Therapeutic Effects of β-Thujaplicin Eardrops on Canine Malassezia-Related Otitis Externa

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ABSTRACT. An eardrop solution of β-thujaplicin was examined for therapeutic effects on canine Malassezia-related otitis externa. Half to one ml of β-thujaplicin solution of 100 μg/ml including DMSO 2% was injected everyday into both external ear canals of 31 cases for test-of-cure agreement. Fifteen score phases were established from the symptoms and cerumen smear biopsy findings, and score changes were recorded at least once a week. The means of the second and third inspection day scores decreased significantly more than the previous value of each. In addition, the numbers of yeast-like organisms clearly decreased. These results suggest that β-thujaplicin eardrops are effective for Malassezia-related otitis externa in dogs.

KEY WORDS: β-thujaplicin, Malassezia, otitis externa.

Malassezia pachydermatis is one of the most common microbes isolated from canine otitis externa cases [2, 7, 8]. M. pachydermatis-related otitis externa is intractable and recurrent antifungal agents must be administrated long-term [1]. Azoles such as ketoconazole, polyene derivatives as nystatin, and allylamines as terrbinafine are antifungal agents available for otitis externa, but recently, the appearance of drug-resistant fungi was reported [10].

β-Thujaplicin is a chemical substance with a tropolone base extracted from Aomori Hiba, a kind of hiba arborvita found in north Japan, and the antimicrobial and antifungal effects of this chemical have been reported [5, 6]. β-Thujaplicin has anti-inflammatory and deodorant effects, and can be used safely and cheaply outside the medical arena in cosmetics, hair tonic, or dental powder [5, 6]. As well as antifungal effects, there is a report of difficulty with microorganism resistance [3]. In our previous report, β-thujaplicin showed mycotic growth inhibitory effects in vitro at a concentration equal to commercial antifungal drugs for M. pachydermatis isolated from canine otitis externa [2]. In this study we inspected the therapeutic effects of auditory canal drops, including β-thujaplicin, on otitis externa in dogs.

Before the clinical test, 4 guinea pigs with a physically destroyed tympanic membrane on one side were injected daily into both ears for five weeks with 400 μg/ml of β-thujaplicin solution (including 2% of dimethyl sulfoxide) at 4X concentration as a therapeutic test, but no abnormal clinical symptoms and no pathological changes in the external, middle and inner ear were observed.

For the clinical test, 31 voluntary otitis externa cases presented at cooperative animal hospitals in Osaka City. In this test, affected dogs were tested only when owners accepted the following conditions of informed consent: 1) Both ears were tentatively diagnosed with Malassezia-related otitis externa based on clinical test findings and cerumen biopsies; 2) Manifestations such as torticollis and eyeball tremor were not present without otitis media or otitis interna, moreover no other apparent diseases such as dermatitis; 3) The owner could give the test dog the eardrop injection daily at home, but no other treatment was permitted; 4) They could visit the hospital for follow-up and biopsies every week; 5) The owner understood that there are some temporary dyscrasias potential in the ear canal, hearing and balance by continuing to inject liquid foreign material even after the safety of β-thujaplicin was confirmed; 6) The owner consented to the publication of the obtained results.

A total of 31 affected dogs were tested. They include 6 each of Miniature Dachshund and mix breed, 4 each of Golden Retriever and Shih Tzu, 3 of Miniure Poodle, 2 each of Beagle, Labrador Retriever and Maltese, and 1 each of American Cocker Spaniel and Cavalier King Charles Spaniel. Clinical scores of the judged effect are presented in Table 1. The color of cerumen, volume of cerumen, inflammation of the external auditory canal, pruritus, odor, and number of yeasts by biopsy were chosen as the score calculation elements, and each element was divided into several phases. By adding these element phases, 15 scores were available. Changes in clinical scores during the test periods were recorded.

The test solution of 100 μg/ml of β-thujaplicin including 2% of dimethyl sulfoxide was prepared for the clinical test. In the first visit to the animal hospital, 0.5 to 1 ml of the solution was injected into each ear, and ear injections were continued once a day at the owner’s home. Clinical scores were recorded at least once a week for 30 days in principle. There were some cases in which the injection was terminated before 30 days because the veterinarians judged the
Table 1. Clinical scores of the judged therapeutic effect of β-thujaplicin on otitis externa

<table>
<thead>
<tr>
<th>Score</th>
<th>Color of cerumen</th>
<th>Amount of cerumen</th>
<th>Inflammation of ear canals</th>
<th>Pruritus</th>
<th>Odor</th>
<th>Number of yeasts/HPF</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not brown</td>
<td>Little</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>1</td>
<td>Slightly brown</td>
<td>Small</td>
<td>Slight</td>
<td>Slight</td>
<td>Characteristic</td>
<td>1–4</td>
</tr>
<tr>
<td>2</td>
<td>Brown</td>
<td>Medium</td>
<td>Medium</td>
<td>Medium</td>
<td>–</td>
<td>5–9</td>
</tr>
<tr>
<td>3</td>
<td>–</td>
<td>Large</td>
<td>Severe</td>
<td>Severe</td>
<td>–</td>
<td>&gt;10</td>
</tr>
</tbody>
</table>

Maximum score is 15 by adding up each score. HPF: High power field (400 × magnification of microscope).

### Results

- **Initial Conditions**: 31 cases (100%) of canine otitis externa were used. The mean age of the dogs was 125 ± 37.5 days, and the mean weight was 5.7 ± 1.4 kg. Ear cerumen samples were collected from all cases on the first presentation day. There were 15 cases (48%) in which ear cerumen smears of over 10 yeasts were counted in a high power field microscope, and 10 cases (32%) in which ear cerumen smears of 5 to 9 yeast counts were counted. Yeast-shape organisms were observed in ear cerumen smears of 23 cases (74%).

- **Therapeutic Effect**: After ear injections of β-thujaplicin solution for canine otitis externa cases revealed clinical effects and decreases in *Malassezia* counts in the ear canals. Yeast-like organism counts in ear cerumen biopsy have been accepted as an important indicator of *Malassezia*-related otitis externa, and the effects of β-thujaplicin were also confirmed by yeast counts of the smears. According to canine otitis externa treatment tests by other antifungal drugs [4, 11], clinical severity of otic disease and yeast counts were significantly decreased. The present results, considering the extremely simple treatment such as dropping into the auditory canals, must be evaluated to reveal little difference from other drugs. Conclusively, an eardrop solution including β-thujaplicin was effective at home as well as in veterinary clinics in the treatment of otitis externa.

### References