Studies on a Bioactive Substance for Epidermal Barrier Improvement Derived from Fermented Barley Extract

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Fermented barley extract (FBE) is the supernatant obtained from barley shochu distillery residues by sieving and filtration, and is rich in amino acids, peptides, organic acids, inorganic salts, and vitamins. Barley shochu is made from barley and brewed with yeast (*Saccharomyces cerevisiae*) and white koji-mold (*Aspergillus luchuensis* mut. *kawachii*). Therefore, various components in FBE are derived from the decomposition products of barley and the metabolites of these two microorganisms. It has been reported that oral administration of fermented barley extract P (FBEP), the fraction of FBE that adsorbs to a hydrophobic resin, to normal mice significantly enhances erythrocyte glutathione peroxidase (GPx) activity and increases hepatic glutathione levels compared to a control group. Since a report indicated that increasing antioxidant activity such as GPx in NC/Nga mice suppresses Th2 cytokine and IgE levels, I inferred that oral administration of FBEP may be useful for the treatment of atopic dermatitis (AD). However, the effect of FBEP on AD-model mice remains unknown. In this study, I identified an FBE component that improves the epidermal barrier function using AD-like hairless mice and elucidated the mechanism of the active compound production to obtain basic knowledge for its industrial production.

CHAPTER I

Identification of a fermented barley extract component with epidermal barrier improvement effects

AD is a chronic inflammatory skin disease characterized by pruritic and eczematous skin lesions. The skin of AD patients is generally in a dried condition. Therefore, it is important for AD patients to manage skin moisturization. In this chapter, I discuss the effects of orally administered FBEP on stratum corneum (SC) hydration and transepidermal water loss (TEWL) in AD-like lesions induced in hairless mice using 2,4,6-trinitrochlorobenzene. Oral administration of FBEP increased SC hydration and decreased TEWL in the dorsal skin of this mouse model. Further fractionation of FBEP showed that a pyroglutamyl pentapeptide, pEQPFP, comprised of all L-form amino acids, is responsible for these activities.

CHAPTER II

Elucidation of the mechanism of pyroglutamyl pentapeptide formation in shochu mash

I investigated the mechanism of the formation of pEQPFP (Mw598) in shochu mash. I revealed that the precursor of Mw598 (QQPFP; Mw615) in shochu mash was leached from barley white koji and was also produced from hordein by the action of enzymes secreted from barley white koji. Although Mw615 was decomposed by enzymes secreted by white koji-mold, Mw615 seemed to be transformed into Mw598, which was not degraded by enzymes from white koji-mold, via cyclization of a glutaminyl residue at the N-terminus. This pyroglutamylation was promoted in the atmospheric distillation process. Furthermore, I found that black koji-mold, which is closely related to white koji-mold by molecular phylogenetics, also produced both peptides.