Evaluation of Site selective release of Probiotics from a Delayed Release capsule

Background & Rationale: Probiotics are "good or friendly bacteria" with several beneficial effects like improved lactose digestions, resist enteric pathogens and preventing infections, immune system modulation. One of the major issues with probiotics is their viability in the GIT, mainly in the acidic gastric environment. Hence, probiotic bacteria / oral probiotic formulation needs to be protected by enteric polymeric coatings. This increases the processing and cost of the final product [1]. XXX capsule is a novel capsule composition which ensures delayed release of the contents by a unique dual triggered mechanism (pH and time dependent) to ensure targeted delivery of contents in the intestine; these capsules can provide an alternative to the coating of probiotics[2]. Aim of this study was to assess the suitability of XXX capsules for probiotic powder and probiotic oil formulations with respect to protection from acidic environment of stomach and ensuring selective release in upper intestine

Methods: **A) Filling of Probiotic formulations in XXX capsules:** Two formulations, viz. Freeze dried powder of the probiotic strain, *L. casei* (100mg equivalent to 2.3×10^6 CFU) and an oil formulation (dispersion in almond oil-0.5 ml equivalent to 2.3×10^6 CFU) were filled in regular HPMC capsules and the novel XXX capsules. The oil filled capsules were sealed by banding.

B) *In vitro* selective release and survival studies of probiotics: These studies were performed in simulated gastric fluid (SGF-pH 1.2) and simulated intestinal fluid (SIF-pH 6.8) [50 ml medium stirred magnetically-60-80 rpm], at 37±2°C. The capsules, after pre-exposure to SGF for 2 hrs, were transferred to SIF and study was carried out for additional 6 hrs. Aliquots were withdrawn at periodic time intervals during each exposure and, after suitable dilution, were assessed for probiotic release and viability by pour plate technique in MRS agar plates.

Results and Discussion: The regular HPMC capsule disintegrated in SGF and very low survival of 7 to 8 % was seen for both powder and oil formulations. The XXX capsules, filled with probiotics in powder form as well as oil dispersion, were intact in gastric fluid throughout the two hour period, which was evident by no growth in MRS agar plates inoculated with aliquots sampled at regular intervals. When transferred to intestinal medium, the capsules disintegrated releasing the probiotics; and the % survival was observed to be 70 to 90 % for up to 360 mins in case of both powder and oil probiotic formulations.

Conclusions: XXX capsules are suitable for protecting probiotics from gastric environment and targeting their release in upper intestine; further it is an alternative to costly and time consuming encapsulation or coating of probiotics.

References:

1. Cook, M.T., et al., *Microencapsulation of probiotics for gastrointestinal delivery.* Journal of Controlled Release, 2012. **162**(1): p. 56-67.
2. Cole, E.T., et al., *Enteric coated HPMC capsules designed to achieve intestinal targeting.* International Journal of Pharmaceutics, 2002. **231**(1): p. 83-95.