Investigating the enteric coating functionality of spray dried ethyl cellulose, HPMC and shellac microcapsules

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INTRODUCTION AND OBJECTIVES

Spray drying is a conventional practice in food industry to microencapsulate a wide range of ingredients from micronutrients to flavours. The release profile of coating materials plays an important role in functionality of the encapsulated system. For example for encapsulated flavours mouth-release enhances taste and acceptability of the product but for coated iron a late release to mask the taste and color of the core is crucial. For pH-sensitive ingredients extra protection against the acidic condition of the stomach is required and hence enteric coating can help the core material to pass intact through GI tract and release the active ingredient where the pH approaches neutral in the intestine.

The choice for food grade enteric coating materials is limited due to regulatory restrictions. The available commercial enteric coating formulations are a combination of either ethyl cellulose or shellac in combination with sodium alginate. However, these products are originally designed for pan coating the dietary supplements and nutraceuticals in solid dosage forms such as tablets.

We report on the results of preliminary work on comparing enteric coating properties of ethyl cellulose, HPMC and shellac-based microcapsules prepared using spray drying technology to produce powders that ultimately could be used as additives for food fortification.

MATERIALS AND METHODS

Ethyl cellulose (EC), hydroxypropyl methyl cellulose (HPMC); and shellac along with Na-alginate were spray dried in a Buchi B290 mini-spray dryer. In the first step a hydrophilic marker (FDC blue #1) was used as the core material. Since currently there is no compendial method for *in vitro* release testing of microspheres (Rawat, 2009), we developed our own procedure simulating the USP disintegration tests for dietary supplements. Performance (disintegration) of the three powders were compared at pH 1.2 and 6.8: the powders were dispersed in HCl 0.1 N (stomach condition) and phosphate buffer pH 6.8 (intestine condition) and shaken at 37 °C for 1 and 4 hrs, respectively. The samples were centrifuged for 15 min and filtered with 0.45µm syringe filters. The release was measured as the UV-VIS absorbance of the solution measured by spectrophotometer. Based on the results obtained in this stage, shellac was used to encapsulate a liquid lipophyllic mixture. Performance and release behaviour of shellac capsules was examined using fed-state simulated intestinal fluid (FeSSIF) as dilution medium and fat-soluble Nile red as the marker. The release was measured as the intensity of fluorescence. The microstructure and surface of the capsules was examined by scanning electron microscopy (SEM).

RESULTS AND DISCUSSION

In this experiment we studied and compared the performance of EC, HPMC and shellac microcapsules obtained by spray drying. As it can be seen in Fig. 1, at pH 6.8, EC, HPMC and shellac formulations released their entire content (blue vials) as desired. EC and HPMC disintegrated in 0.1N HCl (pH 1.2) and released 93.8 and 98.2% of the dye (green vials). Only the shellac formulation was resistant under acidic conditions with a negligible release rate of only 1.5% in 1 hr (colourless vial).

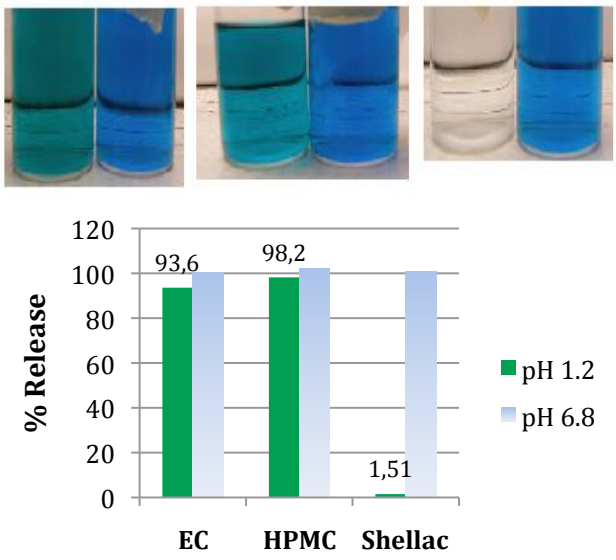

Fig. 1 - The release rate of the EC, Shellac and HPMC capsules in pH 1.2 and 6.8.

The SEM imaging of the capsules revealed the microstructure of the capsule surface. The HPMC capsules collapsed with deep dents, the EC capsules were shrivelled at the surface and shellac capsules looked smooth (Fig. 2). The particle size for all three types was in the range of 1-7 µm with a moisture content of 4-6%.

The failure of enteric functionality of the EC/ Alginate formulation is in agreement with results reported by

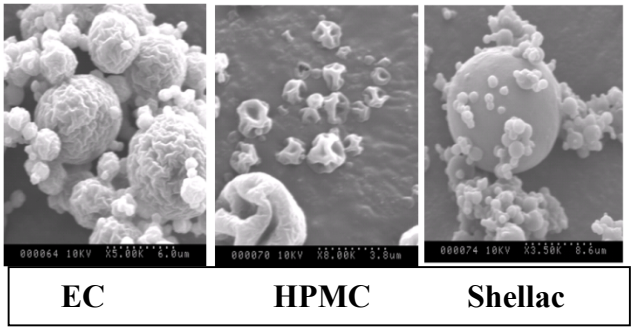

Fig. 2- SEM micrograph of capsules

Ali-Merchant (2009) but contradicts the manufacturer's claims.

Different release profile in acidic pH roots in their different solubility profiles: Ethyl cellulose is insoluble in water and the capsules when mixed with water form a suspension, HPMC capsules are totally soluble and form a solution but the aqueous solubility of shellac is pH-responsive: it may make a solution, colloidal suspension or suspension depending on the pH. So in EC and HPMC capsules, EC and HPMC are just film/matrix formers and the only pH-responsive component is alginate. But in shellac-based capsules, both shellac and alginate are pH-responsive which results in an effective delayed release profile. The coating remains intact in acid and can protect and transport the active complex from the stomach to the small intestine.

Based on the above results, the shellac formulation was chosen for encapsulation of droplets of a fine emulsion. The experiment was done for three loading levels (20%, 30% and 40%). The results revealed that release rate from capsules was largely correlated to capsule concentration in the dilution medium, and to a lesser extent it depended on the payload (Fig. 3).

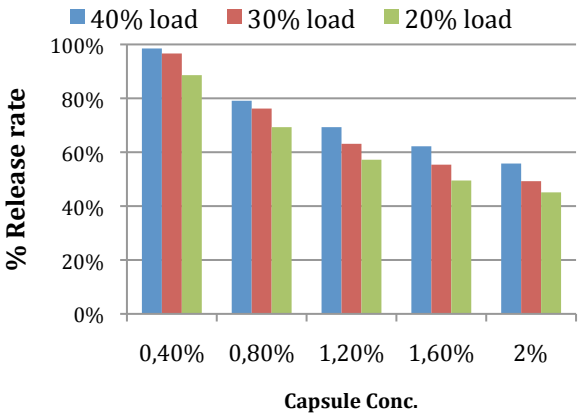

Fig. 3- The effect of capsule concentration and pay load on release in 4 hours.

In the spray dryer feed, the oil droplets were dispersed as sub-micron-particles surrounded by coating polymers. After passing through the atomizer, micron-size solid spheres formed, each containing numerous droplets. The results suggest that microcapsules formed by the entrapment and distribution of oily droplets within a shellac/alginate matrix, rather than by a simple reservoir-type core/shell model. The results indicated that upon exposing the capsules to a pH 6.8 medium, the matrix gradually dissolves. This allows the entrapped lipophilic system to diffuse from the capsules. Obviously, in a dilute system, polymers dissolve more readily and allow the droplets to diffuse out more easily. This may explain the high release rate in dilute systems. At 0.4% capsule concentration, almost all of contents released in 4hr from 40% loaded capsules (Fig. 3).

The SEM imaging showed that at higher payload the surface shrunk, increasing the proportion of uncoated components at the surface. It was also noted that more than 80% of the release occurred in the first hour of wetting the capsules. (Fig. 4)

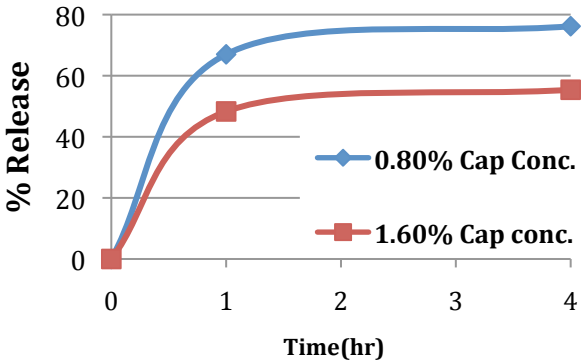

Fig. 4- The effect of time on release rate

CONCLUSION

Microencapsulation with ethyl cellulose, HPMC and shellac based formulations has been successfully demonstrated. Spray-coating based on a shellac/alginate complex produced microcapsules that, at proper dilution, released the entire contents at neutral pH after protecting them under acidic conditions similar to that in the stomach. More studies are required to optimize the spray drying parameters and the release profile. The work paves the way to improving the protection and absorption of pH-sensitive compounds and micronutrients.

REFERENCES

- Ali-Merchant et al, *Efficacy of an enteric coating system suitable for nutraceutical applications,* in 2009 AAPS Annual Meeting and Exposition, American Association of Pharmaceutical Scientists, Nov. 8–12, 2009 - Los Angles.
- Rawat, A.et. al. (2009). Standardization of USP apparatus 4 method for performance testing of microspheres. The AAPS Journal, 11(S2).