Griseofulvin Taste Masked by Hot Melt Extrusion for Pediatric and Geriatric Reconstitutable Suspension

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Purpose
The objective of this project was to investigate the potential of Kleptose Linecaps DE17 (a pea maltodextrin with a DE range of 15 – 20) in masking the bitter taste of antifungal drug, griseofulvin (GRI) by Hot Melt Extrusion (HME) and to formulate a reconstitutable suspension for pediatric/geriatric patients.

Methods
Thermogravimetric studies were performed on the Kleptose Linecaps DE17, plasticizers and GRI to determine thermal stability during extrusion. The physical characterization of pure GRI, Kleptose Linecaps DE17 (KLD), plasticizers and extruded formulations was performed by differential scanning calorimetry (DSC). In order to increase KLD extrudability different plasticizers (Glycerol, Xylitol and Maltitol) were used in a ratio of 10-20% w/w. GRI at 10% -20% w/w drug loads were pre-mixed with KLD and plasticizer using a V-shell blender and further extruded using co-rotating twin screw extruder (16 mm Prism Euro Lab, ThermoFisher Scientific) at screw speeds of 50-150 rpm over a temperature range of 135-150°C. Milled extrudates were studied for in vitro dissolution release in simulated saliva fluid (pH 6.8) using USP Type-I apparatus at 37 ± 0.5°C, and 100 rpm and samples were analyzed using a Waters HPLC-UV system (Waters Corp).

Results
Thermogravimetric studies confirmed the stability of GRI, KLD and polyols at the employed extrusion temperatures. The DSC studies revealed a characteristic melting endotherm of GRI at 218-220°C in the physical mixtures as well as in all extrudates over the period of study, indicating the crystalline nature of drug. HME of KLD was achieved only in the presence of plasticizer (torque lower than 60%). Among the investigated plasticizers xylitol showed improved processability of KLD at all concentrations. Dissolution studies with xylitol (10-20%w/w) as plasticizers and at 10%-20% w/w GRI load exhibited less than 5% release of the API in simulated saliva fluid

Conclusion
HME of GRI at varying drug load using Kleptose Linecaps DE17 as a matrix and Xylitol as a plasticizer demonstrated very good extrudability. Lower release of micronized GRI could suggest the potential use of Kleptose Linecaps DE17 in development of taste masked formulation by HME for a reconstitutable suspension.