Sweetness of recombinant human lysozyme

Here, we reported that lysozyme found in human milk elicits sweet taste as well as chicken lysozyme with 20-folds more sweetness than sucrose by weight.

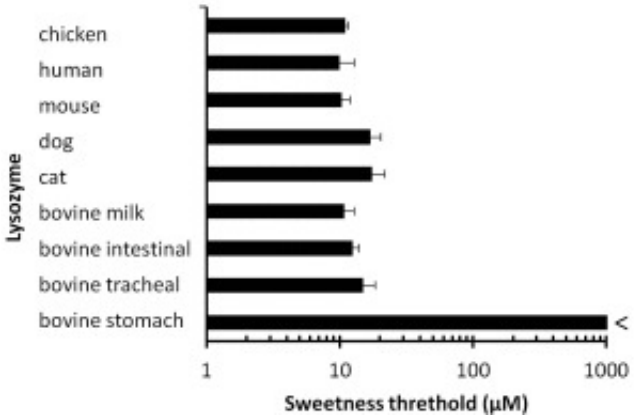

Fig. 1. Sweetness threshold values determined using a human sensory test.

Lysozyme is an enzyme that degrades the bacterial cell wall and thereby accounting for its main biological function of protecting the host from bacterial infection. We have already reported that chicken egg-white lysozyme elicits a sweetness. Sweetness is a pleasant sensation for most animals and is believed to be a signal for high caloric substances in foods because sugars are representative of natural sweet compounds. However, there are numerous structurally diverse compounds that elicit sweetness other than sugars. Some proteins such as monellin and thaumatin that are present in tropical fruits of West Africa elicit intense sweetness. Because they elicit 2,000–3,000-fold more sweetness by weight than sucrose, these compounds may replace low-calorie artificial sweeteners. The nutritional value of these specific proteins is yet unknown because proteins are not high-calorie substances. Monellin and thaumatin are structurally and evolutionarily related to the protease inhibitors and antifungal proteins, respectively, that are involved in plant defense, although neither protein elicits sweetness. These limited examples for sweet proteins of plant origin; however, lysozyme is the only sweet protein of animal origin.

In mammals, lysozyme is present in the breast milk and most other body fluids. In addition, lysozyme occurs in excess in the human colostrum and contributes to the reduction of microbial infections in the gastrointestinal tract of breast-fed infants. Milk provides a nutritious diet for mammalian infants, and lysozyme is present as a nonspecific host defense factor, regardless of the animal species. We prepared recombinant lysozymes to asses their sweetness. Recombinant human lysozyme and other mammalian lysozymes of mouse, dog, cat and bovine milk elicited similar sweetness as determined using a sensory test, whereas bovine stomach lysozyme did not. Assays of cell cultures showed that human lysozyme activated the human sweet taste receptor,

whereas bovine stomach lysozyme did not. Point mutations confirmed that the sweetness of human lysozyme was independent of enzyme activity and substrate-binding sites, although acidic amino acid residues of bovine stomach lysozyme played a significant role in diminishing sweetness. Therefore, we conclude that elicitation of sweetness is a ubiquitous function among all lysozymes including mammalian lysozymes.

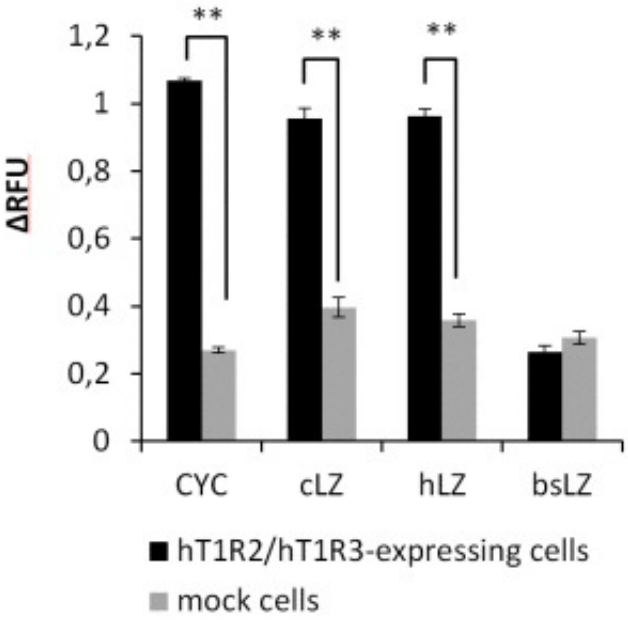

Fig. 2. Responses of cells expressing the human sweet taste receptor to lysozymes. CYC, cyclamate; cLZ, chicken lysozyme; hLZ, human lysozyme; bsLZ, bovine stomach lysozyme.

The sweetness of lysozyme is not considered to be an attractive signal that indicates high-calorie substances such as sugars; therefore, it should be considered whether the sweetness of lysozyme works without oral sensation. Components of the taste signaling pathway are present in other organs such as the intestinal cells, and the activation of sweet receptor regulates appetite, insulin secretion, and gut motility. Therefore, we believe that it is reasonable to assume that mammalian lysozyme in milk may be associated with the nutrition of infants by activating sweet receptor in the oral cavity or gastrointestinal tract.

We showed that seven lysozymes derived from five mammalian species elicited sweetness that was independent of enzyme activity. It was also indicated that sweetness elicitation of lysozyme is not associated with the food habit and fertility trait of its host animal. We speculate that a critical structure that imparts sweetness may be conserved among lysozymes of diverse species, although this remains to be proven. The current study reveals a novel and ubiquitous characteristic of the molecular basis of the sweetness of lysozyme, which may provide novel insights into the biological

function of perceiving sweetness in the oral cavity as well as in the gastrointestinal tract. Whether lysozyme regulates the nutrient-responsive secretion of gut hormones through the activation of sweet receptor will be addressed in the future.

Publication

Sweetness characterization of recombinant human lysozyme.
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