Solubility of Delphinidin in Water and Various Organic Solvents between (298.15 and 343.15) K

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The solubilities of 2-(3,4,5-trihydroxyphenyl)chromenylium-3,5,7-triol (delphinidin) in water, methanol, ethanol, and acetone have been measured spectrophotometrically at various temperatures ranging from (298 to 343) K under atmospheric pressure. Delphinidin is most soluble in methanol, followed by water, ethanol, and acetone at all measured temperatures. The experimental data were correlated using the modified Apelblat equation. The calculated solubilities for all solvents showed good agreement with the experimental data in the temperature range studied.

Introduction

Delphinidin [2-(3,4,5-trihydroxyphenyl)chromenylium-3,5,7-triol, CAS Registry No. 13270-61-6, Figure 1] is one of the major anthocyanidin molecules contained in the vacuolar sap of the epidermal tissues of flowers and fruit, to which they impart a pink, red, blue, or purple color.[1] It is the principal and basic skeleton of flower color pigments, so it is the most widespread in nature. It belongs to the group of polyphenolic antioxidants since it contains at least one hydroxyl group attached to a benzene ring and has been reported to possess antioxidant, antiinflammatory, and antiangiogenic properties in vitro.[2] It is commonly administered orally.[1,2] To ensure that the release of this drug material fits the patient needs, researchers try to formulate a dosage form of this drug into controllable release granules. Conventional micronization of drug through recrystallization and comminution have several drawbacks, such as wide size distribution, high thermal and mechanical stress, environmental pollution, large quantities of residual organic solvent, and multistage processes.[3] One of the better methods of preparing controllable release granules is supercritical fluid granulation, which utilizes carbon dioxide as an antisolvent.[4,5] Supercritical fluids offer considerable advantages as solvents or antisolvents in crystallization and precipitation processes. This is why their role has been upscaled and their use as solvents and antisolvents has been nowadays in the center of attention. In the sensitive area of pharmaceuticals processing, various requirements need to be fulfilled: use of the smallest possible amounts of organic solvents, molecular control of the process, one-stage technique that leads to pure product with no residual solvent, control of the properties of the formed microparticles, and application on a large field of pharmaceutical compounds.[6] Since delphinidin is usually obtained from its natural sources through solvent extraction, the knowledge of delphinidin solubility in water and certain organic solvents is important. Furthermore, this information is also necessary in the selection of the most appropriate supercritical antisolvent methods that could be applied. However, from a thorough study on delphinidin literature, it was found that no experimental solubility data of delphinidin in aqueous or organic solvents have been reported.

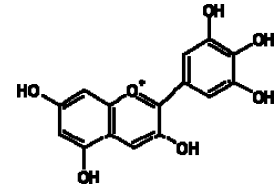

Figure 1. Structure of the delphinidin molecule.

The solubility of delphinidin in water and various organic solvents and at temperatures near the critical point of carbon dioxide was investigated. Solubility measurements were conducted by the pH differential spectrophotometric method.

Experimental Section

Materials. Delphinidin (CAS Registry No. 13270-61-6, > 0.99 mole purity) was purchased from Sigma-Aldrich and used as received without any further treatments. Deionized water, absolute ethanol (CAS Registry No. 64-17-5, > 0.998 mole purity), anhydrous methanol (CAS Registry No. 67-56-1, > 0.998 mole purity), and acetone (CAS Registry No. 67-64-1, > 0.998 mole purity) were purchased from Scharlab S.L., Mallinckrodt, and Merck, respectively, and were also used as solvents without further purification.

Apparatus and Procedure. The solubility of delphinidin was determined using the same apparatus that was described in the literature[7] and explained briefly here (see Figure 2). The experiment was conducted in a glass tube immersed into a constant temperature water bath, which was controlled at the desired temperature by continuous forced water circulation from a thermostat. A mercury-in-glass thermometer (uncertainty of ± 0.1 K) was used for the measurement of the actual temperature inside the glass tube. A predetermined excess amount of delphinidin was charged into 100 mL of solvent contained in a sealed glass tube. The mixture was then agitated using a magnetic stirrer for 1.5 h. The solution was then left for 2 h, to allow the undissolved solids to settle. Prior to the solubility study, some different agitation and settling times were tested to determine a suitable equilibrium time. It was found

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