Dissolution Shelf Life of Packaged Pharmaceutical Tablet by Prediction and Experiment

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ABSTRACT

This research was designed to find a way to estimate shelf life of packaged pharmaceutical tablets by using package permeation and dissolution as a function of moisture content and storage time. Shelf life was estimated by the amount of time required for the moisture content of the pharmaceutical product to increase until it reached an arbitrarily-selected critical moisture content (permeation time) plus the time that the product could tolerate that storage condition (exposure time) in an open dish study. Permeation time can be calculated by using information from a sorption isotherm for the product, WVTR of the package and other parameters, including product dry weight, storage conditions, initial and critical moisture content.

In this study, prednisone, a moisture-sensitive uncoated tablet, was stored in an open dish at 75%RH at 25°, 30° and 40°C to determine exposure time. To prove the validity of the calculation, the actual permeation time was determined by measuring the moisture content of prednisone packaged in PVC and PVC/0.6 mil Aclar blisters at certain intervals. The calculation provided an error of less than 10%. Therefore, this calculation is useful to select candidate packaging materials that provide enough moisture barrier to a product for the stability test. The actual dissolution shelf life was arbitrarily chosen by using as the failure point a 10% reduction in dissolution. When the predicted shelf life and the actual shelf life were compared, the predicted shelf life was from 8 to 44 percent less than the experimental result.

Key words : Dissolution, Shelf Life, Prednisone, Blister

INTRODUCTION

The shelf life of a drug is the time lapse from manufacturing to the specified expiration date during which the characteristics of the drug product will remain within the approved specifications (Chow and Shao, 1991; USP 23 <1151>). Certain physical properties that can cause failure are appearance, palatability, uniformity and suspendability (USP <1191>). Acceptability in appearance, (for example, turning yellow in tablets, stickiness in capsules or cracking in coated tablets) can be determined easily by visual or tactile means. Failure to meet these limits can result in recall of the product (Murthy and Ghebre-Sellassie, 1993). Dissolution is another physical property that is listed as a criterion for acceptable levels of stability in the monograph for every drug product listed in the United States Pharmacopoeia (USP).

In many researches, dissolution has been found to be susceptible to change (loss of ability to dissolve) during storage (Nakabayashi et al., 1981; Chowhan, 1994; Qian, 1996;