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What Effects Do Gelatin Preparations Have?

Therapy of Osteoarthritis

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Degenerative osteoarthritis of the locomotor system is one of the major rheumatic ailments presented today to the general practitioner. Mostly, the hip and knee joints are affected. Bradytrophic tissues (tendons and cartilage) are frequently inadequately or not at all supplied with blood and, due to their slow metabolism, cannot react either in an inflammatory or regenerative way to external noxious elements. Are gelatin preparations capable of influencing such symptoms and able to provide therapeutic support? In the study described, patients suffering from joint disease were given three different gelatin preparations; these were compared with a test substance made of egg albumin.

Pertaining to pathogenesis there are primary and secondary types of osteoarthritis; the causes of the former are mostly unknown, or at least it is not possible to clearly specify primary etiological factors that may be responsible [7]. On the other hand, there are a number of causal factors, e.g. mechanical stress, acute and chronic trauma and inflammatory joint processes that may well result in secondary osteoarthritis [14]. The slowly progressing process gives rise to a number of symptoms which in turn result in typical functional osteoarthritic disturbances and pain. In cases where the osteoarthritic syndrome is accompanied by synovitis, this is known as active osteoarthritis.

Therapy is mainly always symptom-oriented

A number of therapy possibilities are available for the treatment of osteoarthritis; however, most of these are designed to treat the symptoms. In conventional medicine, especially during the acute phase, non-steroidal anti-inflammatory/anti-rheumatic drugs are frequently used; these are designed to quickly reduce pain and to inhibit the inflammatory process [5]. However, as such drugs tend to accelerate the degenerative process [15] over the longer term and as they are frequently accompanied by substantial side-effects, individual physiotherapy is often used to relieve the symptoms. Surgical intervention is normally a last resort.

Increasing interest being shown in "chondro-protective therapy"

Increasing interest has been shown in recent years in the more specific "basic" treatments for degenerative osteoarthritis; these include e.g. chondro-protective drugs that also stabilize cartilage. These drugs are designed to inhibit the catbolic degradation of the cartilage mass, improve the nutrient and energy supply to cartilage tissue, stimulate build-up processes and slow down the progression of the degenerative process in the affected joints.
In recent years, gelatin and gelatin-containing substances (sometimes combined with L-cystine) have been included in this type of therapy. Gelatin, produced from collagenous raw materials of animal origin, is characterized by its high content of various amino acids (e.g. hydroxyproline, hydroxylysine and arginine) that play an important role in the biosynthesis of collagen [6, 8]. It is widely known and has been exhaustively described in the literature that the regular intake of gelatin has a positive effect on hair and nail growth [9, 11, 12]. There are also a number of empirical (e.g. [2]) and clinical [1, 6, 10, 13] studies that indicate that gelatin can play a supportive and pain-reducing role in the treatment of degenerative joint disease.
In the study described below, these findings were checked by investigating the effect of three different gelatin preparations (manufacturer: Deutsche Gelatin-Fabriken Stoess AG, Eberbach) and a substance containing egg albumin on patients suffering from osteoarthritis.

Patients and their symptoms

Of the 52 patients evaluated in the study (24 women, 28 men, mean age 56) suffering from degenerative hip or knee disease, 10 had unilateral Cox-arthritis, 31 degenerative changes of both hips and 21 severe osteoarthritis of the knee. In more than half the cases, the condition had persisted for over 5 years; only 10% had had the condition for less than 2 years. With the help of x-rays, osteoarthritis of the first to third degrees was diagnosed; in all cases this was diagnosed as the activated form of the disease. Table 1 gives an overview of the relevant clinical diagnoses of the pool of patients.

Therapy

In a controlled double-blind study using parallel groups, the following test substances were compared:

a) Highly purified collagen hydrolysate produced using enzymatic hydrolysis; the substance, like gelatin, contains a high proportion of the amino acids arginine, glycine, hydroxyproline, proline and hydroxylysine.
b) Gelatin
c) Gelatin + glycine + $CaHPO_4*2H_2O$
d) Egg albumin

Each of the four substances was administered in a randomized manner over a period of 60 days with a treatment-free interval of ca. 2 months between treatments with each substance. Each day, the patients were given 10 g of substance in the form of 20 tablets (each of 0.5 g) distributed over the day.
Analgesics/anti-inflammatory drugs taken by the patients in various doses before the start of the study were able to be taken in controlled form over the duration of the study; however, no anti-rheumatic drugs could be taken during the study and indeed for 1 year prior to the start of the study.

(picture: Industrial production of gelatin: jelled gelatin subsequent to the cooling process)

Criteria

The following symptoms were taken into account in assessing the success of treatment:
- Pain on starting to walk
- Stiffness on starting to walk
- Pain during the night
- Sensitivity to weather
- Exhaustion
- Sensitivity to cold
- Stress pain
- Tiredness pain
- Muscle pain
- Pressure pain over the articular joint
- Pain in the trochanter
- Pain on movement
- End phase pain

These subjective criteria were entered on a scale by the patients as "not present" <0>, "moderate" <1> or "severe" <2>. The initial score, entered by each patient at the start of a cycle, was then compared with the one entered at the end. To obtain a total overall score, all of the pain scores (the same weighting for all pain types) were taken into account. These were then used to indicate the degree of general "quality of life". In addition, the mobility of the affected joints was measured at the beginning and at the end of the study; this was done by measuring the angle between basic and final position in several planes.

The mean consumption of analgesics (tablets per day) at the beginning and end of the study was also used as a parameter.
In addition, in all patients, the erythrocyte sedimentation, transaminase, alkaline and acid phosphotase and the serum antibodies against types I, II and III collagen were measured before and after the study.

Results

Pain status

The most important criterion of successful treatment was the pain status as assessed by patients on the pain scale both before and after each phase of treatment. These were statistically compared using the Lehmacher test. Overall, it was shown that administration of test substance D (egg albumin) had an insubstantial and insignificant influence on the condition of the patient whilst the three other treatments resulted in substantial reduction of symptoms (see tables 2 & 3). This differentiated statistical comparison (CHI quadrat test) with respect to changes in pain scores (pre- and post-treatment in each phase) of the four test substances showed that substance D (egg albumin) was significantly different compared to at least one other test substance with respect to all criteria (with the exception of "sensitivity to weather"). However, it has to be noted that, with respect to "tiredness pain" only substance A (collagen hydrolysate) and to "pain during the night" only substance B (gelatin) differed from substance D. In addition, treatment with substance C (gelatin + glycine + $CaHPO_4{}^*2H_2O$) showed no difference to substance D with respect to "exhaustion". The four substances could best be statistically differentiated using the criterion "pain on movement". All test substances were significantly different (except for the comparisons A/C and B/D); however, in 10 patients, an improvement in the score was noted subsequent to treatment with substance D (egg albumin).
In the course of the various treatments, a maximum reduction in the score of 17-18 points in comparison with the initial values was noted with substance A (sum of scores from 3 patients with respect to collagen hydrolysate). In contrast, with substance D (egg albumin), the increase in the score was only 2 points. The scores with the various gelatin preparations (A, B, C) were reduced on average by 7.4-9.0 points; however, there was no statistically significant difference between the three treatment forms. Again, there was a significant difference between the gelatin preparations and substance D (egg albumin), the latter having a negligible influence on pain (table 4). It should be noted that in all 12 patients where a reduction in the score subsequent to treatment with substance D was > 26%, treatment with another preparation had already been given. In a separate action (not described here in detail) the substance D was administered exclusively; it was shown that the reduction in the score was below 26% in every case.

Table 1: X-ray diagnoses – incidence in 52 patients prior to the start of the study

Narrowing of articular joint cavity	52
Osteophytosis	41
Sub-chondral sclerosis	28
Cysts	10
Prostusio acetabuli	6
Erosion	3

Table 2: Pain status – pre-and 2 months after administration of substances

(No. patients with symptoms)

Treatment

Pain status	A	B	C	D
Pain on starting to walk	48/38	51/46	46/37	41/45
Stiffness on starting to walk	49/42	45/37	35/28	42/42
Exhaustion	22/15	34/20	13/06	27/27
Sensitivity to cold	31/20	41/24	25/07	31/31
Stress pain	52/44	52/51	51/45	52/49
Tiredness pain	52/44	51/44	45/40	51/45
Muscle pain	35/24	47/29	38/18	34/34
Pain during the night	32/22	47/22	29/13	32/28
Sensitivity to weather	40/24	47/32	39/34	43/38
Pressure pain - over articular joint - in trochanter	 46/36 39/23	 49/41 44/33	 46/38 40/42	 45/46 35/39
Pain on movement	42/30	44/35	32/26	37/38
End phase pain	49/32	50/38	47/37	47/46

Table 3: Pain score changes – intra-individual differences pre- and post administration of test substances

Treatment

Change in pain score	A	B	C	D
Increase	0	1	0	21
Reduction: < 26% 26-50% > 50%	10 17 25	7 15 29	10 18 24	19 7 5

Consumption of analgesics

The consumption of analgesics at the end of every cycle was observed to be reduced compared to the initial consumption (table 4). Here also, substance D resulted in the lowest effect (non-parametric Friedman test). In the other treatments, a significant reduction in the consumption of analgesics/anti-inflammatory drugs was recorded – in sequence A < B < C (highest percentage reduction).

One positive marginal effect was the fact that several patients lost weight over the treatment period. In addition, relief of backbone pain and an improvement in general well-being were registered.

In these observations also, a certain sequence was noted: B < A < C (lowest effect).

Table 4: Consumption of analgesics – intra-individual changes illustrated as a % reduction at the end of each treatment phase compared with initial score

Reduction (pre- / post)	Treatment A	B	C	D
< 26%	11	6	7	13
26-50%	5	7	8	21
50-75%	18	16	15	14
> 75%	18	23	22	4

Mobility

The degree of mobility of hip and knee joints at the end of the study could only be compared with the initial values. Flexion of the hip joint improved slightly (71.7° - 73.5°) whilst mobility remained either static in other planes or no worsening of the condition was noted.
Neither positive nor negative changes were observed using x-ray techniques.
During the study, only slight changes were observed in the clinical chemical parameters, erythrocyte sedimentation rate, transaminase/phosphatase values and antibody titers against the three types of collagen.

Discussion

In all 52 patients involved in the study, a clear and statistically relevant improvement in the various test parameters was established at the end of the study.
Overall, the substances containing gelatin were significantly different from that containing egg albumin (D).
These positive findings can be underpinned by the consideration that, as a result of the cartilage protection therapy, the enzymatic and/or mechanical generation and release of irritation factors (tissue fractions) and inflammatory mediators are reduced in the osteoarthritic joints. The result in fact was an individually observed analgesic effect. It is also conceivable that the administration of gelatin-containing preparations results in the build-up of a pool of amino acids within the body. This would substantially improve the nutrient supplied to cartilage tissue, thus enabling chondrocytes to form increased amounts of cartilage matrix [3, 4].

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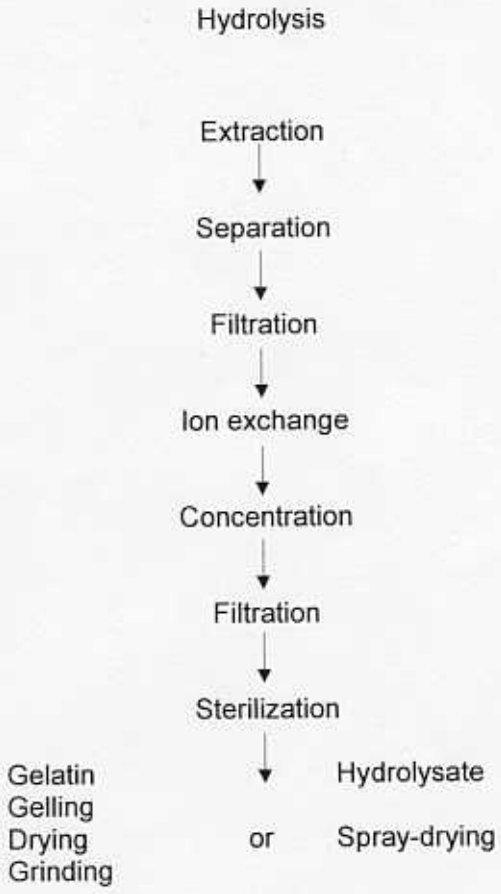
Gelatin manufacture

Gelatin is a pure protein obtained from collagenous materials such as the connective tissue, bone and hide of slaughtered animals. The materials are subjected to a complex extraction and purification process. The gelatin and gelatin hydrolysate are obtained using thermal and enzymatic hydrolysis. The following process steps are involved:



Gelatin application areas:

Gelatin is a foodstuff with special technological properties. In the food industry, gelatin plays a major role as an odor- and taste-neutral gelling and thickening agent for desserts, pastries, aspic products, confectionery and dietetic foodstuffs.

In pharmaceuticals, gelatin capsules represent an "elegant" and important dosage form. Also, gelatin and, particularly, gelatin hydrolysate, are used as excipients in tableting, film-coating and the micro-encapsulation of sensitive substances. Special types of gelatin are chemically modified for use as plasma expanders. Foamed gelatin sponges are suitable for use as styptic agents.

The use of gelatin in the area of photography remains important. Synthetic materials have not been able to replace natural gelatin with its special technological properties. Recently, special forms of gelatin have been used for the manufacture of extrusion foil and injection-molded articles.