# Alginate-prednisolone controlled delivery systems: design and *in vitro* characterization

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Purpose: The current study aimed to develop a controlled release formulation for the oral administration of prednisolone (P), potentially useful for the treatment of chronic inflammatory diseases.

Methods: Prilling was selected as micro-encapsulation technique to produce drug loaded hydrophilic microparticles (gel-beads). The influence of process parameters such as composition and viscosity of the aqueous feed solutions (sodium alginate 2.0-2.75% w/v in different ratio with P 1:10-1:4), aqueous bulks for ionotropic gelation and cross-linking time (5-10 min) on the obtained particles was evaluated. Beads morphology, size and solid state characteristics were analysed (SEM microscopy, FTIR, DSC). *In vitro* release study was assessed in conditions simulating the gastrointestinal environment (USP XXVII).

Results: Particles morphology as well as release kinetics of alginate formulations were strongly related to the amount of alginate and P loaded into the feed solutions. Best results were obtained increasing alginate and P content in order to achieve a compact polymeric matrix able to better retain the drug. The best formulation, F6 released around 20% of P in simulated gastric fluid (SGF, pH=1); complete drug release is achieved after pH change in simulated intestinal fluid (SIF, pH=6.8) in about 3.5 h. This behavior may be explained by a combination of alginate pH-dependent solubility, cross-linking properties of $Zn^{2+}$ and polymeric matrix density in #F6; beads did not swell or erode in SGF and still keep intact matrix, whereas in SIF (at pH 6.8) they started to swell and further erode due to the ion-exchange. Moreover, in order to further improve the release kinetic, the formulation F6 has been insert into suitable capsules able to protect the drug in acidic medium and to extend anti-inflammatory activity.

Conclusions: Conventional therapies of chronic inflammatory diseases (such as arthritis arthrosis) consists of multiple daily administrations of prednisolone leading to a variable drug blood level and ineffective therapy. This study suggested that prilling is an appropriate technological approach to manufacture drug delivery systems able to control prednisolone release. The best formulation F6 could be proposed as self-consistent formulation or as a dosage form hosted into suitable capsules for the treatment of inflammatory chronic diseases.