Predicting the glucophores of sweet proteins

Annalisa Pastore and Pierandrea Temussi

Division of Molecular Structure, National Institute for Medical Research, MRC, Mill Hill, The Ridgeway, London NW7 1AA, U.K. and Dip. Chimica, Universit Federico II, via Mezzocannone 4, I-80134 Naples, Italy.

Taste receptors have been studied less than those of other stimuli. However, the availability of many agonists and the practical relevance of sweeteners have stimulated indirect studies of the interaction of sweet agonists with their receptor and the development of general models of the sweet receptor active site. Most sweeteners are small molecular weight compounds but there are also sweet macromolecules, both synthetic and natural, i.e., sweet proteins. Do they interact with the same receptor of low molecular weight compounds? There are several sweet proteins: miraculin , monellin, thaumatin, curculin, mabinlin, pentadin and brazzein, but only three of them, i.e. thaumatin, monellin and brazzein, have been studied from a structural point of view. Multiple alignment of the sequences of sweet proteins shows no similarity. There is also no obvious similarity among the structures of thaumatin, monellin and brazzein. How can we identify the protein glucophores? We made the assumption that they are similar to those of low molecular weight compounds and that all sweet compounds interact with the same receptor. In fact, our model for the sweet receptor (Temussi et al., 1984, 1991) is consistent also with macromolecules since the active site is depicted as an open cavity with a flat bottom. When trying to explain the sweet taste of a protein it's natural to assume the existence of some kind of "sweet finger", i.e., a protruding structural element hosting one or more glucophores. We sought to identify sweet fingers in the three sweet proteins whose structure is known. Detailed structure comparison of all loops in the structures of thaumatin, monellin and brazzein by means of DALI shows that each protein hosts a likely sweet finger in which the spatial arrangement of three key residues (an aromatic a hydrogen bond donor and a hydrogen bond acceptor) is consistent with our model of the receptor active site.

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