

トコフェロールニコチン酸エステルカプセルにおける 溶出挙動の経時変化に関する検討

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Changes in Dissolution Behavior of Tocopherol Nicotinate Capsules during Storage

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Summary

Many drugs have recently been recalled from the market because of dissolution problems. In the past three years, 27 cases of recall due to decreased dissolution rate after storage have been reported.

Dissolution seems more likely to be altered during storage than any other product requirement. Thus, we examined the changes in the dissolution of tocopherol nicotinate capsules during storage under various conditions, and investigated the causes of variations.

Four products were stored under 3 conditions (25°C/60% RH, 40°C/75% RH, and 25°C/75% RH), and dissolution tests were performed after 0, 3, and 6 months. Using 4 types of dissolution medium, dissolution curves were prepared according to the Orange Book (Japanese Edition).

After storage at 25°C/60% RH, 1 product did not pass the dissolution test. Furthermore, 2 other products showed changes of dissolution behavior from the results of quality reevaluation, although they still met their dissolution test requirements. Among the storage conditions examined, storage at 40°C/75% RH for 6 months caused marked changes, and the most marked differences among the products were observed in pH 1.2 dissolution medium.

When dissolution tests were performed with the capsule contents, there was no delay or reduction of dissolution after storage. Thus, dissolution tests under the same conditions were performed, using samples prepared by exchanging the capsular shells and contents with those of other products. The results indicated that the changes in the dissolution behavior of stored capsules were due to alterations in the capsular film or contents, or both.

Key words

Tocopherol nicotinate, Hard capsule, Dissolution behavior, Time-course changes, Storage test, Accelerated storage condition, Quality reevaluation, Japan edition of Orange Book