IN VITRO DISSOLUTION OF CEPHALEXIN EXTEMPORANEOUS SUSPENSIONS DURING SIX MONTHS OF STORAGE

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INTRODUCTION

Most problems linked with extemporaneous suspensions are associated with physical stability. In general, suspension stability studies consider only changes in chemical stability, pH, caking, and re-dispersability (1, 2), with no focus on dissolution stability (3). Previous studies carried out on suspension dissolution do not consider changes during the administration period of the constituted suspension (stored at room temperature as well as under refrigeration) throughout the shelf life of the powdered product (4-10). During aging, absence of dissolution changes suggests that bioavailability could remain intact (3).

Our research attempted to evaluate dissolution stability of three cephalexin extemporaneous suspensions from Argentinian market, throughout the recommended administration period of constituted forms, during six months of powders storage under natural and accelerated aging conditions (11).

MATERIALS AND METHODS

Two samples (B and C) of cephalexin extemporaneous suspensions (250mg/5mL) were purchased from pharmacies in Bahía Blanca city, a third sample (A) was produced by a local state laboratory. Cephalexin content, dissolution profiles, pH, specific gravity and organoleptic characteristics were determined (12-14) at constitution time, after 7 days of storage at room temperature and 14 days under refrigeration, repeating this scheme at time zero, and throughout the storage of the powders for oral suspension (3 and 6 months). The formulations were stored under ICH accelerated (40°C/75% R.H.), and natural conditions (25°C/60% R.H.).

Dissolution profiles were compared in terms of Dissolution Efficiency (DE). Analysis of variance (ANOVA) was used to compare both assay average results (chemical stability) and DE values (dissolution stability).

RESULTS

Color changes and unpleasant odor were observed during aging of all constituted suspensions, and pH values remained in the range of 3.0–6.0, satisfying pharmacopoeia specifications.

Due to major changes in appearance after three months of storage under accelerated aging conditions, studies could not be continued on sample A. Microbiological assays and chemical interaction tests are being performed.

A cephalexin content decrease trend was observed during the administration period, throughout the storage of powders, but in almost all cases the values were between 90.0-120.0%. For sample A, there were two assay values lower than 90.0%, in accordance with the results of maximum percentage dissolved and DE, possibly due to reconstitution volume.

In all cases, a 100.0% was dissolved in 5 minutes. Almost all DE values were above 100.0%, which indicates an excellent dissolution performance. In some cases, statistical comparison showed differences between DE values during the administration period of the suspension.

DISCUSSION / CONCLUSIONS

Cephalexin concentration remained within 90% of the initial value throughout the stability study, in all brands. All samples showed a high dissolution rate with large dissolved percentages at early time points of the dissolution profile. Although statistical differences were found between DE values throughout administration period, they do not have an important clinical significance.

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The constituted forms were chemically stable and had acceptable dissolution stability during the administration period, throughout the powders aging study.

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REFERENCES