Containing "glucosamine and proteoglycan," assisting health in the joints

# Validation of Proteo G.C

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### - Introduction of the Best Materials Used to Produce a Supplement for Arthritis "Proteo G.C." and Report on the Clinical Cases -

A truly effective veterinary supplement for joints focusing on the following points based on the experiences/results from 20 years of research and development of materials for human/veterinary supplements.

- Glucosamine is garnering attention as a human supplement; is it really effective?
- What are the materials for glucosamine, and how are they purified?
- What is proteoglycan, a substance garnering attention in recent years?

Clinical data from administration of "Proteo G.C.," which contains glucosamine and proteoglycan, are reported.

## What is proteoglycan?

When a bear catches salmon, it usually eats the salmon from the nose as a habit. This is said to be because salmon heads contain a high amount of "proteoglycan."

Proteoglycan exists in all parts of the body, and the amount is particularly high in the joint cartilage. The joint cartilage is bluish gel-form tissue that covers the tips of the bones, with a structure of collagen fiber net skeleton tangled with "chondroitin sulfate-form proteoglycan." It has 4 to 6 mm thickness and is softer than the bone, containing joint fluid (synovial fluid) mainly composed of hyaluronic acid. Its surface friction coefficient is lower than that between ice surfaces to offer lubricity.



Proteoglycan is constructed with core protein and about 100 molecules of chondroitin sulfate bound to it.

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The existence of joint cartilage allows smooth movement of bones without direct contact between them. The bones and the joints are protected by such joint cartilage. And the joint cartilage is protected by "proteoglycan."

"Proteoglycan" serves as a logistic center in the living organ to provide nutrients for the joint cartilage, which has no veins, as well as to suppress activities of enzymes that degrade the joint cartilage and enhance production of new joint cartilage (**Fig. 1**).

## **Outline of glucosamine**

"Glucosamine," a substance well known on TV and in newspapers, varies in raw materials, characteristics, prices, and place of origin. It would not be an exaggeration to say that such differences are not properly understood not only by general users but even by doctors or veterinarians. We avoid mentioning the raw materials used in human/veterinarian glucosamine products from other manufacturers, but we have reached the conclusion that glucosamine is difficult for the body to absorb unless a large amount of high-quality product is ingested, because its molecular weight is large.

As a "high-quality product," we have determined that "glucosamine re-purified in Japan" is effective, although it is expensive. Generally speaking, products purified overseas are insufficiently purified and may contain remaining impurities (contaminants). Most glucosamine products distributed in the market are produced in China, and they contain high amounts of minerals such as silicon (Si) and barium (Ba) due to difference in water quality between China and Japan. However, it was revealed that these minerals can be eliminated through re-purification (**Fig. 2**).



Fig 2

"Glucosamine" has two forms: "glucosamine hydrochloride" coupled with hydrochloride group and "glucosamine sulfate" coupled with sulfate group. In Japan, glucosamine is classified as "spontaneous specification for existing additives" and its manufacturing process is determined as "glucosamine is produced by hydrolysis of chitin." In Japan, therefore, only "glucosamine hydrochloride" is distributed (overseas glucosamine sulfate products can be imported and used personally). Glucosamine sulfate is distributed as a drug or supplements mainly in Europe.

As described above, glucosamine hydrochloride is produced by hydrolyzing chitin with hydrochloric acid. In general, the sulfate product is manufactured not through direct reaction with sulfuric acid and "glucosamine" but by a method where glucosamine hydrochloride is once produced and then substituted to form sulfate. However, in Western markets including Europe, a lot of products produced by only mixing the hydrochloride with sodium sulfate, without a special reaction process such as substitution, are distributed. You should be careful when using such products because they often contain only 200 to 300 mg of glucosamine per capsule, although they indicate that "Each capsule contains 500 mg of glucosamine."

Accordingly, a glucosamine product re-purified in Japan seems to be more effective. Our "Proteo G.C." uses glucosamine purified in Japan, and only legs of Chionoecetes japonicus caught in Tottori Prefecture are used as raw material. Clinical data obtained by actually administering "Proteo G.C." containing glucosamine and proteoglycan are reported.

# Validation of clinical effects

#### 1) Evaluation by pet owners

First, a monitoring survey was performed in owners of 26 animals with arthritis symptoms within the Scarecrow members.

Material: Proteo G.C. (Fig. 3)

Major raw materials: glucosamine, proteoglycan, non-denatured type-II collagen, chondroitin, glutathione yeast extract

Containing 100 mg of high-quality glucosamine/pill (140 mg)

Dose:

Age:	1-18 years;	Body weight: 2.1–25 kg
Cases:	25 dogs and	one cat
•	Period:	One month
	≥ 30 kg:	6–8 pills/day
	≥ 20 kg:	4–6 pills/day
	≥ 10 kg:	2–4 pills/day

#### ♦ Results

Improved:	22 cases	(84.6%)
Not changed:	4 cases	(15.4%)
Worsened:	0 cases	(0%)

#### Cases with marked improvement: 4 cases

#### [1] Chihuahua, male, 8 years, 1.8 kg

**Before administration:** It had pain in the anterior limbs and gait difficulty. It limped even after medication and stopped jumping.

After administration: Two weeks after starting administration, the anterior limbs were improved while walking. It played more often and brought a stuffed toy by itself. No limping was observed after starting administration.



#### [2] Miniature pinscher, female, 5 years, 5.2 kg

**Before administration:** It had had severe pain in the anterior legs for 3 years. It hated to be even touched and bit when only being touched in the anterior legs.

A steroid was administered when the pain was strong.

After administration: No dragging of legs was observed immediately after waking up. It did not hate to be touched in the anterior legs and the condition was improved so that it can run around the house.

#### [3] Miniature dachshund, male, 7 years old, 4.6 kg

**Before administration:** It was diagnosed as having dislocation of the kneecap 5 years ago. It dragged its legs while walking and ran moving the posterior legs exactly the same way. The posterior legs sometimes shook.

After administration: No tremor condition such as dragging the legs was observed after starting the administration.

#### [4] Chihuahua, male, 1 year old, 2.7 kg

**Before administration:** It had had knee joint pain since its birth. It walked as though skipping while being walked and dragged its legs on its way home.

After administration: It stopped skipping from Day 10 of administration and could go home without dragging its legs.

Clinical symptoms	Before adm	ninistration	Evaluation after administration				
Vomiting	Yes	/No	Marked improvement/slight improvement/no change				
Diarrhea	Yes	/No	Marked improvement/slight improvement/no change				
Polydipsia/polyuria	Yes	/No	Marked improvement/slight improvement/no change				
Limping/abnormal gait	Yes	/No	Marked improvement/slight improvement/no change				
Wobbling/oblique	Yes	/No	Marked improvement/slight improvement/no change				
Local fever/swelling	Yes	/No	Marked improvement/slight improvement/no change				
Abnormal muscle (right vs. left)	Yes	/No	Marked improvement/slight improvement/no change				
Mental status	Stable/Ag	ggressive	Marked improvement/slight improvement/no change				
Body weight change	Week 1 kg	Week 2 kg	Week 3 kg	Week 4 kg			

#### 2) Evaluation by veterinarians of clinics

To evaluate the improvement rate of 84.6% in pet owners objectively, an administration study was performed in 14 animals in cooperation with 10 veterinary clinics. QOL was evaluated for evaluation results for limping/abnormal gait in Clinical symptoms (**Table 1**). Results were as shown in **Table 2**.

Since results were favorable, showing that 86% had some form of improvement, with 50% having a marked response and 36% slight improvement, Proteo G.C. was suggested to have efficacy as a supplement for arthritis (**Fig. 4**).



Table 2

										* Marke	d improvement	0	Modest alleviation $\Delta$ No change
Species	Sex	Age	Body weight	Admini stration number	Period	Drugs	Bone deform ation	Affected sites	X-ray	Weight change	Clinical Symptoms		General comment
Yorkshire terrier	Female	15	3.3	2	112	-	Present	Four limbs	-	-	Abnormal gait	*	Difficulty in walking improved in a month to be able to walk.
T. poodle	Male	1	3.7	2	210	-	-	Posterior legs	-	3.5	Abnormal gait	0	It became able to run although slightly unstable and wobbling.
M. dachshund	Male	6	5	2	60	_	-	Hip joints	-	-	Abnormal gait	*	Improved and recovered in a month. Easy to administer every day.
G. retriever	Contrace pted	9	32	8	30	-	Present	Hip joints	-	-	Abnormal gait/muscle	0	Limping symptom was improved in 2 weeks.
Border collie	Female	13	20	20	30	-	-	Hip joints	_	-	Abnormal gait/muscle	0	Limping symptom was alleviated.
Mix	Male	12	16	4-6	30	-	-	Hip joints	_	-	Abnormal gait	Δ	Good preference although no marked improvement.
Labrador	Contrace pted	17	20.5	6	20	Rimadyl or previcox	Present	Left hip, shoulder, and elbow joints	Present	-	Abnormal gait/muscle and wobbling	*	It is animated with reduced wobbling.
Sheltie	Castrated	13	14	4	15	_	_	Hip and elbow joints	_	_	Hating to be touched in the legs	0	Although hating to be touched, it was more animated than before.
Yorkshire terrier	Male	16	2.6	2	40	Meloxic am	-	Knee joints	-	2.45	Abnormal gait	*	Although joints were unstable, condition was good without limping or pains.
Mix	Male	19	15	3	40	-	-	Hip joints	_	-	Difficulty in standing	0	After a month, it smoothly stands with improvement in walking.
Mix	Male	14	13	4	30	_	_	Low back	_	-	Abnormal gait	*	It was slightly wobbling before, but started to pull the lead while walking from Day 5.
T. poodle	Contrace pted	15	2.2	3	22	-	Present	Shoulder and knee joints	-	2.1	Abnormal gait	*	It became able to jump as it had been in its youth.
Labrador	Castrated	12	28	8	20	-	-	Hip and wrist joints	_	-	Abnormal gait	*	Standing and walking speed became faster.
Corgi	Castrated	13	11.5	5	25	_	_	Hip joints	_	11.4	Slight difficulty in moving on stairs	Δ	Switched from Boma Zeal but no change when compared.

## **General statement**

Scarecrow has been a research and development company of veterinary supplements for 10 years since its establishment, and the veterinary supplement market seems to have expanded compared to 10 years ago. While the pet food market is said to be 400 billion yen-scale, it seems that the supplement market has also grown to 10 billion yen-scale, although smaller. Supplements are an area expected to grow in the future, and characterizing this growth, purchase in reliable pet shops and sales via counseling by veterinarians will form important markets.

We will continue to make every effort to introduce the clinical effects of our products, such as "Panfenone S," "Ippet S," and "LPS Dr," through academic presentations and the present journal.

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