SPECIFIC®

DISSE TEGNENE KAN TYDE PÅ AT DYRET HAR LEDDPROBLEMER

SPECIFIC™ JOINT SUPPORT CJD

Økte mengder næringsstoffer som støtter leddbrusken
gir bedre støtte for artrose og andre leddproblemer

- Tilsatt **hydrolyserte kollagenpeptider**
- **Økt innhold av kondroitinsulfat** erstatter **glukosaminen**, og gir den **samme totale mengden GAG som før** samt økt støtte for **leddfunksjon** og **forbedret smertelindring**
- **Økt mengde Antarktisk krill -** en **premium kilde til omega-3** som har **høyere biotilgjengelighet** i kroppen og gir en **økt total mengde EPA**
- Tillsatt **betaglukaner**

SPECIFIC™ CJD JOINT SUPPORT

GIR FORBEDRET STØTTE FOR ARTROSE
OG ANDRE LEDDPROBLEMER:

- **Unikt høyt innhold** av **omega-3 fettsyrer** fra **fisk** og **krill** som støtter den **naturlige antiinflammatoriske prosessen** og **reduserer aktiviteten til brusknedbrytende enzymer.**
- **Hydrolyserte kollagenpeptider** for **vedlikehold** av **bruskvev** og **forbedret mobilitet.**
- **Betaglukaner** - støtter hunder med artrose ved å redusere de **inflammatoriske** og **brusknedbrytende mediatorer.**
- **Økt nivå kondroitin**, som er en **viktig komponent i brusk** som effektivt **støtter leddfunksjon i smertefulle ledd.**
- **Høye nivåer av antioksidanter** hjelper til med å nøytralisere **brusknedbrytende frie radikaler**
- **Høyt innhold** av **mangan**, en **co-factor** i syntesen av **proteoglykaner.**
- Støtter **optimal vektkontroll** gjennom **lavt fett-** og **høyt fiberinnhold** sammen med tilsatt **L-karnitin** - et aminosyrederivat som kan **øke fettforbrenningen.**

KOLLAGEN**PEPTIDER**

- **SPECIFIC™ CJD inneholder PETAGILE®**, høyrensete hydrolyserte kollagenpeptider, med en molekylstørrelse på gjennomsnittlig 6000 Dalton
- **Kollagenpeptider har veldig høy fordøyelighet** og kan tas opp som aminosyrer, dipeptider og til en viss grad som inntakte molekyler og **akkumuleres i bruskvevet** [1]
- In-vitro studier med kondrocytter fra svin, storfe og hund, viste at **kollagenpeptider øker biosyntesen av bruskvev og reduserer inflammatoriske cytokiner, aktiviteten hos proteaser og nedbrytning av brusk** [2-4]
- I en studie med **artroseutsatte mus** (STR / ort), **bremset**, eller til og med **stoppet kollagenpeptider nedbrytningen av brusk** [5]
- I kliniske studier på **hunder med artrose**, minsket **hydrolyserte kollagenpeptider haltheten og forbedret bevegeligheten** [4,6,7]. Den observerte forbedringen assosieres med reduserte plasmanivåer av MMP-3, en biomarkør for nedbrytning av brusk [6]

1. Oesser S et al. (1999) Oral administration of ^{14}C labeled gelatin hydrolysate leads to an accumulation of radioactivity in cartilage of mice (C57/BL) J Nutr 129: 1891-1895.
2. Oesser S & Seifert J (2003) Stimulation of type II collagen biosynthesis and secretion in bovine chondrocytes cultured with degraded collagen. Cell Tissue Res 311: 393-399.
3. Schunck M et al. (2009) Collagen peptide supplementation stimulates proteoglycan biosynthesis and aggrecan expression of articular chondrocytes. Osteoarthr Cartilage 17: S143.
4. Schunck M et al. (2017) The effectiveness of specific collagen peptides on osteoarthritis in dogs – Impact on metabolic processes in canine chondrocytes. Open J Anim Sci 7: 254-266.
5. Oesser S et al. (2007) Orally administered collagen hydrolysate halts the progression of osteoarthritis in STR/ort mice. Osteoarthr Cartilage 15: C61-C62.
6. Weide N (2004) Der Einsatz von Gelatinehydrolysat bei klinisch-orthopädisch gesunden Hunden und Hunden met chronischen Erkrankungen des Bewegungsapparats. PhD Thesis, Hannover.
7. Beynen AC et al. (2010) Influence of dietary beta-1,3/1,6-glucans on clinical signs of canine osteoarthritis in a double-blind, placebo-controlled trial. Am J Anim Vet SCi 5: 90-94.

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1. ORAL ADMINISTRATION OF 14C LABELED GELATIN HYDROLYSATE LEADS TO AN ACCUMULATION OF RADIOACTIVITY IN CARTILAGE OF MICE (C57/BL)

Steffen Oesser,1 Milan Adam,* Wilfried Babel† and Ju¨rgen Seifert

ABSTRACT: Several investigations showed a positive influence of orally administered gelatin on degenerative diseases of the musculo-skeletal system. Both the therapeutic mechanism and the absorption dynamics, however, remain unclear. Therefore, this study investigated the time course of gelatin hydrolysate absorption and its subsequent distribution in various tissues in mice (C57/BL). Absorption of 14C labeled gelatin hydrolysate was compared to control mice administered 14C labeled proline following intragastric application. Plasma and tissue radioactivity was measured over 192 h. Additional "gut sac" experiments were conducted to quantify the MW distribution of the absorbed gelatin using SDS-electrophoresis and HPLC. Ninety-five percent of enterally applied gelatin hydrolysate was absorbed within the first 12 h. The distribution of the labeled gelatin in the various tissues was similar to that of labeled proline with the exception of cartilage, where a pronounced and long-lasting accumulation of gelatin hydrolysate was observed. In cartilage, measured radioactivity was more than twice as high following gelatin administration compared to the control group. The absorption of gelatin hydrolysate in its high molecular form, with peptides of 2.5–15kD, was detected following intestinal passage. These results demonstrate intestinal absorption and cartilage tissue accumulation of gelatin hydrolysate and suggest a potential mechanism for previously observed clinical benefits of orally administered gelatin. J. Nutr. 129: 1891–1895, 1999.

2. STIMULATION OF TYPE II COLLAGEN BIOSYNTHESIS AND SECRETION IN BOVINE CHONDROCYTES CULTURED WITH DEGRADED COLLAGEN

Steffen Oesser · Jrgen Seifert

Abstract The functional integrity of articular cartilage is dependent on the maintenance of the extracellular matrix (ECM), a process which is controlled by chondrocytes. The regulation of ECM biosynthesis is complex and a variety of substances have been found to influence chondrocyte metabolism. In the present study we have investigated the effect of degraded collagen on the formation of type II collagen by mature bovine chondrocytes in a cell culture model. The culture medium was supplemented with collagen hydrolysate (CH) and biosynthesis of type II collagen by chondrocytes was compared to control cells treated with native type I and type II collagen and a collagen-free protein hydrolysate. The quantification of type II collagen by means of an ELISA technique was confirmed by immunocytochemical detection as well as by the incorporation of 14C-proline in the ECM after a 48 h incubation. Chondrocytes in the control group were maintained in the basal medium for 11 days. The presence of extracellular CH led to a dosedependent increase in type II collagen secretion. However, native collagens as well as a collagen-free hydrolysate of wheat proteins failed to stimulate the production of type II collagen in chondrocytes. These results clearly indicate a stimulatory effect of degraded collagen on the type II collagen biosynthesis of chondrocytes and suggest a possible feedback mechanism for the regulation of collagen turnover in cartilage tissue.

3. COLLAGEN PEPTIDE SUPPLEMENTATION STIMULATES PROTEOGLYCAN BIOSYNTHESIS AND AGGRECAN EXPRESSION OF ARTICULAR CHONDROCYTES

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Purpose: Over the past years hydrolyzed collagen has been used in the treatment of OA and positive effects on joint health were demonstrated in pre-clinical experiments and clinical studies. The therapeutic mechanism, however, is still unknown. The aim of this study was to investigate the influence of a specific Collagen Hydrolysate (FORTIGEL®) on the proteoglycan metabolism of the extracellular matrix (ECM) of chondrocytes.
Methods: Primary articular chondrocytes were isolated of porcine ankle joint cartilage and cultured under reduced oxygen conditions. The culture medium was supplemented with 0.5 mg FORTIGEL®/ml according to recommended daily dose of patients. At different time points of the culture period the amount of secreted and cell-associated proteoglycans (PGs) were quantified by measuring 35S-sulphate incorporation. Total proteoglycan biosynthesis was measured by specific staining of sulphate groups with Alcian blue. Moreover, the expression of aggrecan was determined by Northern Blot analysis and the amount of aggrecan in the ECM was analyzed via Western Blotting.
Results: Supplementation of the culture medium with FORTIGEL® resulted in a statistically significant ($p<0.05$) increase of total PG synthesis. The amount of secreted and cell-associated PGs was significantly increased up to 1.6-fold after FORTIGEL® treatment compared with the control cells. In particular, administration of FORTIGEL® was associated with a statistically significant increase ($p<0.05$) of aggrecan biosynthesis shown by RNA expression and accumulation of aggrecan intermediates and of native aggrecan in the ECM as well.
Conclusions: These results indicate a stimulatory effect of FORTIGEL® on the metabolism of proteoglycans in chondrocytes. Thus FORTIGEL® may be helpful reducing degenerative changes of the ECM by stimulating anabolic processes in cartilage tissue.

4. THE EFFECTIVENESS OF SPECIFIC COLLAGEN PEPTIDES ON OSTEOARTHRITIS IN DOGS-IMPACT ON METABOLIC PROCESSES IN CANINE CHONDROCYTES

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Abstract: In clinical trials over the past decade, the beneficial effect of orally administered collagen peptides in osteoarthritic dogs has been clearly demonstrated [1] [2] [3]. Although a statistically significant improvement in the lameness and vitality of dogs in general has been documented, the mode of action of the collagen peptide treatment is still under discussion. A previous study [3] indicated that the reduction in lameness and increased mobility in dogs after collagen peptide treatment were associated with a statistically significantly lowered plasma content of MMP-3, which is involved in collagen degradation. In addition, the content of the MMP-antagonist TIMP-1 increased slightly after collagen peptide supplementation, suggesting a direct impact on the cartilage metabolism, particularly on the decrease of extracellular matrix degradation. Based on these findings, the impact of specific collagen peptides (PETAGILE ®) on cartilage metabolism was tested in canine chondrocytes in the current investigation. In addition to the biosynthesis of various matrix molecules effects might help to explain the previously reported clinical improvements after collagen peptide supplementation. Furthermore, the beneficial effect of (type II collagen, aggrecan and elastin), the RNA profile of inflammatory cytokines and degenerative matrix molecules was investigated. The results howed clearly that the supplementation of specific collagen peptides reduced catabolic processes, as indicated by a statistically significant decrease in inflammatory cytokines and proteases in canine chondrocytes compared with untreated control experiments. In addition, a statistically significantly enhanced biosynthesis of type II collagen, elastin, and aggrecan was observed. Hence, the current data supports the suggested anti-inflammatory effect of specific collagen peptides, but also clearly demonstrates a pronounced stimulatory impact on matrix molecule synthesis. A combination of both observed effects might help to explain the previously reported clinical improvements after collagen peptide supplementation. Furthermore, the beneficial effect of the specific collagen peptides was also confirmed in case reports on osteoarthritic dogs that demonstrated decreased lameness and increased vitality in the affected animals after PETAGILE treatment.

5. ORALLY ADMINISTERED COLLAGEN HYDROLYSATE HALTS THE PROGRESSION OF OSTEORATHRITIS IN STR/ort MICE

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Purpose: Experimental investigations on various chondrocyte and cartilage explant models have demonstrated a clear stimulatory effect of Collagen Hydrolysate on chondrocyte metabolism and cartilage growth. The objective of this study was to investigate the efficacy of orally administered Collagen Hydrolysate on the development and progression of osteoarthritis (OA) in an appropriate animal model.
Methods: The inbred mouse strain STR/ort spontaneously develops osteoarthritic lesions of the knee joint by 35 weeks of age resembling human osteoarthritis. The efficacy of Collagen Hydrolysate was tested in a randomly assigned placebo-controlled animal study. In 6 month old male STR/ort mice 0.15 mg Collagen Hydrolysate or BSA/g body weight was orally administered once a day over a treatment period of 3 months. Thin sections of the knees were analyzed for osteoarthritic changes by haematoxylin-eosin staining. OA joint damage was assessed by a well-defined semi-quantitative histopathological score. Additionally, the progression of osteoarthritis in male mice at different ages was determined and the correlation between grade of OA and body weight was investigated. A total number of 48 male STR/ort mice were analyzed in this study.
Results: According to the literature the progression of the determined grade of OA in the non-treated STR/ort mice correlated with the aging of the animals. While female mice developed only mild forms of OA, 85% of the non-treated males showed extensive OA-like lesions at the end of the study. The oral administration of Collagen Collagen Hydrolysate over 3 months led to a pronounced decrease in cartilage tissue degeneration in the knee joints. The incidence of severe joint destruction was clearly reduced after Collagen Hydrolysate treatment and the determined grade of OA decreased statistically significantly in comparison to the untreated control animals. Interestingly, a more detailed analysis of the data suggested a correlation between the determined grade of OA and the body weight of the STR/ort mice.
Conclusions: The results indicate that orally administered Collagen Hydrolysate was able to slow or even halt cartilage destruction in STR/ort mice. The data suggest that Collagen Hydrolysate may prevent the progression of joint degeneration in OA and could possibly be a potential disease-modifying agent for the treatment of degenerative joint diseases.

7. INFLUENCE OF DIETARY BETA-1,3/1,6-GLUCANS ON CLINICAL SIGNS OF CANINE OSTEOARTHRITIS IN A DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Abstract: Problem statement: There are indications for a beneficial effect of beta-1,3/1,6-glucans on the clinical signs of dogs with osteoarthritis. Data from a controlled trial were necessary to prove or disprove the indications.
Approach: A double-blind, placebo-controlled trial with privately owned dogs was carried out to assess the efficacy of a preparation of beta-1,3/1,6-glucans in the treatment of osteoarthritis. With the use of a questionnaire, the clinical signs were evaluated by the owners. For a period of 8 weeks, the test dogs daily received a complete dry food without or with 800 ppm beta- 1,3/1,6-glucans. There were 23 dogs per experimental group.
Results: When compared with the baseline values, the administration of beta-1,3/1,6-glucans significantly improved activity (vitality) and significantly reduced stiffness, lameness and pain. In the placebo group there only was a significant change in the clinical signs of stiffness. When the changes over time for the two groups were compared, there were no statistically significant differences, but the test group showed greater numerical improvement as to the scores for activity, stiffness, lameness and pain.
Conclusion: Beta- 1,3/1,6-glucans can be considered safe and it is suggested that a dose of 800 ppm in a dry food would be beneficial for dogs with osteoarthritis.