Fabrication of Hierarchical Polymeric Thin Films by Spin Coating toward Production of Amorphous Solid Dispersion for Buccal Drug Delivery System

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Purpose
Thin films are progressing towards an attractive dosage form, especially in the area of self-administration via oral or transdermal route, to enhance patient compliance and adherence. The present work reports incorporation of drugs into hierarchal polymeric thin films to screen amorphous solid dispersion formation, in an attempt to be easily released in relatively small surface area of the oral mucosa of buccal route of administration. Spin coating technology was used to tap the advantages of a fast and consistent production mean of this innovative pharmaceutical form.

Methods
Spin coated films were prepared by dispensing defined volume of solutions on substrates. The combination of spin speed for sufficient dwelling time, respective solution concentration and dispensing layers were used to ensure full coverage of the substrate and formation of uniform flat-films. Bottom-up assembly of the layers was employed, so as the second layer was spin coated on a top of completely dry first layer using the same conditions. As substrates, conventional glass coverslips (Citoglas, Germany) in 22x22mm were used. Some surfaces of these substrates were covered with wax paper to enhance removal of the thin films. Subsequently spin coating was performed using G3P-8 programmable spin coater (Specialty Coating Systems, USA). Chlorpheniramine maleate, Theophylline and Famotidine were used as model drugs and mixed with matrix polymers of Opadry ® Amb II or Macrogol-PVA grafted copolymer. Drug/polymer weight ratios of 10/90, 25/75, 40/60 and 50/50 (w/w) in appropriate solvents were spin coated. Acryl-Eze ® II or Zein solutions were also spun onto the surface (design-I) or the surface and the base (design-II) of the aforementioned drug-polymer mixtures.Polarized light microscopy and differential scanning calorimetry (DSC) were used to characterize solid dispersion(s). Dissolution studies of the resulted films were performed in distilled water (pH 6.8, 37°C), using an optimized experimental setup to monitor drug release without delays in sampling.

Results
The absence of drug endothermic peak in the thermal analysis by DSC, supported by polarized microscopy images that exhibit no drug crystals, were used to indicate drug amorphization. Of all the drug- Opadry ® Amb II combinations, only Chlorpheniramine maleate was fully dispersed up to 25 % (w/w) drug loading. In contrast, Macrogol-PVA grafted copolymer resulted in solid dispersion of all the tested drugs at different composition (10% w/w Famotidine and Theophylline, and 25% w/w Chlorpheniramine maleate), suggesting that it has a better capacity for drug solubilisation of spin-coated solutions upon drying. Solid dispersions that have been sandwiched between two layers of Acryl-Eze ® II or Zein (design-II) at drug-Opadry ® Amb II or drug-Macrogol-PVA grafted copolymer compositions, respectively, reached a cumulative percent release level more than 95% within 150 min in water. On the other hand, dispersed formulations topped with a layer of Acryl-Eze ® II or Zein (design-I), gave lower drug concentrations over 3 h. This indicates that lower content of these polymers significantly decreased the cumulative drug release from the spin coated thin films.

Conclusion
Two kinds of consistent and homogeneous polymeric thin films, with surface and surface-bottom polymeric layers of Acryl-Eze ® II or Zein, were designed and successfully prepared via spin coating. The use of surface-bottom design, and depending on the type of polymeric matrices (Opadry ® Amb II or Macrogol-PVA grafted copolymer) as well as drug concentration, may be able to produce stable amorphous dispersion, thus allowing enhanced drug release of acceptable size dosage form for buccal delivery.