Development and Evaluation of an Oral Fast Disintegrating Anti-Allergic Film Utilizing Melt Extrusion Technology
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Purpose
The main objective of this study was to develop a continuous manufacturing process for oral fast disintegrating films (ODF) and to evaluate their performance by in vitro and in vivo studies.

Methods
Chlorpheniramine maleate (CPM, 5-10 %), citric acid and Lycoat® RS 780 were dry mixed using a V-shell blender (GlobePharma, Maxiblend, New Brunswick, NJ) after passing through an ASTM #30 mesh. The plasticizer (glycerol with dissolved sucralose and Magnasweet®) were incorporated slowly into a high shear mixer (Model RSI 3VG, Robot Coupe Industrial Division, Ridgeland, MS) containing the previously mixed blend with all excipients and allowed to blend for 10 minutes. The blends were melt-extruded using a co-rotating twin-screw extruder (16 mm Process, Thermo Fisher Scientific, Pittsburgh, PA) at 30-50 rpm over a temperature range of 100–110 °C. The physical blend of formulation was manually fed into the hopper and films were collected, wrapped in wax paper, sealed and stored in polyethylene bags at 25°C, 40% relative humidity. The mechanical properties of the films were evaluated using the texture analyzer (TA.XTPlus, Texture Technologies, Scarsdale, NY) equipped with 5 kg load cell. The disintegration and dissolution of the films were performed in artificial salivary fluid. X-ray diffraction (XRD, Bruker D8 Advance, Madison, MI) was utilized to determine the physical state of drug, excipients and film formulations. Palatability was studied by an in vivo model using rats (Protocol number 15-026) and a human taste panel (Protocol number VIPS/2013/12).

Results
All of the formulations exhibited excellent extrudability with significantly lower torque values (4.8 – 7.2 Nm) than typically encountered. This was attributed to the plasticization effect of glycerin and the other excipients. The films were transparent, thin and odorless without any entrapped air bubbles. The film formulations demonstrated appropriate mechanical properties and excellent disintegration times (6-11 seconds). Also, all the formulations released more than 95% of the drug within the first 5 minutes. XRD studies revealed that CPM was present in the amorphous form in all of the formulations. Both human and rat models (Figure 1) confirmed the significant reduction of bitterness in optimized formulations. Moreover, in vitro disintegration results were correlated with human taste panel outcomes.

Conclusion
This study demonstrated the utility of melt extrusion technology for the manufacturing of fast disintegrating films. An appropriate selection of formulation and processing parameters helped to extrude below the conventional extrusion temperature with minimal torque. Moreover, the data for disintegration time and release profiles were comparable with published results for commercial film products. Film formulations exhibited satisfying physical, mechanical and palatable qualities, which are the critical parameters for fast disintegrating dosages forms.

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