THE DEHYDRATION AND HYDRATION OF FERROUS SULPHATE

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Two salts of ferrous sulphate are included in the BP, Ferrous Sulphate, $FeSO_4,7H_2O$, and Dried Ferrous Sulphate. The monograph states that the latter is Ferrous Sulphate deprived of part of its water of crystallization by drying at a temperature of 40°. The limits $\geqslant$ 80.0% and $\leqslant$ 90.0% $FeSO_4$ correspond to material consisting mainly of $FeSO_4,H_2O$ plus variable amounts of higher hydrates.

Commercial samples of Dried Ferrous Sulphate examined by X-ray diffraction, thermal analysis and the USP assay consisted essentially of the monohydrate. Ferrous Sulphate heated at 40° formed the tetrahydrate however and not the monohydrate as required in the BP. The dehydration reaction was complete within about three hours and even after seven days at 40° no further dehydration occurred. The tetrahydrate also formed on drying in a desiccator or under vacuum at room temperature.

Dried Ferrous Sulphate is used in tablet manufacture but rehydration may lead to the formation of a concrete-like surface layer which retards dissolution (Stephenson 1965). Dried Ferrous Sulphate is used because the heptahydrate in uncoated tablets would effloresce in dry air and when coated the release of water vapour might attack the coat. The choice of hydrate therefore has an important bearing on stability and bioavailability and the tetrahydrate may have advantages over the official salts.

The dehydration and hydration of Ferrous Sulphate and Dried Ferrous Sulphate were compared with that of the tetrahydrate salt by measuring the changes in weight after storage at 25° over various saturated salt solutions which gave relative humidities of 12, 33, 43, 54, 65, 75, 84, 92 (RH%).

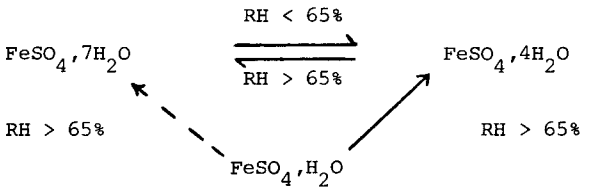

Fig. 1 Dependence of phase changes of ferrous sulphate on RH% at 25°.

Ferrous Sulphate dehydrates to form the tetrahydrate at RH < 65% but prolonged storage at low RH does not cause further dehydration to the monohydrate. Dried Ferrous Sulphate is stable up to 65% RH but at some RH between 65-75% changes to the heptahydrate through the intermediate formation of the tetrahydrate. In tablets made from $FeSO_4,H_2O$ such a phase change may cause dissolution problems, and produces an increase in mass of 64 percent. The increase in volume can change the tablet structure. The tetrahydrate also rehydrates between 65-75% RH but the increase in mass is only 24 percent.

Intrinsic dissolution rates determined using a rotating disc method showed no significant differences between the three hydrates. Preliminary studies on uncoated tablets prepared using Avicel pH 102 as a direct compression agent showed that tablets with acceptable hardness, disintegration times and dissolution times could be prepared from either the mono or tetrahydrate salts. $FeSO_4,4H_2O$ may be a suitable alternative to $FeSO_4,H_2O$ and drying the heptahydrate at 40° would give this salt and not the monohydrate as described in the BP.

Stephenson, D. (1965) Pharm. J. 195: 69-75

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