

The efficacy of Pycnogenol-containing Pinfenon S in the treatment of intractable diseases of dogs*

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Measurement of platelet aggregation revealed a relationship between the measured values and various diseases of dogs. We report here therapeutic benefit that was observed with administration of Pinfenon S (Pycnogenol and citrate-fermented sesame extract) by measuring platelet aggregation in dogs in whom conventional Western medical treatment did not show therapeutic benefit. Absorption of Pycnogenol in Pinfenon S appears to be enhanced by combining it with citrate-fermented sesame extract, which has a chelating effect. Pycnogenol has benefits for various diseases by exerting an inhibitory effect on platelet aggregation as well as anti-virus and immune-adjustment effects such as on the interferon activity.

Keyword: Pycnogenol, platelet aggregation inhibition, veterinary field

Introduction

Pycnogenol contained in Pinfenon S is a material extracted from the bark of a pine botanically called *Pinus pinaster* (French maritime) growing in a limited area in the southwest of France and is a safe and water-soluble natural food, which has very high bioactivity. The proanthocyanidins and more than 40 types of organic acids contained in Pycnogenol are low-molecular antioxidants with special flavonoid properties and are powerful active oxygen removers belonging to the polyphenol group. More than 130 research papers from investigational institutes around the world have been published on Pycnogenol, which demonstrates anti-inflammatory effects,¹ peripheral vasodilator effects,² inhibitory effects on platelet aggregation,³ peripheral vascular resistance-lowering effects,⁴ immune adjustment effects,⁵ connective-tissue-strengthening effects⁷ and vitamin C enhancing effects⁸ on biological processes. Accordingly, Pycnogenol is widely used as in alternative and complementary therapies in human medical practice. In the ophthalmologic field, study papers have reported that Pycnogenol is effective for diabetic retinopathy and cataracts. In gynecology and obstetrics, patents for therapeutic drugs to treat endometriosis and dysmenorrhea have been granted.^{9,10}

This time, we decided to investigate to which diseases Pinfenon S is efficacious in the veterinary field, where Pycnogenol is a major ingredient of Pinfenon S and noted for its efficacy in the medical field.

Methods and Materials

Study 1

We first measured platelet aggregation in 119 dogs to find the relationship with diseases in dogs. We used a whole blood platelet aggregation measuring device (made by SSR Engineering Co., Ltd.), which adopted a screen filtration pressure (SFP) method. Adding aggregation-inducing substances (including ADP and COLL) from low concentration to high concentration (4 channel [4 concentration levels]) to aliquots of whole blood (a condition closer to in vivo under an existence of unaltered blood = erythrocytes, and leukocytes with hyperlipidemia), the whole blood was sucked through a micro-mesh filter. Platelet aggregation tests were conducted to evaluate platelet aggregation by measuring and analyzing vacuum pressure caused by clogging micro-mesh filter holes with platelet clots.

As a judgment scale, “±0” was defined as the safety margin in an appropriately healthy condition; plus trend value “+2” as the strong elevation requiring prevention measures to thrombosis, heart failure, diabetes, and dementia; and minus trend value “-2” as the declining trend for platelet aggregation capability requiring attention to bleeding during surgery.

From the results of Figure 1, the mean value of tumor-related diseases ranging from lymphoma (No. 1) to mastocytoma (No. 7) is “+2” showing an elevation trend, and the mean value of items ranging from mitral insufficiency (No. 8) to filariasis (No. 16) is “+2” showing an elevation trend for platelet aggregation capability. The mean value of items ranging from thrombocytopenia (No. 17) to Cushing’s disease (No. 22) is “-1” and this shows platelet aggregation capability is

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in declining trend. When considered with disease status, the results above appeared to show high correlation in general between the measured value and disease status.

Mean values, total of 119 dogs

Collaborated institutes: Nippon Veterinary and Life Science University and nation-wide veterinarians in private practice

No.	Diagnosis	Number of dogs	Rating by Type						
			+3	+2	+1	±0	-1	-2	-3
1	Lymphoma	14		•					
2	Intra-abdominal tumor	3		•					
3	Leukemia	5		•					
4	Thyroid cancer	6			•				
5	Liver tumor	3		•					
6	Non-epithelial malignancy	3		•					
7	Mastocytoma	5			•				
8	Mitral insufficiency	7			•				
9	Chronic renal failure	6		•					
10	Hepatic fibrosis	3			•				
11	Diabetes	10		•					
12	Dementia	13		•					
13	Pancreatitis	5			•				
14	External otitis	5			•				
15	Cystitis	5		•					
16	Filariasis	5		•					
17	Thrombocytopenia	5				•			
18	Hypothyroidism	2					•		
19	Intravascular sarcoma	3					•		
20	Pemphigus	3					•		
21	Portal vein shunt	3					•		
22	Cushing's disease	5						•	

Figure1(above)

Study 2

Based on study 1 data, we decided to study the effect of Pinfenon S via administration to animals with intractable diseases in whom improvement had not been observed using conventional medical therapies.

Test material

Pinfenon S tablet 140 mg (Pycnogenol and citrate-fermented and -extracted complex of sesame) was used as a test drug.

Method of use

Basically, 2 tablets per dose of Pinfenon S was administered once daily to dogs less than 10 kg in bodyweight and 3 to 6 tablets per dose once daily for 10 to 20 kg. Dogs were given Pinfenon S alone and limited to those without concomitant drugs or supplements. The test period was set to 4 weeks, and platelet aggregation values were measured before and after administration. Also at sites unable to perform platelet aggregometry, QOL and hair-coat status were observed.

Animals studied

A total of 19 dogs with intractable diseases who presented at two animal hospital sites from September 2004 to June 2006 were included in the study.

Results

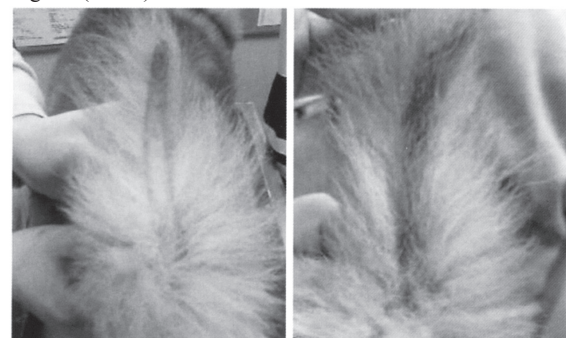
The dog population consisted of 18 dogs who underwent platelet aggregometry after administration of Pinfenon S alone, and one dog without undergoing platelet aggregometry; the total of 19 dogs showed 6 with complete remission, 8 with partial remission, 5 with no change, and 0 with deteriorated. (Figure 2)

Case	Breed of dog	Age	Sex	Disease name	Platelet aggregation measurement value	Efficacy (complete response = ⊙, Partial Response = ○, No Change = △)	Clinical symptom
1	Hybrid	2	M	Lithuresis	+1→+1	△	Cystitis remained
2	Toy poodle	14	F	Mitral insufficiency	+2→±0	○	Coughing disappeared
3	Maltese	9	F	Mitral insufficiency	+2→±0	○	Caught up lost bodyweight
4	Pomeranian	9	F	Cushing's disease	+2→+1	○	Abnormal amount of drinking decreased
5	Shih Tzu	13	F	Mitral insufficiency	+2→±0	⊙	Coughing disappeared
6	Toy poodle	16	F	Diabetes	+2→±0	⊙	Vigor recovered from death-bed status
7	Pug	1	M	Atopy	+2→+2	△	Still bleeding and swelling, No change
8	Shiba	15	F	Atopy	+2→+1 or slightly more	○	Itching and scaling off disappeared
9	Shiba	17	M	Dementia	+2→+2	△	Died later
10	Golden retriever	11	F	Pain of arthritis	+2→+1	⊙	Condition to be able to walk without pain lasted
11	Labrador retriever	10	F	Atopy	+1→±0	○	Itching disappeared
12	Shih Tzu	4	F	Atopy	+2→+2	△	Still itching
13	American cocker spaniel	8	F	External otitis	+1→±0	○	Sore Improved
14	Miniature dachshund	1	F	Atopy	+1→+1	△	Still itching
15	Cavalier King Charles spaniel	9	M	Mitral insufficiency and thyroid tumor	+2→+1 or slightly more	⊙	Coughing disappeared
16	Miniature dachshund	2	M	Gastritis	+2→±0	○	Vigor returned
17	Boston terrier	2	M	Anterior uveitis	+2→±0	⊙	Gum and tear in eyes improved
18	Chihuahua	8	M	Gonarthrits	+1→±0	○	Complete remission from pain after 3 months one-foot disability to stand on the ground
19	Shiba	12	M	Unknown cause Alopecia of tail	No measurement (Evaluation picture Fig. 3)	⊙	

Figure2(above)

One dog without undergoing platelet aggregometry presented with alopecia of the tip and underside of the tail of unknown cause on January 28, 2005. Administration of ointment and Reishi caused no change, and hence Pinfenon S alone was administered at a dose of four tablets twice daily from March 4, which resulted in 90% to 100% of hair growth in one month with 70% of length recovery of the hair coat. (Figure 3)

Figure3(above)



January 28, 2006

April 1, 2006

As comprehensive evaluation,

$$\frac{\text{Complete remission} + \text{Partial remission}}{\text{All dogs}} \times 100 = \text{efficacy ratio for all dogs}$$

Efficacy ratio = 73.6%.

Discussion

Pine bark is used as traditional folk remedy that Canadian natives administered by drinking a pine bark and needle decoction before Pycnogenol was developed. Pycnogenol contained in Pinfenon S was used as a dietary supplement. It has been granted Generally Recognized As Safe (GRAS) status, which is food safety criteria in the USA, and granted approval of Therapeutic Goods Administration (TGA), the strict safety criteria of Australia. A clinical trial is underway using the national budget regarding “Lymphedema of the arm after operative treatment of breast cancer” in the National Center for Complementary and Alternative Medicine (NCCAM), one of the National Institutes of Health (NIH) centers in the United States. Pycnogenol contained in Pinfenon S is considered to be absorbed efficiently from the intestine in animals due to the combination with citrate-fermented sesame extract, which has a chelating effect. Pycnogenol has benefits for various diseases by exerting an inhibitory effect on platelet aggregation, as well as anti-virus and immune-adjustment effects such as on modifying interferon activity.

This time, we administrated Pinfenon S alone to 19 dogs with intractable diseases. We performed platelet aggregometry and investigated the change in appearance. Results showed improvement in platelet aggregation with a high efficacy ratio of 73.6% in 18 dogs along with improvement of symptoms, including hair growth, in one dog. However, we did not sufficiently perform other examinations in 18 dogs who underwent platelet aggregometry. Therefore, in the future we plan to increase the number of dogs and investigate the relationship between changes in platelet aggregation and improvement in symptoms caused by administration of this health food supplement.

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