CGRP ANTAGONIST PEPTIDE'S FORMULATION IN CHITOSAN MICROPARTICLES

Vera D'Aloisio, Christopher Coxon, Gillian Hutcheon

School of Pharmacy & Biomolecular Sciences, Liverpool John Moores University, Liverpool, L3 3AF, UK

Contact Email V.Daloisio@2017.ljmu.ac.uk

AIM: to develop a dry powder, mucoadhesive drug carrier for the nasal administration of small peptide CGRP (calcitonin gene-related peptide) antagonists to treat migraine.

METHODS: A truncated version of CGRP was synthesised using SPPS. Peptide-containing microparticles (MP) were prepared by spray drying peptide (1%) and low molecular weight (LMW) chitosan (2%) from a solution of 0.5% acetic acid using a Büchi B-290 spray dryer. Moisture content was determined by thermogravimetric analysis. The morphology and MP diameter was observed using scanning electron microscopy. Average particle diameter was calculated measuring 100 particles for each sample.

To assess the release of the peptide, Three MPs samples (10 mg) were suspended in 1 mL of deionised water and mixed (20 rpm, 37˚C, 24 h) and centrifuged (13200 rpm for 10 min). The supernatant was analysed by RP-HPLC, utilising the unloaded MPs as blanks.

Peptide stability was investigated using human serum. Aqueous peptide stock solution (2 mg/mL) was added to 25% pooled aqueous human serum and incubated at 37˚C. At specific time intervals samples were precipitated (6% TCA), centrifuged (13,200 rpm, 2 min) and the supernatants were analysed using an RP-HPLC.

RESULTS: LMW chitosan was selected due to its biocompatibility, mucoadhesiveness and non-toxicity. Chitosan MPs containing 5mg of peptide in 0.5 g LMW Chitosan were prepared with a 45% yield. The water content of the powder was 8.2%. Microparticles were spherical with an average diameter of 10.7 µm. In water, 70% of the peptide was released over 24 h. The stability of the peptide over 30 minutes was analysed by RP-HPLC and LC-MS indicating a percentage degradation of 43%.

CONCLUSIONS: Chitosan microparticles loaded with peptide were successfully prepared by spray drying, achieving a size suitable for nasal delivery.

Back to Programme