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## ***In Vitro* Evaluation of Extended Release HPMC Matrix Tablets and Correlation with *In Vivo* Data**

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Due to complexity and interplay of variable gastrointestinal conditions with matrix tablets which are predominantly erosion controlled it is often difficult to predict in vivo release profile [1]. Nascent gel layer of matrix tablets is prone to mechanical stress which is difficult to simulate in vitro.

Present study describes approaches to establish a biorelevant in vitro test for evaluation of two different matrix tablets containing a BCS class 2 model drug. Mechanism of release was also evaluated. Obtained results were compared with in vivo pharmacokinetic data ( $C_{max}$ ) and possibilities for IVIVC or IVIVR were explored.

The tablets were first tested with conventional dissolution tests. Secondly, a test that simulates mechanical stress potentially occurring during transition of tablets through GI tract was performed [2]. This test incorporates glass beads manipulation. Additionally, a new approach using dissolution apparatus USP3 with plastic beads was also explored.

Obtained results were used to elaborate the mechanism of release from the tablets. One formulation was accelerated after applying the mechanical stress, while the other formulation exhibited no changes and followed a 0. order release. This was proven by calculating the Korsmeyer-Peppas release rate constants.

The release mechanism was further examined by inspecting the rates of dissolution  $\Delta Q/\Delta t$  before and after mechanical stress manipulation. IVIVR with  $C_{max}$  results was also shown, the dissolution profile when approximately 70% of the drug is released being relevant for in vivo.

The results from dissolution apparatus USP3 and plastic beads test were used to develop an IVIVC model. Based on this model the maximal plasma concentration ( $C_{max}$ ) was predicted and compared with the observed values from the in vivo BE study. The average absolute percent prediction value for each tested matrix tablet was less than 15%, which demonstrates a good internal predictability of the IVIVC model.

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