

Dissolution TECHNOLOGIES

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Release Studies On
Semisolid Formulations

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Summary

In vitro release testing of semisolid formulations is currently used as a QA tool to ensure batch-to-batch uniformity. This article gives examples of several techniques and apparatuses that could be employed in release testing of semisolid drug products.

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Performance Testing Of
Transdermal Systems

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Summary

Transdermal performance testing is an important part of both development and control. This article discusses performance testing in relation to the system design, the theoretical release profile, the chemistry of the drug substance, and the types of apparatuses used for testing.

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ABSTRACT

Crosslinking Of Gelatin Capsules And Its Relevance To Their In Vitro/In Vivo Performance

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The chemistry of the crosslinking of gelatin is a complex phenomenon, the nature of which is dependent on several factors. The present manuscript represents an attempt to answer some specific basic science issues.

Two "stress" conditions are commonly known in connection with gelatin capsules. The first condition is induced by exposure to formaldehyde. The second stress condition is created by exposing the gelatin capsules to high moisture and elevated temperatures (i.e., stressed storage conditions).

The adverse effect of prolonged storage on in vitro disintegration and on subsequent drug release from gelatin capsules has long been known. Changes in in vitro dissolution due to exposure to high humidity have been observed in capsules containing chloramphenicol, tetracycline, nitrofurantoin, and either water insoluble or relatively water soluble agents. The principal concern is to determine the effect of stressed conditions on the bioavailability and/or the clinical efficacy of a drug from gelatin capsules or gelatin coated tablets.

It has been shown recently that hard gelatin capsules tested in a dissolution medium containing enzymes such as pepsin and pancreatin would negate the adverse effects or adverse storage conditions (such as high humidity and temperatures, and also severe light conditions) on the in vitro dissolution performance of capsules.

The studies performed on stressed hard gelatin capsules are overly discriminatory and do not reflect the in vivo performance of the product. On the other hand, dissolution of stressed capsules in the presence of enzymes is fairly rapid, nearly

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Crosslinking Of Gelatin Capsules

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the same as in pre-stress condition, and is a reflection of the in-vivo behavior of the product.

Several examples exist in the literature that demonstrate that while the rate of the in vitro dissolution (in media containing no enzymes) of drugs from hard gelatin capsules was decreased under stressed storage condition, no differences in bioavailability of these drugs were observed in vivo.

These findings strongly suggest that dissolu-

tion studies with hard gelatin capsules should be conducted in two stages, one in a dissolution medium without enzymes and secondly, in dissolution media containing enzymes (pepsin at pH 1.2, or pancreatin at pH 7.2 representing gastric and intestinal media respectively). Testing for contamination with formaldehyde as well as low molecular weight aldehydes should be a standard part of excipient evaluation procedures.