Evaluation of a Modified Hyaluronan Biopolymer (MHB3™) on Cartilage Loss and Osteophyte Formation in a Knee Instability Model

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Background: Osteophytes, commonly called bone spurs, are bony projections that develop along the edges of bones accompanying cartilage loss. They may form on any bone including vertebrae, and often form where bones meet at joints. Osteophytes may also develop where ligaments and tendons connect to bone. Range of motion is frequently limited in the affected joint and although osteophytes themselves are not painful, they frequently rub against nerves and cause pain. All vertebrate species are subject to the development of osteophytes.

Osteophyte formation has been classically related to any sequential and consequential changes in bone formation due to aging, degeneration, mechanical instability, and osteoarthritis. For Forty two percent of the adult human population, degeneration and development of osteophytes will lead to symptoms of neck and back pain, radiating arm and leg pain and weakness in the extremities during their lifetime.

Medical treatments for cartilage loss and osteophytes are typically palliative and not directed at the underlying problem. Osteophytes that limit range of motion or cause other problems that limit ability may require surgery to prevent further joint damage. Surgical options are determined by the location of the osteophyte. Osteophytes are often removed as part of a more comprehensive surgery for osteoarthritis. For example with osteoarthritis in an elbow the surgeon may remove osteophytes while making other repairs to the joint. Access to the joint for removal of osteophytes may be via arthroscopic surgery or with an open procedure.

A study was designed and conducted to examine the effect of an orally administered exogenous hyaluronan biopolymer (MHB3, Cogent Solutions Group) on cartilage loss, bone remodeling and osteophyte development.

Methods: A total of 10 inbred laboratory mice were obtained and housed according to accepted laboratory animal standards. The mice underwent an aggressive knee instability surgery. The medial collateral and anterior cruciate ligaments were identified and transected followed by a partial meniscectomy. Following surgery mice were randomly assigned to two groups. Control Group (N5) was gavaged 5 days/week for 4 weeks with saline. Treatment Group (N5) was gavaged 5 days/week with MHB3 at a dose of 10mg/kg, for five weeks. During the five weeks post-surgery, it was anticipated that all animals would have severe cartilage loss, bone remodeling and osteophyte development. After five weeks of treatment the mice were euthanized, their knees decalcified, paraffin embedded, stained with Saffrin-O, evaluated on slides (Figure 1) and scored on a scale of 1 to 24 (Pritzker *et al).* A histopathological score of 1 indicates pristine articular cartilage such as might be found in a very young healthy subject; a score of 24 indicates complete cartilage loss, poor bone reformation, and likely osteophyte formation.

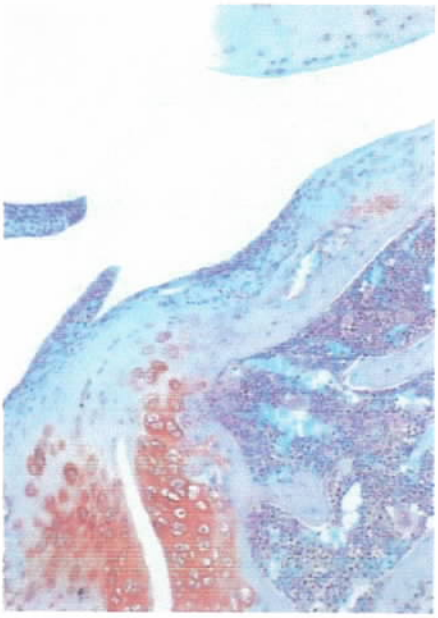
Results: All of the control mice showed complete cartilage denudation and the formation of osteophytes scoring 24/24 at the effected joint. The treatment group averaged scores of 5/24 showing significant healthy cartilage and no osteophyte formation.

Disscussion: As shown in Figure 1 Control Mouse (left), the red-staining tissue with poorly defined margins on the interior of the bone tissue is indicative of a failed attempt to remodel the bone and the formation of osteophytes leading to severe instability. On the other hand, the sample Treatment Mouse (right), which was orally administered the hyaluronan composition exhibits well-defined bright red-staining tissue on the surface of the bone. The well-defined margins of red-staining tissue are indicative of intake and healthy cartilage and bone surfaces.

Conclusions: These results strongly demonstrate the effectiveness of the oral administration of MHB3 in protecting healthy cartilage and bone, and the prevention of osteophytes in mice having undergone knee instability surgery, as compared to those mice receiving a saline control composition. This is the first time, to our knowledge, that an orally administered, exogenous hyaluronan biopolymer has been shown to have cartilage and bone protecting benefits including osteophyte prevention.

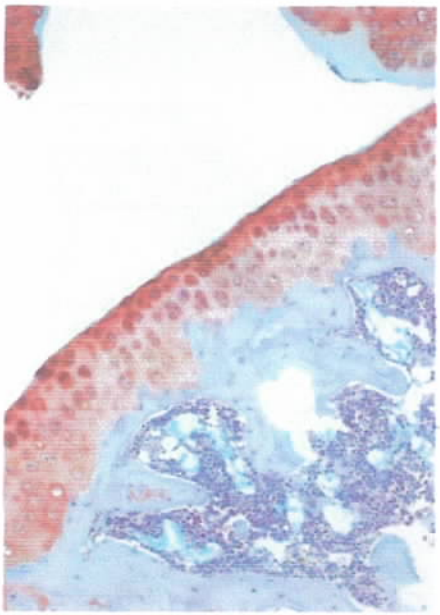
FIGURE 1

Saline Control Group Sample



Sagittal section of knee joint post-MCL/ACL resection showing loss of articular cartilage, poor bone remodeling, and formation of osteophytes.

MHB3™ Treated Group Sample



Sagittal section of knee joint post-MCL/ACL resection showing healthy articular cartilage with no indication of poor bone remodeling or osteophyte formation.