

# ORAL CHONDROITIN SULFATE THERAPY IN OSTEOARTHRITIS OF THE KNEE: ALGO-FUNCTIONAL AND STRUCTURE MODIFYING EFFECTS

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Symptomatic Slow-Acting Drugs for the treatment of Osteoarthritis (SYSADOA) are compounds which are prescribed as drugs in European countries since many years, whereas they are sold as nutraceuticals in USA. In Europe, the publication of the EULAR Recommendations for the treatment of knee OA in 2003 has listed oral chondroitin sulphate as evidence 1A and strength of recommendation A which represents the highest level for a therapeutic strategy (Ann Rheum Dis 2003; 62: 1145-1155).

Symptomatic slow-acting drugs are intended to be used as ground therapy for osteoarthritis; these compounds are not rapidly acting agents such as NSAIDs and their clinical efficacy on algo-functional symptoms can only be demonstrated after a couple of weeks of regular intake. Interestingly, once the administration is stopped, they do show a carry-over effect of various duration, from about 3 months with the oral formulations to 6-9 months with intra-articular formulations. The main rationale behind the use of the SYSADOA therapeutic class is the reduction of NSAIDs in the overall drug management of OA disease and therefore consequently to limit the very significant risks of upper GI tract erosions, ulcers with bleeding and/or deleterious renal effects in elderly patients.

The evidence for clinical efficacy of oral chondroitin sulfate as a drug able to significantly improve the algo-functional symptoms of OA disease does come from a set of randomized clinical studies published a couple of years ago. Indeed, it was demonstrated that the drug was effective in knee (Bourgeois P et al., 1998; Bucsi L., Poor G., 1998; Uebelhart D et al., 1998) and finger osteoarthritis (Verbruggen G et al., 1998), whereas previous data suggested that hip OA patients could also benefit from it (Conrozier T. et Vignon E, 1992). In addition, oral chondroitin sulfate supported the comparison with NSAIDs such as diclofenac sodium in a medium/longterm clinical study in patients with knee OA (Morreale P. et al., 1996). A dose-finding study in patients with knee OA did provide strong data supporting the administration of 800 mg of chondroitin sulfate orally which had nearly the same effects as 1200 mg/day (Pavelka K. et al. 1999), whereas the use of a sequential 3 months administration mode, twice a year was also shown to provide the same results as a continuous treatment (Malaise M et al, 1999; Uebelhart D. et al, 2004).

Taken these important points into account, we definitively have enough clinical available data supporting the view that oral chondroitin sulfate is a valuable and safe symptomatic treatment for OA disease.

More recent data based on a couple of previous trials and two pivotal studies (Michel BA et al, 2005; Reginster JY et al., 2006) do provide further evidences that oral CS does also have structure modifying effects in knee OA patients.

A couple of other compounds such as hyaluronan, diacerein, avocado and soja unsaponifiables, doxycycline have also been tested with respect to their potential disease modifying effects. Additional compounds including RANK Ligand inhibitors, Cathepsin K inhibitors, Bisphosphonates are further assessed regarding their structure modifying effect.

