Oral Delivery of Anticoagulant Dabigatran via a Mg-Micromotor Encapsulant Within a Gastric-Resistant Tablet for Ischemic Stroke Treatment

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A novel, targeted, therapeutic oral delivery system was designed as a blood-thinning treatment to prevent ischemic stroke, caused by blood clots. Dabigatran (Db), is an anticoagulant medication that inhibits free and fibrin-bound thrombin. However, the drug is not able to withstand gastric fluids, and effectively reach the small intestine for absorption. To provide stable and effective delivery of Db past the stomach, it was uniquely encapsulated on magnesium micromotors, with SiO2, PLGA, and chitosan layers, producing 30μm Db-PLGA-SiO2-Mg microparticles. Dissolution studies in simulated intestinal fluid demonstrate timely release of Db from microparticles within 6 min following arrival. 1mg of these microparticles were incorporated into 80%-starch/20%-baking soda to create a 10mg Db-minitablet (DMT). In a simulated in-vitro experiment within gastric fluid, the treatment was successfully delivered to the intestine after withstanding stomach fluid for 1-2 hours. Once in the small intestine, the DMT dissolved, releasing Db-PLGA-SiO2-Mg microparticles for H2-gas self-propulsion towards the intestinal walls, for Db absorption. To support the functionality of the encapsulated Db delivery, experiments were designed to measure the blood-thinning capability of Db-PLGA-SiO2-Mg microparticles, versus untreated and free-Db. While untreated-blood coagulated in 5 min, blood treated with free-Db coagulated in 11.4 min. Finally, analogous-dose Db-PLGA-SiO2-Mg microparticle-treated blood coagulated in 19.0 min, likely due to the microparticle’s unique dissolution properties. The results of this work highlight the stable delivery of Db-PLGA-SiO2-Mg microparticles through the stomach gastric fluids, where it then self-propels through the small intestine, and is quickly absorbed.

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