perpendicular to the water planes and parallel to the axis of the columns. The chloride ions are coordinated with three hydrogen bonds from 3/2 water molecules.

Presumably the same structure was earlier attributed to a tetrahydrate [W.H. Taylor, *Z. Krist. 91* (1935) 450]. A phase transition between the pentahydrate and a second polymorphic form was described to occur near 30°C in aqueous suspension [S.W. Bodman, S.P. Kodama, P.C. Pfeil, R.E. Stevens, *J. Chem. Eng. Data 12* (1967) 500]. The second form was also obtained by vacuum drying of the pentahydrate at room temperature, and its water content was indicated to amount to approximately 1 mol/mol.

The solid state form of a compound is of great importance for pharmaceutical applications. It may influence the chemical and physical stability of the compound itself and of its formulations, may have an impact on pharmacokinetics and bioavailability. In the case of hydrates, the composition has also an influence on the correct dosage of the active pharmaceutical ingredient.

Methylthioninium chloride used in pharmaceutical compositions is described as a trihydrate (USP Material Safety Data Sheet for Methylene Blue (Catalogue Number 1428008), 2005), which is thought to be methylthioninium chloride pentahydrate admixed with other components. The mixture or components in the mixture are stable under different conditions, they may convert to other polymorphic or pseudopolymorphic species and hence change their composition, so that correct dosage is a problem and storage stability may be considered to be insufficient.

SUMMARY

In an aspect, there is provided a crystalline methylthioninium chloride dihydrate as Form C having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	8.1
2	11.1
3	17.6
4	25.9
5	27.2

In another aspect, there is provided a process for the preparation of methylthioninium chloride dihydrate substantially in form C as defined herein, wherein a water-containing methylthioninium chloride or a mixture of various hydrates or a specific hydrate thereof is suspended and stirred at ambient temperature in a solvent selected from the group comprising isopropanol, 1-propanol, 1-butanol, 2-butanol, tert.-butanol, tetrahydrofurane, dioxane, acetone, 2-butanone, and acetonitrile containing a small amount of water, for a time sufficient to generate form C; the solid is then isolated; and the solvent is removed from the solid.

In another aspect, there is provided a pharmaceutical composition comprising methylthioninium chloride dihydrate form C as defined herein.

In another aspect, there is provided a pharmaceutical composition comprising methylthioninium chloride dihydrate form C as defined herein, and a pharmaceutically acceptable carrier, excipient or diluent.

In another aspect, there is provided a methylthioninium chloride dihydrate form C or D as defined herein, for use in therapy.

In another aspect, there is provided the use of methylthioninium chloride dihydrate form C as defined herein, in the manufacture of a medicament for the treatment of a disease condition.

In another aspect, there is provided the use of methylthioninium chloride dihydrate form C as defined herein, in the manufacture of a medicament for the treatment of a tauopathy, Alzheimer's disease (AD), skin cancer, melanoma, Hepatitis C, HIV or West Nile virus.

DETAILED DESCRIPTION

The present invention provides specific polymorphic forms of methylthioninium chloride hydrates, as well as safe and reproducible processes for their preparation. The present invention also provides specific polymorphic forms of methylthioninium chloride hydrates, which are stable under defined conditions, and which have good solubility and bioavailability. The present invention provides specific polymorphic forms of methylthioninium chloride hydrates, which can be easily metered to arrive at defined contents in pharmaceutical compositions in order to administer exact amounts of the active compound.

A first aspect of the present invention is MTC substantially in crystalline Form B of methylthioninium chloride dihydrate.