquid, is one of the most commonly used vehicles in soft gelatin capsules.[2–4] The solid forms of PEG, with MWs ranging from 1000 to 8000, are used as vehicles for solid dispersions or solid solutions of poorly water-soluble drugs.[5]

A potential problem with the use of PEG as a solvent is the precipitation of drug (phase separation and aggregation) on dilution with water.[6] Such a situation could have an adverse impact on the dissolution of drugs in aqueous media and, consequently, the desired bioavailability enhancement might not be possible.[7] The aggregation of drugs after phase separation can be minimized if a surfactant is used as a neat vehicle or as a mixture with another vehicle. Because of the surface activity of such a vehicle, any drug sepa-

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