CAP
Companion Animal Practice
CAP2011.10

Anti-Tumor Effects of IPET-S (with Taheebo) on cancer-bearing dogs and cats

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In the March 2010 issue of this journal, we published the effective results of IPET-S on 84 cases at 28 operating animal hospitals. However, given the lack of clarity as to dosage timing, whether IPET-S was administered in conjunction with other pharmaceuticals, and the relatively few cases of IPET-S-only treatment, we recognized the need to collect more data. In this study, we had caregivers dose 15 tumor-bearing dogs and cats with IPET-S. Our study reflected administration timing and other factors, investigating IPET-S palatability, anti-tumor effects, QOL improvement, and presence of metastasis, determining whether IPET-S is an effective dietary supplement. The following is a report of our study and results.

Key words : Taheebo tumor promotion inhibitor IPET-S

◯ Introduction

TAHEEBO, contained in IPET-S, is a polyphenol extract from the bignoniaceae tabebuia avellanedae tree that grows natively in Brazil. Taheebo includes NQ801, an active component that not only inhibits the growth of cancer cells, but also presents selective toxicity that does not affect normal cells. Patents have been awarded in four countries (see Fig. 1), and the extract is used widely as a complementary and alternative medicine for cancer treatment in humans. Tohoku Fukushi University professor Dr. Takusaburo Ebina (formerly of the Miyagi Cancer Center) published a journal article describing the metastasis invasion inhibition effect of Taheebo on cancer cells, Taheebo's apoptosis induction, and antiangiogenic effect. University of Sao Paulo honorary professor Dr. Walter Radames Accorsi, a noted scholar on South American medicinal plants, reported that his research showed Taheebo to demonstrate a variety of effects in addition to anti-cancer properties, such as anti-inflammatory, analgesic, and diuretic properties.

In a prior issue of this journal (March 2010) we studied the effects of IPET-S containing Taheebo NQ801 on small animals in a clinical setting. We reported this same anti-tumor and underlying disease effects in small animals, as well as expected increase in QOL in animals. However, we did not have sufficient data regarding IPET-S-only dosages, and we could not claim to have proper support to claim effectiveness. Accordingly, here, we present our study reflecting the collection of more data, dosage administration timing and other factors, investigating IPET-S palatability, anti-tumor effects, QOL improvement, and presence of metastasis

Fig. 1 Japanese, American Patents

Fig. 2 IPET-S (containing Taheebo)

◯ Test Specimens, Animals

● Test Specimens

PET-S (containing bulk powder) 1 Tab 150mg **(Fig. 2)**

Wt. less than 5kg	1 Tab
5kg to 10kg	2 Tabs
10kg to 20kg	4 Tabs
20kg to 30kg	6 Tabs
30kg or more	8 Tabs

● Test Animals

We utilized 15 animals (11 dogs, four cats) diagnosed histologically or clinically with tumor masses. Of these, 13 animals were diagnosed with malignant tumors, and two were indeterminate unknown.

Dogs Aged 9 to 16 yrs., avg. 13.2 yrs., median 13 yrs.
Wt. 2.8 to 33.0kg, avg. 15.8kg, median 11.7kg

Cats Aged 3 to 13 yrs., avg. 9.8 yrs., median 13 yrs.
Wt. 2.5 to 4.6kg, avg. 3.8kg, median 3.9kg

◯ Studied Items, Methodology

● Studied Items

Palatability, Q OL, anti-tumor effect, presence of metastasis during dosage period

● Methodology

Group 1: IPET-S-only dosage after surgery or cessation of chemical treatment **(five subjects)**

Group 2: IPET-S-only dosage with no aggressive treatment after diagnosis **(seven subjects)**

Group 3: IPET-S administered with chemical treatment for an underlying disease **(three subjects)**

● Determination of anti-tumor effect

We used the RECIST (Response Evaluation Criteria in Solid Tumors) standard to evaluate the anti-tumor effects. Namely,

CR: Tumor completely disappears after four weeks or longer, based on visual or image inspection

PR: Tumor reduces 30% or more after four weeks or longer, based on visual or image inspection

PD: Tumor increases 20% or more, based on visual or image inspection

SD: Changes not categorized as PR or PD

Improvements according to impression preparation are evaluated as PR, PD or SD according to ratio of cells.

◯ Results

◯ Palatability

All 15 subjects accepted their dosages without issue. The small size of the tablets (5mm diameter x 3mm height) allowed for mixing them in with food for easy acceptance.

◆ Group 1: IPET-S-only dosage after surgery or cessation of chemical treatment: **Five subjects**

Dosage Period 66 to 269 days (avg. 172 days; median 186 days)

◯ Anti-Tumor Effect

All five subjects exhibited a favorable effect, passing the dosage period without a recurrence of tumors or occurrence of new tumors.

No metastatis in any subject during the dosage period

◯ QOL

Of the five subjects, one exhibited diarrhea, and four exhibited improvement

◆ Group 2: IPET-S-only dosage with no aggressive treatment after diagnosis: **Seven subjects**

Dosage Period 60 to 262 days (avg. 153 days; median 168 days)

◯ Anti-Tumor Effect

Clear disappearance or reduction:	One subject (PR)
No change:	One subject (SD)
Increase:	Five subjects (PD)

No metastasis in four subjects, metastasis in three subjects during dosage period

◯ QOL

Improvement:	Five subjects
Stable:	One subject
Aggravation:	One subject

◆ Group 3: IPET-S used in conjunction with chemical treatment for underlying disease: **Three subjects**

Dosage Period 33 to 573 days (avg. 213 days; median 73 days)

◯ Anti-Tumor Effect

Clear disappearance or reduction:	No subjects
No Change:	One subject
Increase:	Two subjects

Two with no metastatis, one with metastatis during dosage period

◯ QOL

Improvement:	One subject
Stable:	One subject
Aggravation:	One subject

○ Observations

There were no issues with palatability for any of the subjects. During IPET-S dosage, one subject exhibited diarrhea, but a temporary reduction in dosage resulted in improvement. A return to the original dosage did not result in a recurrence of symptoms, leading us to conclude that there are no strong side effects.

Making a clear judgment of the effects of IPET-S-only dosage in Group 1 and Group 3 was difficult. Accordingly, we once again administered dosages for evaluation, adding four subjects to the IPET-S-only group reported in our study published in a prior journal issue (March 2010) for a total of 11 subjects for analysis. As a result:

● Anti-Tumor Effect

Clear Disappearance or Reduction: Three subjects (27.3%)
No Change: One subject
Increase: Seven subjects

Of the three subjects exhibiting a clear disappearance or reduction: CR: One subject PR: Two subjects.

Metastasis during the dosage period (all seven; since four subjects from prior year were indeterminate)

(**Fig. 3**)

None: Four subjects (36.4%)
Present: Three subjects

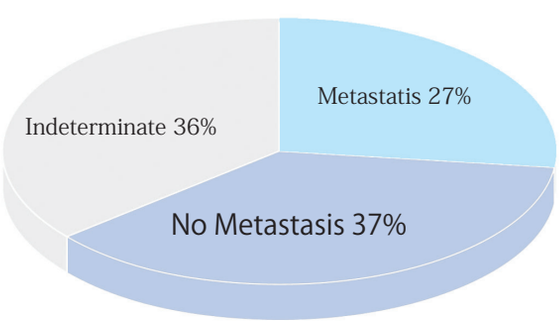
○ QOL

Improvement: Eight subjects (72.7%)
Stable: One subject
Aggravation: Two subjects

The response rate for the subject group administered an IPET-S-only dosage (CR + PR) was three of 11 subjects (27.3%). QOL improvement was eight of 11 subjects (72.7%). **(Fig. 4)**

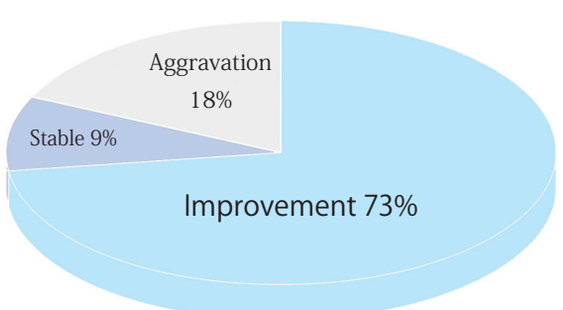
In this study the response rate of the anti-tumor effect of IPET-S-only dosage was a CR of one subject and a PR of two subjects (27.3%). Of the two PR subjects, one was evaluated via impression preparation. Removing this case results in a response rate of two out of 11 subjects (18.2%). The tumor indicating CR was dog transitional cell carcinoma of the urinary bladder. The PR was a dog digestive tract plasma cell neoplasm evaluated by impression preparation as dog mammary gland cancer. The behavior of the dog transitional cell carcinoma of the urinary bladder was extremely locally invasive, with a high metastasis rate. However, having confirmed with hospitals that used the supplement, two years later, there have been no confirmed local recurrence or metastasis. Of the two subjects indicating PR, the two cases of mammary gland cancer showed gradual reduction over the two months after the start of dosage. However, there was a gradual increase subsequent, including a metastasis to the lungs, resulting in the death of the subject 160 days after the start of dosage. The other subject experienced a cessation of mucous and bloody stool, and continues to be doing well.

Comparing our response rate with the response rate of piroxicam (a commonly used cycoxygenase inhibitor for dog squamous cell carcinoma of the oral cavity) in a veterinary clinic setting, it is unclear whether it is the same level or whether it is greater. In other words, where Schmidt et.al. used piroxicam (an anti-infammatory analgesic) only for dog squamous cell carcinoma of the oral cavity, three of 17 subjects (17.6%; CR:1, PR:2) were reported to have responded. From this result, we can say that IPET-S is a dietary supplement exhibiting anti-tumor effects for cancer-bearing animals similar to piroxicam, which is used as an effective anti-



Presence of Metastasis	Subjects
Metastasis	3
No Metastasis	4
Indeterminate	4

Fig. 3 Presence of Metastasis



QOL	Subjects
Improvement	8
Stable	1
Aggravation	2

Fig. 4 QOL

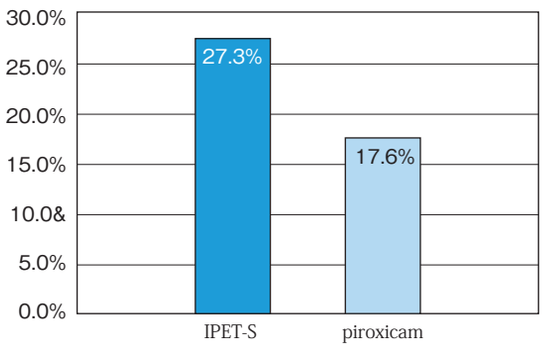


Fig. 5 Anti-Tumor Effect

tumor pharmaceutical in dog squamous cell carcinoma of the oral cavity and dog transitional cell carcinoma of the urinary bladder, etc. (Fig. 5)

In this study, we administered an IPET-S-only dosage to dogs and cats with tumors. As a result, we can conclude that there are no significant side-effects with IPET-S. We can also conclude that there is an expected improvement in QOL, and further that IPET-S is a dietary supplement that provides an expected anti-tumor effect in cancer-bearing dogs.

Moving forward, we believe it is necessary to increase the number of cases of IPET-S-only dosage including cancer-bearing cats, conducting evaluations for types of tumors and in different clinical stages.

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◆ Acknowledgments

We wish to thank the following hospitals for their cooperation in our study (listed in random order):

Kotoku Animal Hospital

Elm Animal Clinic

Mori Animal Hospital

Seta Animal Hospital

Yasuda Animal Hospital

Shiba Animal Hospital

Yurigaoka Animal Hospital

Nanao Veterinary Clinic

Sobue Animal Hospital

ARK Animal Hospital

The following summarizes IPET-S dosages based on our experience.

Weight (Kg)	**General Health Genetic Concerns**		**Strengthen Immunity before Surgery Post-Surgical Care/ Recurrence Prevention Reduce side effects of chemical treatment (chemotherapy) Reduce side effects of radiation therapy When aggressive treatment is not desired**	
	Guideline		Guideline	
- 5		1 tab		2 tabs
5 to 10		1 to 2 tabs		3 tabs
10 to 15		2 to 3 tabs		4 tabs
15 to 20		2 to 4 tabs		5 tabs
20 to 25		3 to 5 tabs		6 tabs
25 to 30		3 to 6 tabs		7 tabs
30 -		3 to 7 tabs		8 tabs