W4158

Prolonged gastric acid resistance using a new double DRcaps approach

CAPSUGEL®

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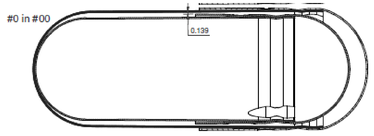
PURPOSE

DRcaps®, HPMC based capsules developed by Capsugel, are well accepted non-animal acid resistant two piece hard capsules.

Extending the time post-dosing at which drug is released from a capsule can potentially help site-specific drug delivery.

The aim of this study was to evaluate the benefit of DRcaps® capsule acid resistance in a double capsule concept and extend the period of delayed release.

DRcaps acid resistant capsules are not affected by the presence of up to 40% ethanol in the dissolution media which may help to prevent alcohol dose dumping in delayed release products.



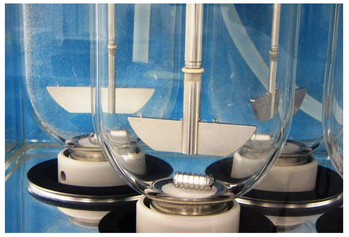
METHODS

A range of different double capsule size options were tested using in vitro dissolution and disintegration tests where capsules were filled with pure acetaminophen.

Acetaminophen dissolution test: pH1.2 USP, 2 hours, then pH6.8 JP2. (USP apparatus 2).
Capsule disintegration test with USP Disintegration apparatus for acid resistance: pH1.2 USP, 2 hours under following conditions respectively: (a) without disc or sinker, (b) with sinker and small disc and (c) with sinker and large disc.

Capsule disintegration behavior at pH6.8 JP2: as delayed dissolution was measured in pH6.8 JP2 with double DRcaps, an additional study was performed to determine the double DRcaps disintegration behavior at pH1.2 USP, for 2 hours followed by pH6.8 JP2 with sinker and with small disc.

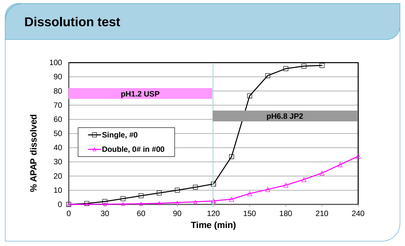
Two criteria were used: visual examination of the capsules after 2 hours pH 1.2 and assay of the amount of acetaminophen released in the dissolution media.



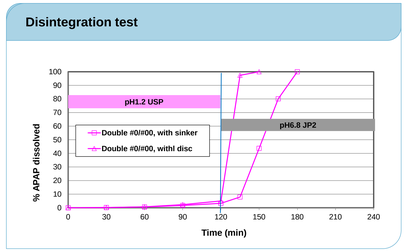
To evaluate the behavior in the presence of 40% ethanol in the dissolution test the double capsule options were tested at pH 1.2 USP with 40% ethanol using dissolution test equipment Sotax AT70 USP apparatus 2, caffeine 100mg formulation and dissolution sinker.

RESULTS

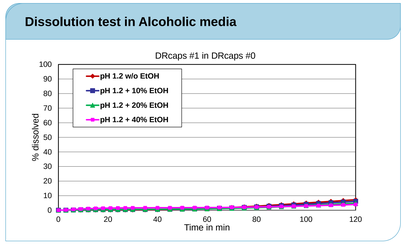
Acetaminophen dissolution: Utilizing a double-wall DRcaps capsule significantly increases the acid resistance (pH1.2 USP) and delays dissolution in pH6.8 JP2 buffer:



Tested under disintegration test conditions, the double DRcaps did not exhibit any significant delay at pH6.8 JP2 stage.



It was confirmed that double DRcaps acid resistance capsules were not affected by the presence of up to 40% ethanol in the dissolution media.



CONCLUSIONS

The test results of double DRcaps capsules confirmed that it can be considered as an option as extended delayed release oral dosage form and the DRcaps acid resistance is not affected by the presence of up to 40% alcohol in the dissolution media.

ACKNOWLEDGEMENTS

We wish to acknowledge Dr. Keith Hutchison for his support.

REFERENCES

a. Performance Qualification of a New Hypromellose Capsule Paragraph 2.5. Mechanical strength evaluation