Preparation and Evaluation of Gastro-Floating Fine Granules Prepared by Melt Granulation and Highly Loaded with Clarithromycin for Helicobacter Pylori Eradication

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Purpose
Gastro-retentive drug delivery systems (GRDDSs) for clarithromycin (CAM) have recently been developed to enhance the efficiency of helicobacter pylori eradication; however, a variety of problems remain unresolved, including low CAM load in the product, poor shelf-life stability, a bulky final product, and a complicated manufacturing process. In the present study, we prepared gastro-floating granules highly loaded with CAM using a melt granulation technique in combination with highly hydrophobic lipids, and then evaluated their physicochemical properties as a novel GRDDS.

Methods
Three lipids were used as meltable binders: glyceryl monostearate (GM), hydrogenated castor oil (HC), and triglyceryl full behenate (TR-FB). Talc was used as a glidant. Components of the formula (75% CAM, 20% meltable binder, and 5% talc) were mixed in a high-shear mixer while being heated to 5 degrees Celsius above the melting point of the binder with a rubber heater. Then the product was cooled and deagglomerated. The following powder properties were measured: particle size distribution, flowability, and the roundness and hardness of the granules. In addition, a floating property test and a drug dissolution test were also conducted.

Results
Fine granules containing 75% CAM with a particle size range of less than 350 µm were obtained in a 10 min granulation process. All of the prepared granules were dense and spherical, and showed better flowability compared to bulk CAM. Granules prepared with either TR-FB or HC with hydrophobicities higher than GM floated on the surface of test fluid for more than 24 hours. On the other hand, granules prepared with GM sank in the test fluid. None of the floating properties of the granules were affected by granule size. Granules prepared with either TR-FB or HC showed sustained CAM release compared to granules prepared with GM, and had a similar CAM release profile to CAM sustained release products already on the market.

Conclusion
Fine floating granules highly loaded with CAM prepared by melt granulation with highly hydrophobic meltable binders can overcome the problems of previous CAM GRDDSs. These granules have the potential to be an efficient GRDDS for enhanced eradication of helicobacter pylori.