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医薬品溶出試験時に用いる界面活性剤の適正使用・保存安定性に関する研究*2

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Study on Proper Use and Storage Stability of Surfactant in Dissolution Test*2

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Summary

Polysorbate 80 (PS80) is one of the most widely used surfactants in the dissolution tests described in the Japanese Pharmacopoeia. It is used to assess the dissolution behaviors of poorly water-soluble drugs from tablets at different pH values, and to improve their dissolution characteristics. However, it has been reported that PS80 decomposes under strongly acidic conditions, which could lead to a potential decrease in the interfacial activity of PS80 and consequent generation of misleading results. To determine whether PS80 affects the dissolution behavior of drugs from commercially available tablets, we investigated the physicochemical stability of PS80 under different acidic conditions, and we also determined the effect of PS80 on the solubility and dissolution behaviors of poorly water-soluble drugs. The decomposition rate of PS80 was determined at pH values of 1.2 and 6.8 in solutions containing 0.1% (w/v) PS80 at 37 ℃. At pH 1.2, PS80 started to decompose immediately, and up to 45% of the original PS80 had decomposed after 8 days. In contrast, PS80 decomposed at a much slower rate at pH 6.8, although the overall level of decomposition was similar to that in the pH 1.2 solution after 10 days. The particle size of the PS80 micelles formed in distilled water was 14 nm, but after incubation of a solution of PS80 at pH 1.2 for 10 days at 37℃ micelles of 23 and 80 nm in size were found. This result could be attributed to the decomposition of PS80; the fatty acids derived from the decomposition of PS80 aggregate to form mixed micelles with large particle sizes. In fact, the addition of oleic acid, which is the main fatty acid component of PS80, to a solution of PS80 led to an increase of the particle size of the PS80 micelles. Interestingly, flufenamic acid, which is a poorly water-soluble acidic drug, showed increased solubility in solution containing 0.1% (w/v) PS80 at pH 1.2. An increase in the dissolution rate of this drug from commercial tablets was also observed. These observations suggest that the size of PS80 micelles influences the solubility and rate of dissolution of this drug. Our results suggest that the decomposition of PS80 should be carefully considered in dissolution tests for tablets containing poorly water-soluble drugs.

Key words

Dissolution test, Polysorbate 80, Solubility, Storage stability, Micelles