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Calorimetric Evaluation of Hydration of Cholestyramine

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Abstract

We have investigated the mechanism of hydration of cholestyramine, a water-insoluble resin used pharmaceutically.

Two types of water of hydration (freezing and non-freezing) and the amounts of heat evolved or absorbed during the hydration of cholestyramine were determined. From differential scanning calorimetry, 0·57 g water was observed to be tightly bound per gram of resin (non-freezing water). The hydration of dry cholestyramine was found to be exothermic. The heats of hydration of cholestyramine with chloride or nitrate counter-anions were found to be $-6{\cdot}05$ and $-3{\cdot}46\,cal\,g^{-1}$, respectively. Some of the partially hydrated cholestyramine samples showed absorption of heat during hydration.

The data generated in the study were utilized to better understand the mechanism of hydration and swelling of cholestyramine.

Interaction of polymers and drug molecules with water is of special interest because of the consequences of hydration on the physicochemical properties (drug stability, transport of drug molecules through polymers) of these compounds (Frank 1972). Slade & Levine (1991) reviewed the effects of water on the development of modern food science technology: food quality, safety, stability and technological performance of food. Joshi & Wilson (1993) recently studied the mechanism of dissolution of hydroxypropylmethylcellulose (HPMC E5) in water. There are possibly three types of water of hydration. Type I water is free water which freezes and its frozen form melts at 0°C. Type II water is the water weakly bound to hydrophilic groups on the substrate, which freezes and its frozen form melts at about −15°C to −35°C. Type III water is tightly bound to hydrophilic and ionic groups on the substrate and does not freeze (Jhon & Andrade 1973). Joshi & Wilson (1993) found that the heat of solution of HPMC E5 was associated mainly with the addition of tightly bound water to the polymer. Endothermic and exothermic components were believed to be present with the dissolution of HPMC E5 and a new model for the dissolution of hydrophilic polymers in water was proposed.

Cholestyramine, an anion exchange resin, is widely used as an orally-active cholesterol-lowering agent. Binding of bile acids and other anions has been studied in detail (Lindenbaum & Higuchi 1975; Kos et al 1991; Benson et al 1993). Cholestyramine consists of a styrene-divinyl benzene copolymer containing quaternary ammonium groups. Cholestyramine is water-insoluble, but absorbs large quantities of water and swells considerably. Because of its wide use, cholestyramine was selected as a model to study the thermodynamics of the hydration process of polymeric resins. Hydration of water-insoluble resins such as cholestyramine was expected to involve the following processes: absorption of water at the most easily accessible reactive sites; breaking of polymer-polymer bonds; creation of polymer-water bonds; and dispersion/swelling of the hydrated polymer chains.

In this study, different types of water in hydrated cholestyramine were determined by differential scanning calorimetry (DSC). Heats of hydration of the hydrated cholestyramine were determined by means of an isoperibol calorimeter. Volume changes in cholestyramine resulting from the absorption of water were also monitored.

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Materials and Methods

Drying of cholestyramine

Cholestyramine obtained had chloride as a counter-anion. Cholestyramine with nitrate as the counter-anion was prepared in the laboratory. The resin samples were dried at 70°C under 125 mmHg for three days. Cholestyramine resin is very hygroscopic and, therefore, during weighing of the samples, special precautions were taken to minimize the absorption of moisture (e.g. weighing as quickly as possible and not working on a humid day).

Preparation of cholestyramine nitrate from cholestyramine chloride

Cholestyramine (chloride counter-anion) was hydrated with distilled water and filtered through Whatman filter paper No. 1. Sodium nitrate solution in water (18%, w/v) was passed over the hydrated cholestyramine bed in the funnel to prepare the nitrate salt.

Characterization of types of water in hydrated cholestyramine

The different types of water of hydrated cholestyramine resins were characterized by DSC (Perkin Elmer, DSC-4, Norwalk, CT). The DSC was calibrated using an indium standard. Standard aluminium pans (Perkin Elmer) for volatile liquids were used in the experiments. Samples were weighed with an automatic electrobalance (model # 23,