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Short communication

Developing gastro-retentive dosage forms by innovative hot-melt technics

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Introduction

Gastro-retentive drug delivery is useful when the active ingredient has a narrow absorption window or gastric targeted release is aimed. One of the retentive mechanisms is floating by low density. If the density is below 1 g/cm^3, the formulation floats on the gastric fluid and avoids the elimination from the stomach (Tripathi et al., 2019). We aimed to develop drug delivery systems based on their high-porosity and low-density foam formations after melting the components.

Materials and methods

Polyethylene glycol 4000 (PEG4000), stearic acid, type 50 (SA), and acyclovir (ACV) were used as a composition base, they were Ph. Eur. grade and purchased from Molar Chemicals Ltd. (Halásztelek, Hungary). Other reagents were analytical grade and purchased from Sigma Aldrich Ltd. (Budapest, Hungary).

The acyclovir samples, that were contained 15% ACV, 75% PEG 4000, and 10% stearic acid, were foamed based on two innovative methods that were described earlier (Haimhoffer et al., 2021; Haimhoffer et al., 2021). Firstly, the pycnometer method was used to determine the density of the solid compositions. Hitachi Tabletop microscope (TM3030 Plus) was used to characterize the broken surface of solid foams and the porosity of the solid foams was measured by SkyScan 1272 compact desktop micro-CT. Finally, the Erweka DT 800 dissolution tester was used to determine the dissolution profile of compositions (900 mL, pH: 1.2, 37 °C rotating paddle method 75 rpm).

Results and discussion

In the beginning, we designed and built the two lab-scale foaming devices (Fig 1.).

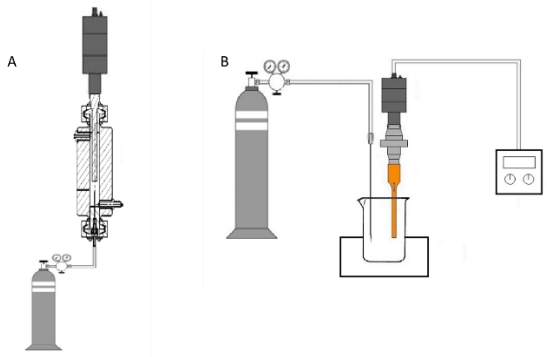

Fig. 1. Sematic structure of foaming devices (A: ultra turrax type, B: ultrasonic type).

After the sample producing the densities were determined, the initial density was 1.10 g/ml, we decreased it to 0.93-0.96 g/ml which is below than 1 g/ml. A lower density was achieved with mechanical mixing ultra turrax than with ultrasonic mixing. While the density for the former was 0.93 g/ml, the density for the latter was 0.96 g/ml.

Our SEM pictures confirmed that we successfully created carriers with entrapped gas bubbles. The cavities

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can be easily separated from the matrix. The shape of the cavities is typically spherical or spheroidal in the melt, somewhere the bubbles' independent boundary ceases and merges.

The closed cells were determined by micro-CT, and the 3D images showed homogeneous distribution of the cavities in the matrix. We achieved a smaller average bubble size with mechanical mixing, in this case, the average particle size was 80.70 µm, while with ultrasonic production it was 533.97 µm.

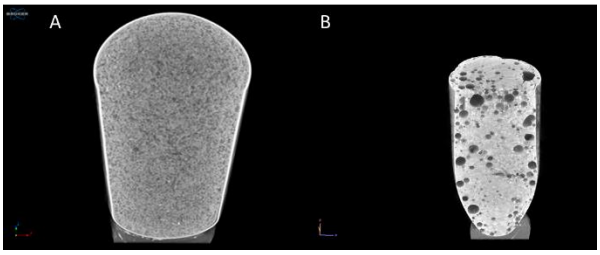

Fig. 2. Micro-CT of samples (A: ultra turrax type, B: ultrasonic type).

The prepared foams had a hard structure even on body temperature. During the dissolution study, the sample was proven to possess zero floating lag time. In case of the ultrasonic production, 70% of the drug was released in 10 hours and the average percentage of the remaining mass of the samples was only 13,3 ± 1,35 %. The ultra turrax samples show a lower dissolution rate, after 10 hours only 50% of the drug was released. The reason for the difference can be found in the formed matrix structure, the larger bubbles increased the opened area of releasing surface per unit of time when the release medium penetrates into the bubbles. The compositions showed continuous buoyancy during dissolution.

Conclusion

We can summarize that we developed novel methods to prepare solid and low-density drug delivery systems with zero floating lag time. The prepared samples showed prolonged drug release and hard structure with the ability to remain in the stomach for several hours.

References

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