

OMEPRAZOLE/SBA-15 MESOPOROUS SILICATE COMPOUND EMBEDDED IN ALGINATE BEADS: A NOVEL VERSATILE GASTRO-RESISTANT PAEDIATRIC FORMULATION.

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Purpose

To formulate a new omeprazole (OME) gastro-resistant oral dosage form for paediatric patients using SBA-15 mesoporous silicate/alginate as a carrier so as to achieve OME improved dissolution rate into the intestinal tract and to obtain a versatile pharmaceutical form for precise dosage control.

Methods

OME was loaded into SBA-15 by kneading in ethanol solution. The OME-SBA-15 complex was dispersed, at 2.5% or 5.0% (w/w), in 2% (w/w) high viscosity alginate solutions and prilled by a Nisco Encapsulator Var D, equipped with a 600 μm nozzle. The alginate was cross-linked with a 0.5M CaCl_2 solution for 5 min. The obtained beads were dried at room temperature overnight. OME-SBA-15 was characterized by TGA, FTIR, and particle size analyses. Beads inner structure was investigated by SEM-EDX analysis after cryofracture in liquid N_2 . Drug content and encapsulation efficiency were evaluated using a HPLC-UV method. Dissolution profiles were obtained using a "pH-change method" assay using USP Apparatus II.

Results

SBA-15 was characterized by 2 μm bean-like homogeneous particles and a high surface area ($\approx 580 \text{ m}^2/\text{g}$). OME was successfully entrapped in SBA-15 mesopores as demonstrated by TGA. Spherical homogeneous particles with mean diameter around 3mm and good encapsulation efficiency (85%) were obtained. SEM-EDX analyses showed that OME is homogeneously embedded in the alginate matrix regardless the loading. OME is a proton pump inhibitor approved for use in children but it is unstable in gastric conditions. Alginate beads were able to limit OME release in the gastric environment to 14% for the first 2 hours. In intestinal simulated conditions, the alginate matrix degradation together with the high OME/SBA-15 surface area strongly increased drug dissolution rate, leading to complete OME release in 3 hours.

Conclusions

This study demonstrates that alginate-OME/SBA-15 beads made by prilling are able to guarantee a very high OME dissolution rate in the intestinal fluid likely resulting in rapid absorption. This is very useful in order to obtain a rapid increase in the pH values of the stomach. Moreover, the alginate-OME/SBA-15 bead use may be expanded to all ages, adapting the needed dose by the number of administered beads.