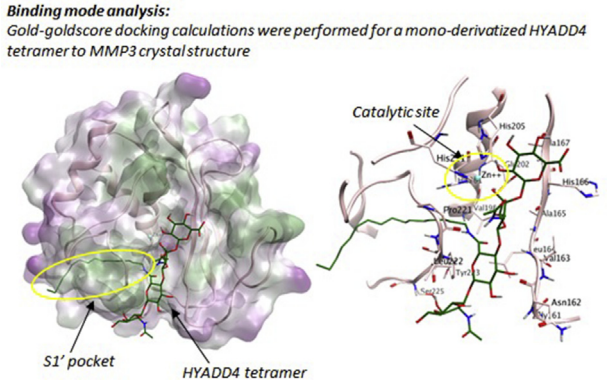
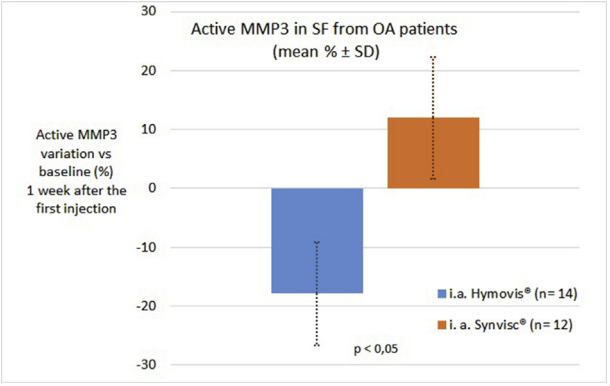
trend resulted in a significant difference when excluding an outlier patient in the Hymovis® group (Chauvenet's method; Mann-Whitney *U* test between treatment groups: $P<0.05$ in favour of Hymovis®).
Conclusions: The HA derivative HYADD®4, contained in the viscosupplement Hymovis®, showed an inhibitory effect on MMP activity *in vitro*; in this study, a specific mechanism for the structural inhibition of MMP3 has been proposed on the basis of molecular simulation studies. In addition, the clinical study outcome has confirmed the pre-clinical results, indicating a decreasing trend in SF MMP3 activity in patients treated with Hymovis®. Therefore, these findings suggest that Hymovis® may prevent local cartilage degradation mediated by MMPs.





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SODIUM SUCCINATE AND HYALURONIC ACID IN KNEE OSTEOARTHRITIS TREATMENT

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Purpose: To investigate the clinical efficacy of combination of hyaluronate and sodium succinate in OA treatment in early stages.
Methods: The study included 126 patients with knee OA (stages I-II, Kelgren and Lawrence), mean age (54.3 ± 2.7) years, among them – 75 women (60%) and 51 men – (40%). All enrolled patients had OA exacerbation (without clinically evident synivitis) and received standard OA treatment (NSAIDs, exercises, orthopedic devices) for 15 days; Gr.1 patients (58) also got 5 intra-articular injections of 1.1% hyaluronic acid, stabilized with sodium succinate (2 ml, once a week); patients of Gr.2 (68) in addition to standard treatment received 5 intra-articular injections of 1,1% solution of non-stabilized HA (2 ml, once a week). Clinical observation and evaluation of the results were performed at the beginning of the treatment, at 6th, 12th and 24th week after the study beginning.
Results: During the treatment period, patients in both groups showed the positive changes in clinical signs and symptoms of OA which led to the lowering of the general WOMAC index (from (78.3 ± 4.1) in Gr. 1 and (75.4 ± 3.8) in Gr. 2 at the beginning of the study to (27.9 ± 2.6) and (29 8 ± 1.9) accordingly at week 12 ($P<0,05$ for both groups). The VAS score in both groups indicated a significant pain reduction, but the stability and duration of the clinical effect in the groups was different. In patients of Gr.1, the pain syndrome continued to decrease after 12 weeks till 24th week, whereas in Gr.2 after the treatment course there was no significant changes in further pain regression after 6th week point. The changes in Lisholm score were also significantly better in Gr.1 than in Gr. 2 (before treatment (21.7 ± 4.6) and (22.6 ± 5.3), at week 6 – (86.4 ± 5.7) and (71.3 ± 4.8), at week 12 – (87.6 ± 6.2) and (63.8 ± 5.3), respectively, $P<0,05$ between groups at week 12th.
Conclusions: Combination of the hyaluronic acide and sodium succinate biochemical and physiologic properties in early stages of knee OA (as intra-articular injections) allows to increase the treatment efficacy, achieve better pain control, and longer remission comparing to use of the hyaluronic acid alone.

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INTRA-ARTICULAR ADMINISTRATION OF HYDROGEN SULPHIDE AMELIORATES SEVERITY OF EXPERIMENTAL OSTEOARTHRITIS

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Purpose: Progressive cartilage destruction leading to joint malfunction is one of the most prominent features of osteoarthritis (OA). At present this pathology has no cure and current treatments are mostly symptomatic, not being able to stop or retard the progression of the disease. Hydrogen sulphide is a small gaseous molecule that has shown to prevent cartilage degradation as well as to exert anti-inflammatory effects in *in vitro* models of OA. The purpose here was to evaluate the effects of administering an H_2S-producing compound, intra-articularly, in an experimental model of OA.
Methods: Experimental OA was induced in a rodent (Wistar female rats) model by transection of the medial collateral ligament and removal of the medial meniscus of the left knee. The right knee was employed as control. Animals were randomized into three groups (6 rats per group). In one group (intra-articular sulphide, IS), GYY4137, a well-known H_2S producing compound, was delivered intra-articularly (200 μM in saline, 50 μl), with one single injection at day 7. The second group (intra-articular control, IC) received vehicle (saline) also in one single injection (50 μl, at day 7) serving as treatment control. The third group received no treatment and served as surgical control (C). Macroscopy clinical evaluation of the animals was performed at days 0 (before surgery), 7, 15 and 40 (euthanasia) including indirect evaluation of pain levels using a Rotarod performance test. Histopathological changes in articular cartilage and synovium were evaluated using a semi-quantitative scoring system (Mankin Score, MS) and a synovitis grading system (Krenn Score, KS), respectively.
Results: Seven days after surgery animals in all 3 groups showed worse performance in the Rotarod test, with significant increases in the number of falls (except IC) and reductions in the time to first fall (Table 1). After 40 days, animals in the C group showed no significant improvement in either of these parameters. In the intra-articular control (IC) the number of falls had returned to pre-surgical levels, and in the animals that received intra-articular H_2S (IS), results were significantly better with respect to both day 0 and both control groups (C and IC) (Table 1). Times to 1st fall were also significantly better in the IS group versus C and IC groups both at days 15 and 40.
Cartilage deterioration as a result of surgery was evaluated with the Mankin Scoring system. Tibial plateaus (TP) and femoral condyles (FC) in both the medial (M) and lateral (L) compartments in each knee were evaluated (Table 2). There were no significant differences among groups in the lateral compartment, neither when considering TP and FC separately nor for the compartment as a whole. Conversely, scores in the medial compartment were significantly better in the animals treated with intra-articular H_2S vs the Control group, both when considering TP or FC separately, and for the compartment as a whole (Table 2). Synovial inflammation was evaluated with the Krenn score, and no significant differences were found among the three groups.
Conclusions: This study demonstrates that a single dose of a H_2S-producing compound (200 μM GYY4137 in 50 μl saline) administered