



[Translator's note: The figures and illustrations have been reproduced in simplified form, so that the German original will be needed for cross-reference to understand the graphs, influence lines and other graphic elements.]

Degenerative joint diseases

# Can a mixture of gelatin and L-cystine stimulate proteoglycan synthesis?

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→ Keywords

Arthrosis

Enzymatic decomposition, gelatin, L-cystine

Degenerative joint diseases confront the physician in practice almost daily. Today they are one of the most important causes of early invalidism of the sick worldwide, and thus also have great economic significance. Half of the populace already suffers from degenerative joint changes by the age of 35. From age 55 on almost everyone is affected. This makes timely, effective therapy which is free of side effects all the more important.

Every arthrosis begins with damage to the cartilage of the joint, which can be caused by many contributing factors (aging processes, overloading of the locomotor system, genetic factors, metabolic diseases, acute and chronic traumas, inflamed joint processes etc.).

Arthrosis usually progresses slowly and causes little problem in the first few years. Only as cartilage wear increases is

there increased limitation of mobility, and later also come intrusively painful inflammations of the joint capsule.

For therapy of the symptoms there are physical measures available such as heat treatment, massage and kinesitherapy, for medicinal treatment there are medications like nonsteroid antirheumatics and corticosteroids. For a number of years there has been considerable interest in the use of substances which provide the body with ingredients which are needed for the maintenance of cartilage substance and functionality. This is based on the following considerations:

Cartilage consists essentially of the chondrocytes (cartilage cells), the collagenous fiber framework, and the homogeneous intermediate material. The chondrocytes are the only living elements in this structure: they produce the other components of

the cartilage. The functionality of the cartilage is therefore crucially dependent on these cells.

What processes lead to degeneration of the cartilage. . . . . ?

The collagen fibers (approximately 50% of the cartilage mass) constitute the framework of the cartilage; they enable the structure of undergo pressure without permanent deformation. The intermediate substance (about 30% of the cartilage mass) which surrounds the collagenous fibers and holds them together, consists of proteoglycans and glycoproteins. It is responsible for the permeability and elasticity of the cartilage. The proteoglycans are macromolecules with a high water absorbing capacity, and consist of mucopolysaccharides and protein. The higher the proportion of proteoglycans, the greater the

water absorbency and water content of the basic substance, and also the better the diffusion conditions in the cartilage and the alimentation of the chondrocytes [5]. The influence of the factors mentioned above can bring about a limitation of the function of the chondrocytes. In healthy cartilage tissues there is equilibrium between the synthesis of collagen and proteoglycans on the one hand and their simultaneous enzymatic decomposition on the other hand. If this equilibrium is disturbed, the decomposition predominates: the cartilage material is reduced and the functionality is limited.

It appears to make sense, therefore, to impose regulation on the disturbed equilibrium and supply the body with building blocks for metabolism of the cartilage substance from outside. Gelatin and L-cystine in particular are available for this purpose.

... how can this be countered by therapy?

Gelatin is made by boiling connective tissue (skins, bones, sinews), by denaturation of the collagen which it contains. Hence it contains the amino acids which are requisite for the new buildup of collagens (especially hydroxyproline and hydroxylysine). The sulfurated amino acid L-cystine is an essential ingredient for the biosynthesis of mucopolysaccharides already mentioned above [2], for example chondroitin sulfuric acid, a

major component of the dry mass of the cartilage tissue. The use of gelatin is already familiar as an old home remedy for the treatment of arthritis; many older people take simple cooking gelatin. In accordance with the make-up and effective mechanism (Fig. 1), only when both gelatin and L-cystine are administered can a stimulation of the synthesis of collagen and proteoglycan be expected.

In the investigation described below, the use of an orally deliverable mixture of gelatin and L-cystine will be tested in various forms of arthritis in a large number of patients, and its efficacy and tolerance examined.

#### Patient corpus and methodology

In the years 1985 and 1986 356 patients were treated by the author with a ready-made mixture of L-cystine and gelatin (L-cystine 10.8 g, gelatin ad 630). The mixture was in granular form (Gela-Feban<sup>®</sup>, Febena GmbH, Cologne).

The dosage was 1 level tablespoon of the granules (approximately 7 g or 10 ml), mixed with yoghurt, fruit juice or milk, in the morning on an empty stomach.

Table 1 indicates the distribution of the diseases among the patients. Multiple listings were possible, so that the total number of indications exceeds the stated number of patients. In particular, the patients with gonarthrosis often also suffered

from polyarthrosis of the hands; coxarthrosis was often accompanied by spinal syndrome, osteochondrosis and spondylosis. Also among the patients were women with osteoporosis.

The treatment period was at least three months, in most cases it lasted six or nine months, and in some cases up to 12 months (see Fig. 2).

The efficacy of the medication was checked primarily on the basis of subjective statements from the patients. In the cases of gonarthrosis in particular it was possible to measure a reduction in the use of non-steroidal antirheumatics and a reduction in the frequency of intra-articular injections as objective criteria.

#### Results

In most cases the effectiveness was rated "good" or "very good" by the patients. In only three cases (0.8%) did the patients report no effect.

Almost all cases of gonarthrosis were sufficiently free of complaints after taking the preparation, normally for six months, that the nonsteroidal antirheumatics which had before been necessary could be discontinued.

The frequency of intra-articular injections, which stood at two per month before the investigation, dropped to 1-2 injections per year under the

treatment with the gelatin/L-cystine preparation. The medications formerly used for injection were phytopharmaca and chondroprotectives, and at the end phytopharmaca and prednisone 10 mg.

The effect of the treatment on patients with polyarthrosis of the hands was also good to very good, a fact which manifested itself in an objectively measurable way in an unmistakable reduction in the use of nonsteroidal antirheumatics (Table 2).

Contrary to these very positive outcomes are the results of treatment of patients with coxarthrosis and spinal syndrome with degenerative changes. Here only a slight reduction in the use of antirheumatics could be registered.

No undesired side effects were indicated by any patient; the gastric tolerance was good without exception. However, some patients developed a certain aversion to the mixture of gelatin/L-cystine with yoghurt as time went on. A gratifying side effect was reported by most of the patients: nail and hair growth improved considerably.

#### Discussion

Can appropriate building materials arrest or retard the destruction of cartilage?

Persons affected by arthrosis generally require constant treatment. The chronic course leads all too often to a certain therapeutic resignation, however. But this is unjustified, since

today there are a multitude of forms of physical and medical therapy which help patients to bear and live with their disease.

The makeup of healthy cartilage is known for the most part. This makes it possible to intervene in the metabolism of the cartilage material with appropriate building materials, to arrest or at least retard further destruction.

That these are not only theoretical considerations is proven by the results of the investigation presented here, using a mixture of gelatin and L-cystine on a large number of patients. The improvements in joint mobility which were attained are impressive, as is the reduction in pain of movement, evident not only in the subjective judgments of the patients but also in the objectively measurable decrease in the use of antirheumatics and the much less frequent need for intra-articular injections. It proved to be important to have a sufficiently long period of treatment, because quick success cannot be expected due to the effective mechanism.

Patient compliance was better than average. Since the medication was prescribed only on user-paid prescriptions, it can be assumed that the substance was also actually taken in all cases.

The results of this investigation agree with earlier studies. In a comparative study over an extended time with 154 patients with chondrophia patellae,

coxarthrosis, gonarthrosis or juvenile growth impairment of the spine, U. Oberschelp [6] tested a preparation which contained L-cystine, vitamin A and gelatin. With physical therapy alone only slight improvements could be achieved in the pain and mobility. A statistically certain, evenly pronounced improvement appeared on the other hand in the groups who were treated with the preparation alone or in combination with physical therapy. The author therefore concludes that in many cases successful therapy is possible with the gelatin material alone. A very clear improvement in subjective complaints and objective measurements was also achieved with this compound by B. Götz [2] when treating youthful patients who were suffering from chondrophia patellae.

Positive results in animal experiments testify in favor of an effect on human cartilage.

The findings are shored up in theory by the fact that it has been possible in animal experiments to prove the presence of exogenously introduced, radioactively marked cystine in the joint cartilage, intervertebral disk and skeletal musculature of mice [8]. This gives reason to believe that the active substances in the medication described here actually reach the intended locus in humans as well. Animal experiments have also succeeded in showing the cartilage protect-

ing and building effect of cartilage-marrow extracts containing a high level of mucopolysaccharides [3].

These results acquire special significance in light of the fact that many nonsteroidal antirheumatics show antianabolic and catabolic side effects on the metabolism of connective tissue and joint cartilage. Some of these medications have an inhibiting influence especially on the proteoglycan synthesis of the cartilage cells [3, 4, 7]. Corticosteroids lead to degenerative changes in the ultrastructure of the chondrocytes and consequently to a limiting of the synthesis action of the cells. Under dexamethasone, for instance, animal experiments showed an increased non-physiological morbidity of the chondrocytes [1].

The other side effects of nonsteroidal antirheumatics and corticosteroids, and the problematic nature of frequent intra-articular injections, are also known.

But especially in long-term therapy, such as the treatment of arthroses, particular value must be placed on the maximum possible freedom from side effects. In these terms, the preparation described here thus represents an alternative or supplemental form of therapy, even if it will not be possible to forego the short-term use of antirheumatics or corticosteroids

in justified cases.

#### Conclusion

The use of the described mixture of gelatin and L-cystine for arthrosis patients has proven to be problem-free and in the great majority of cases extraordinarily effective, especially in cases of arthrosis of the knee and finger joints. It is practically free of side effects, is accepted well by the patients, leads to a clear improvement in the complaints and to a drastic reduction in the need for additional medications. The number of intra-articular injections can be reduced to a minimum. Due to the effective mechanism it can also be expected that further cartilage degeneration can be arrested or at least significantly slowed. And for this reason the compound should be put into use as early as possible.

#### Literature

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(See German original for arrows and lines of influence. —Transl.)

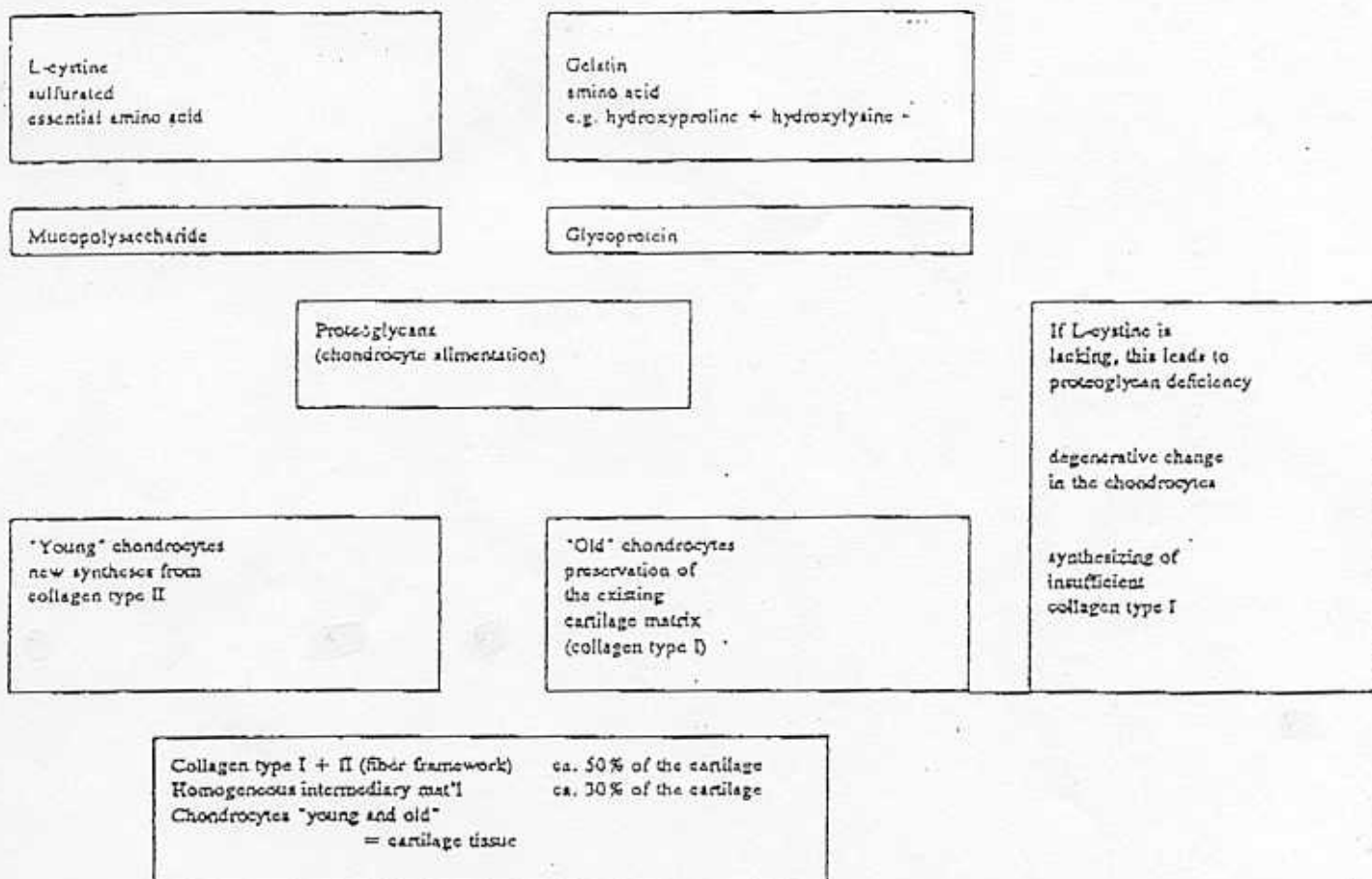


Figure 1 Effective mechanism — greatly simplified representation. Since gelatin contains almost no L-cystine, according to the effective mechanism, a stimulation of the collagen and proteoglycan synthesis can be expected only from providing both substances (gelatin and L-cystine).

Table 1 Distribution of the diseases among the patients (n = 356); multiple listings possible

Indications	Number of cases
Gonarthrosis	289
Chondropathia patellae (youth)	56
Osteochondrosis dissecans (youth)	3
Polyarthrosis of the hands (Heberden-Bouchard)	
Tarsal arthrosis	172
Coxarthrosis with spinal syndrome and osteochondrosis	143

Table 2 Improvement of complaints and reduction of additional medication

Indication	M. =	after 3 mo.	after 6 mo.	after 9 mo.
Gonarthrosis	289	+ +	+ + +	+ + +
Polyarthrosis	172	+	+ +	+ + +
Coxarthrosis	143	(+)	+	+

(+) not unquestionable, + slight, + + clear, + + + strong

[See German original for column graph]

Number of patients

250

200

150

100

50

0

3

6

9

12

Months

Figure 2 Length of period in which preparation is taken (n = 358)