

DEVELOPMENT OF ORAL FAST DISINTEGRATING TABLETS USING DIRECT COMPRESSION AND EXTREME VERTICES METHOD IN DESIGN OF EXPERIMENT (DOE)R. BHATNAGAR¹, S. RIZK¹, P. MAJUMDAR¹, A. PHAM¹, A. KANE¹¹Patheon Inc.**Purpose.**

Development of Oral Fast Disintegrating Tablets by Conventional Direct Compression Method and Using Extreme Vertices Mixture Method

Methods.

A multivariable design called the Extreme Vertices Design method of Design of Experiments (DOE) was chosen to optimize the formulation for Oral Fast disintegrating tablets. Pre-selection of lead formulation was completed using placebo formulation (100mg/tab) with several known excipients. The placebo tablets were screened on basis of fast disintegration time, friability <1 % and acceptable hardness. From this study, the best formulation, with the fastest water uptake disintegration time of 5 seconds in 0.4 mL water, was the one with MCC-301, Dicalcium Phosphate, Ac-Di-Sol, L-HPC, Magnesium Stearate (Mg Stearate) and Colloidal Silicon Dioxide (Colloidal SiO₂). This lead formulation was combined with Drug "X" to develop the drug product formulation.

Initial plan for the DOE was to bracket the study between low and high strength formulation and to vary (a) % Dical in MCC : Dical, and (b) % Ac-Di-Sol in L-HPC : Ac-Di-Sol at 2 different levels each. The preferred option was to examine the vertices (extreme points) to ensure compacts could be compressed and that the critical parameters of flow and disintegration time were achievable within these excipient limits. A total of 8 experiments were planned. For each experiment tablets of 100 mg weight were made and tested for hardness, thickness, weight, disintegration and friability.

Results.

Optimization study showed that an optimized formulation with short DT (<20 secs), desirable hardness (3-5 KP) and satisfactory friability (<1.0%) could be manufactured for the 7.5 mg strength but the disintegration time was much higher (>30 seconds) for the tablets of 30 mg strength.

The technique of examining the vertices (extreme points) can lead to defining of the formulation design space and help in the optimization of the planned formulation.

Conclusion.

Better results were obtained with lower strength than higher strength tablets because the API may be exerting a higher influence in the properties of tablets for higher strength tablets. The results suggest that statistical design of experiment is a valuable tool to design suitable fast disintegrating tablets, with some limitation.

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