ABSTRACT

Mebendazole is a broad spectrum anthelmintic, and is reported to exist in three different polymorphic types in the solid state, i.e. polymorph A, B, and C.

The United State Pharmacopoeia (USP) monograph prescribes various tests such as identification, loss on drying, residue on ignition, heavy metals, chromatographic purity and assay, to assess the quality of mebendazole raw material. Even thought the quality of material conform with the monograph of the USP active ingredient , it was observed that the quality of the finished product i. e. mebendazole, tablets 500 mg varies drastically in different consignments of mebendazole raw material. The variation mainly shows in the results of dissolution test which has been prescribed under the USP monograph of mebendazole tablets. The preliminary investigations revealed that the problem caused due to the different polymorphic types of mebendazole raw material but none of the test parameters prescribed under the mebendazole monograph in the USP were able to differentiate the polymorphic type of the mebendazole raw material.

The main objective of this study was to develop a simple, quick and industrially favorable method to screen mebendazole raw material for identifying the polymorphic type. Secondly, solve the low dissolution problem of mebendazole, tablets 500 mg. In this study three raw material samples of mebendazole active ingredient and two samples obtained from raw material consignments which were purchased by State Pharmaceuticals Manufacturing Corporation (SPMC) in the years 2003 and 2004 were used for investigation.

The characteristic differences in FTIR spectra in regions of (1700-1730) cm^{-1} and (3340-3410) cm^{-1}[30] in each sample and the main XRPD peaks angles obtained (17.99 A, 15.20 A and 11.52 A)[31.32], have led to identify the polymorphic type of the three test samples. The results obtained in FTIR and XRPD studies of two consignment samples revealed that there are mebendazole raw materials in the market which consist of mixtures of three polymorphic types. The screening of polymorphic type of mebendazole raw material by the above methods is unrealistic due to lack of such instrumentation in most of the industrial scale manufacturing plants.

Hence the Intrinsic Dissolution Rate (IDR) studies were carried out for 120 minutes time period in different media for each sample and the results showed that there is a possibility of distinguishing three pure polymorphic types by using 900 mL of 0.1 N HCl as a dissolution medium. The lowest IDR value showed by the material mainly consists of polymorphic type A and the highest IDR value showed by the material mainly consists of polymorphic type B.

The simple formulation studies of three test samples showed that the material consisting of polymorphic type A gives the highest dissolution rate (more than 75 % of the labeled amount within the 120 minutes) as per the conditions prescribed under the USP monograph of mebendazole tablets, where as the dissolution results obtained for other two materials are considerably lower than the specified limit in the USP monograph.

In such a manner it was able to find out an industrially favorable method to screen the mebendazole raw material for its polymorphic type and also able to solve the problem of low dissolution in mebendazole tablets 500 mg by selecting polymorphic type A.