

## PHARMACOKINETICS OF CHONDROITIN SULFATE

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CS is a very heterogeneous natural polysaccharide in terms of structure, molecular mass, biological and pharmacological properties. Furthermore, besides the properties, also the purity of the preparations may change deeply during the extractive processes and influence pharmacological activities. CS is actually classified as a symptomatic slow-acting drug (SYSADOA), a compound that has a slow onset of action in alleviating osteoarthritis symptoms due to its anti-inflammatory activity and capacity to affect cartilage metabolism [1-3].

As well known, CS is orally administered and the possibility to determine its pharmacokinetic parameters is strictly related to specific and sensitive analytical procedures. In fact, the determination of oral adsorption of exogenous CS is a very difficult task, due to its heterogeneous and complex structure [1], for the presence of endogenous plasma CS [4, 5], and for its capacity to interact with tissue and cellular components due to the presence of numerous negative charges on the carbohydrate backbone [1].

We in particular developed different analytical techniques to quantitatively and qualitatively evaluate endogenous CS in small volumes of plasma such as agarose-gel electrophoresis separation with a detection limit of approx. 200 ng [6], HPLC separation of CS disaccharides with post-column derivatization and fluorimetric detection, having a detection limit of about 200 ng with a linearity ranging from 200 to 1000 ng [7], and FACE (fluorophore-assisted carbohydrate electrophoresis) analysis, with a detection limit of approx. 100 ng [4].

A total number of 20 healthy male volunteers participated to two studies, consisting of oral adsorption of 4 g of CS from bovine or from fish cartilage. The healthy volunteers were caucasian males aged 18-30 years. By using the very sensitive analytical procedures previously illustrated, we were able to measure qualitative and quantitative variations of CS in normal human plasma after oral administration of CS of different origin. We found that exogenous CS is also absorbed as a high molecular mass polysaccharide (greater than approx. 2,000 Da as determined by agarose-gel electrophoresis), together with low molecular mass products and, very probable monosaccharides, due to a partial depolymerization and/or desulfation. Furthermore, we also found that the adsorption and the pharmacokinetics and bioavailability parameters are strongly influenced by the structure and characteristics of CS, such as in particular molecular mass and charge density [8, 9].

These results give evidence that structure and properties of polysaccharides strongly influence their absorption and bioavailability by oral route. Furthermore, these studies extend previous results obtained by other researchers in man and experimental animals, both with CS and other polysaccharides (such as heparin, heparan sulfate, dermatan sulfate and mixtures of glycosaminoglycans) confirming that molecules possessing high molecular mass and charge density can be orally absorbed.

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