

Hair growth promotion effect of *Pantoea agglomerans* LPS (lipopolysaccharide)

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Background: We are studying hair growth with natural immunity activators, which have wound healing promotion effect, infection-fighting effect, and antiallergy effect, to improve pets' hair loss or thinning hair due to various diseases. Through our studies, we have screened functional food materials that improve hair loss or thinning hair, and found high efficacy of a combination preparation whose active ingredients are *Pantoea agglomerans* lipopolysaccharide (LPS) and *Pinus pinaster* polyphenol. The result of this study is now patent-pending.

Method: Hair growth study was done with the aid of practicing veterinarians. Thirty-nine dogs with hair loss were included in this study. They were divided into monotherapy groups receiving LPS (10 µg/kg) alone or polyphenol alone or combined therapy group receiving LPS + polyphenol, and took their test article orally for about 30 days. Evaluation of hair growth was done by visual observation and photo determination. Hair growth effect was determined to be present when increase in the rate of hair growth area in the thinning hair area is 61% or more. Administration of pet food and medicinal products was not restricted, but combination of other supplements was prohibited.

Results and discussion: The rate of hair growth was 39.1% in LPS monotherapy group (9/23), 28.6% in polyphenol monotherapy group (2/7), and 100% in LPS + polyphenol combination therapy group (9/9). The combination therapy group showed a significantly high hair growth effect ($P < 0.01$). Since hair loss was not improved spontaneously before administration, it was shown that LPS monotherapy has a considerably high hair growth effect. Nevertheless, its combination with polyphenol showed significantly high hair growth effect. This combination is expected to be effective as hair-loss treatment food/drug.

Keywords: *Pantoea agglomerans* LPS; trichogenous; *Pinus pinaster* polyphenol.

INTRODUCTION

Since hair loss or extremely thinning hair due to skin disorders seriously damages pets' appearance, it is an emotional strain for pet owners. The known causative disorders of hair loss include atopic dermatitis, parasitic dermatitis, fungal or bacterial infections, hormonal disorders, stress, and sebaceous

gland inflammation. In 2013, we reported in this seminar LPS derived from *Pantoea agglomerans*, plant-symbiotic gram-negative bacteria, as a new material to regulate natural immunity, and its improvement effect on allergic disorders in dogsⁱ. In 153 cases diagnosed as atopic dermatitis, oral administration of LPS showed efficacy rate of 58.8%. In addition,

when LPS was orally given prophylactically before the onset of canine parvovirus infection, improvement in survival rate was observed: 85.7% in LPS group versus 50% in control group.

In the investigative study of canine atopic dermatitis (CAD), association with mite allergen or fungus β -glucan was not found, but reverse association with LPS exposure was reported. This suggests endotoxin exposure exerts suppressive effect on the onset of CADⁱ. Today pets are kept indoors. So lowered LPS consumption due to sanitary environment and changing food are thought to cause increase in allergic disorders jointly with physical inactivity and stress. Then, we compared improvement effect on skin condition, especially on hair growth, between the LPS monotherapy group and the combination group with LPS and highly antioxidative polyphenol under the supervision of a practicing veterinarian.

MATERIALS AND METHODS

The LPS used was an animal food material (Institute of Applied Technology for Innate Immunity) prepared by hot-water extraction of the cultured *Pan-toea agglomerans*, which had been isolated from wheat. *Pinus pinaster* polyphenol used was extracted from the cortex of pines growing on the coast of France (Horphag Research). LPS alone (about 10 μ g/kg in terms of LPS amount) or a mixture of LPS and *Pinus pinaster* polyphenol were orally administered in tablet form to 39 dogs included in this study once a day for 30 days. Hair growth effect was evaluated as follows. First, skin condition before use was determined by visual observation or photo determination. Then, skin conditions were compared between before and after the consumption of the supplement to determine the decrease rate of hair loss area, which was then used for evaluation of hair growth effect.

RESULTS

In the LPS monotherapy group, hair growth effect was confirmed to be present in nine out of 23 cases (39.1%). Meanwhile, hair growth effect was confirmed in two out of seven cases with polyphenol monotherapy (28.6%) and in nine out of nine cases with administration of LPS-polyphenol mixture (100%). Administration of the mixture showed higher hair growth effect than for monotherapy, with statistically significant difference ($P < 0.01$). We also administered the mixture to other hair loss cases (two

cats, one rabbit, and one guinea pig), and the mixture showed hair growth effect in all cases.

DISCUSSION

Hair repeats growth and loss (anagen, catagen, and telogen) at a constant frequency. In anagen hair, IGF-1 (insulin-like growth factor 1) secreted by hair papilla maintains hair matrix cells, while TGF- β is thought to become dominant in telogen hair. In addition, macrophages are thought to prepare for anagen by phagocytizing melanin pigments and cellular fragments during telogen. Though the hair growth promotion mechanism by oral administration of LPS has not been clarified yet, first, skin normalization by LPS' anti-inflammation effect against atopic dermatitis and resulting tissue repair is thought to contribute to hair growth. In the mite antigen stimulation model using NC mice, inhibition of periostin, which is thought to be involved in induction of atopic dermatitis, by LPS is revealed. It is thought to be one of the examples (3ⁱⁱⁱ). Second, macrophage's phagocytic capacity promoted by LPS may improve the quality of preparatory stage for anagen. In addition, the antioxidative effect of *Pinus pinaster* polyphenol is thought to promote anti-inflammatory action.

It is known that macrophages' irregular phagocytic elimination action in tissue regeneration deteriorates the regeneration ability of many tissues including muscles, bones, and corpus luteum. We think it is fully possible that enhanced phagocytic ability by LPS improves the quality of skin transition from telogen to anagen. At the same time, *Pinus pinaster* polyphenol is also thought to contribute to hair growth by exerting antioxidative effect and blood circulation promotion effect. From now on, we are going to collect more cases to confirm the usefulness, and investigate hair growth mechanism by LPS in combination with polyphenol.

REFERENCES

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