MULTILAYERED SYRUP GRANULES - A METHOD FOR IMPROVING PRODUCT STABILITY

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The separation of incompatible ingredients of a product by incorporating them into different layers of a multilayered granule has been attempted. Initially magnesium carbonate and copper sulphate were used as models for the two compounds to be separated, and their position in the granule studied using a JXA Microprobe Analyser. The technique was then applied to the separation of a drug substance and a preservative.

Magnesium carbonate (145.5g) and castor sugar (5.6 kg) were granulated by wet massing with a 0.5% w/v aqueous solution of Amaranth in a planetary mixer. The dye was included to provide a visual indication of the progress of the subsequent coating. Examination of the granules by optical microscopy indicated that the magnesium carbonate was evenly distributed over the sugar.

Using a fluid bed granulator, 9 kg of syrup B.P. were sprayed onto the fluidised wet massed granules. Examination using an optical microscope and a Stereoscan Electron Microscope showed a complete coating of sugar over the granule. The ratio of weight of syrup sprayed to weight of sugar used in the wet massing was set as high as reasonably practical, to maximise separation of the incompatible ingredients.

Finally a thin outer coating of copper sulphate solution was sprayed onto the granules.

The granule structure was examined by setting a number of granules in a resin mould, and, after hardening, grinding down using an abrasive cloth until a satisfactory smooth flat surface was obtained. The samples were splattered with carbon and examined by electron microscopy using a JXA Microprobe Analyser.

The method employed was to direct a finely focussed beam of high energy electrons onto a particular point on the surface of the granules whose chemical composition was to be examined. The small volume of material irradiated by the electron beam, about one micron cube, then emits X-rays whose energy and wavelength is characteristic of the elements present within this region.

Photomicrographs have shown the magnesium carbonate to be separated from an outer copper sulphate shell by a layer of sugar.

In the second stage of the investigation, the process was applied to a syrup granule formulation which had previously shown poor stability due to a reaction between the drug substance and a preservative. In this case, the drug substance was incorporated into the core granule, and the preservative into the outer shell.