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Preparation, *in vitro* evaluation, statistical optimization and *in vitro* absorption mechanism of carvedilol-loaded solid lipid nanoparticles for oral delivery

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The availability of reliable high throughput screening methods for rapid evaluation and prediction of the absorption mechanism is needed with lipid based drug delivery systems especially for solid lipid nanoparticles. Carvedilol-loaded solid lipid nanoparticles (SLN) were prepared using solubility parameter (δ) to select the lipid, and hot homogenization to fabricate SLN. The effect of concentration of Compritol 888 ATO (COMP) and Poloxamer188 (P-188) on particle size of blank SLN was studied using design of experiments (DOE). Further narrow concentration range of COMP and P-188 was selected and carvedilol-loaded SLN were prepared to obtain an optimized formulation which was lyophilized (L-SLN), transformed into enteric compression coated tablet and evaluated for drug release, x-ray diffraction and cellular uptake mechanism. To elucidate the absorption mechanism in detail, cells were subjected to different pretreatments and transport studies. COMP was chosen as lipid due to its least value of Δδ with carvedilol. The optimized formulation (7.5% COMP, 5.0% P-188 and 1.11% carvedilol) had 161 nm particle size and 94.8% entrapment efficiency. The enteric-coated carvedilol-loaded SLN tablet protected carvedilol from acidic environment and similar prolonged release profiles were obtained from L-SLN, core tablet and enteric coated tablet. Absence of crystalline carvedilol XRD peak indicated presence of amorphous carvedilol in SLN. Based upon the results of uptake, pretreatments and transport studies, the main absorption mechanism of carvedilol-loaded SLN could be endocytosis and, more specifically, clathrin mediated endocytosis. Higher carvedilol uptake from SLN compared to drug solution in Caco-2 cell line exhibited a potential prolonged drug release in the body following the lymphatic uptake of carvedilol-loaded SLN which will avoid first pass metabolism and hence higher oral bioavailability.

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A study of the effects of oral spray of papaya enzymes in patients with dysphagia and malnutrition with consideration to bacterial colonization and immunological response

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Rationale: Current practice indicates that at the discretion of the speech Pathologist patients experiencing dysphagic symptoms in association with saliva viscosity and dry mouth may be prescribed paw extract, pineapple or grape seed juice.

Aims: To investigate the effects of papaya enzymes in patients with dysphagia and issues regarding saliva viscosity and dry mouth, to determine the association of microbiological and immunological outcomes with the clinical data from the study participants and to investigate quality of life of the participants and consider mental health wellbeing as a result of the consumption of papaya enzymes.

Methods: 100 participants with dry mouth or viscous saliva were able to participate. Samples of mouth swabs and nasal swabs were collected to determine candida albicans, coliforms and flow rate of saliva. 100 of participants were completed a pre and post quality of life survey and objective measures for dry mouth were obtained.

Results: 100% of participants reported improved quality of life, pleasant taste and a marked improvement regarding decreased thirst and dry mouth quality. Saliva flow rate increased for 100% of the participants with decreased saliva flow. The results of the mouth swabs also indicated that there was an improvement by reducing the amount of candida albicans and coliforms found in the mouth within a one week period as a result of spraying the papaya enzymes, therefore decreasing or eliminating oral thrush.

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