



Development and Evaluation of Extended Release Herbal Drug Pellets for Treatment of Urolithiasis using Gansons Fluidized Bed Processor (GFBP)

Background

Urolithiasis is a disorder characterized by the formation of calculi in the urinary tract (kidney, bladder and/or urethra) that causes variable degrees of pain, bleeding and secondary infections. Several treatment options are available for this disorder including diuretics and stone inhibitors, however they show incidences of relapse, side effects and drug interactions. Hence, the current therapy for urolithiasis focuses on the use of herbal drugs which exhibit better efficacy coupled with reduced side effects. Until now, only conventional dosage forms such as powders or crude herbs exist in the market for the herbal drug (*Bergenia Ligulata*) selected for this study.

Rationale

Modified release dosage forms extend the drug release and reduce the frequency of dosing in patients, consequently leading to reduction in side effects associated with conventional drugs. Hence, the goal of the project was to develop stable delayed release pellets of herbal drug for incorporation in capsules. In this case, the drug-loaded pellets were prepared using a solution/suspension layering technique in a Gansons fluid bed processor with the help of wurster coating technology.

Present Approach

The pellet formulation was optimized using varying proportions of Eudragit RS 30D (extended release coating polymer), triethyl citrate (plasticizer), talc (anti-tacking agent) and titanium dioxide (opacifier) via 2^2 factorial design. The developed pellets were evaluated for parameters such as percent yield, angle of repose, bulk and tapped density. Additionally, the pellet-filled capsules were assessed for weight variation,



disintegration time, in-vitro drug release, in-vitro anti-urolithic activity and stability studies.

Results

Bottom-spray (wurster) process is a well-recognized fluidized bed technique for pellet coating in the pharmaceutical industry. The design for Gansons wurster assembly is depicted in Figure 1.

Figure 1: Design of Wurster Assembly Supplied by Gansons



The practical yield of formulated pellets was found to be in the range of 95 - 98%, bulk density was in the range of 0.71 - 0.79 g/cc, tapped density was in the range of 0.74 - 0.83 g/cc and angle of repose was in the range of 25.60 - 29.19°. These values indicate that the formulated pellets had good flow properties.

Additionally, the mean particle size of drug loaded extended release pellets was found to be in the range of 707 - 841 μm . The weight variation of all batches was found to be within the limits set by the United States Pharmacopoeia (weight of individual capsules lies within 90-110% of the average weight). The disintegration time of capsules was found to range from 2 to 5 minutes.

Dissolution studies were carried out for all coated formulations to assess the effect of formulation parameters on drug release characteristics. It was observed that the



polymer and plasticizer concentration had a negative impact on drug release and it was found to be faster at lower concentrations of each of these components.

The optimal drug release of 98% at 8 hours was observed for pellets with 40% Eudragit RS 30D and 25% TEC. The in-vitro anti-urolithic activity of the developed formulations was tested in terms of inhibition of calcium oxalate crystal formation by the herbal drug. The developed formulations had significant anti-urolithic activity owing to the presence of phenolic compounds in the active moiety.

Herbal drug-loaded capsules were subjected to stability conditions as per ICH guidelines ($30^{\circ}\text{C} \pm 2^{\circ}\text{C}$, $65\% \pm 5\% \text{RH}$; $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$, $75\% \pm 5\% \text{RH}$) for one and three months. The results of stability studies indicated absence of physical change in the capsules. In addition, there was no significant change in the drug release after 3 months, thus indicating the stability and integrity of the formulated pellets.

Conclusion

The extended release pellets of herbal drug were successfully formulated using Eudragit RS 30D in Gansons Fluidized Bed Processor by solution suspension layering technology. The developed formulations exhibited sustained release up to 8 hours and were stable for 3 months. Moreover, these herbal formulations exhibited significant anti-urolithic activity indicating their potential in treatment of urolithiasis.

Please contact us for more information:

Global: sales@gansons.com

Europe: engineeringUK@gansons.com