

[P26] Pharmacophore Study of a Blending six-Component Odor Mixture

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The first step of odor perception is an interaction between odorants and olfactory receptors [1]. The corresponding transduced olfactory signals, conveyed by olfactory sensory neurons, are then processed by the brain [2]. It is now accepted that the main strategy used to discriminate thousands of odors results from a combinatorial coding [3]. Moreover, odors perceived in our environment are mainly the result of mixtures of odorants; however, the specific mechanisms involved in their processing remain poorly understood [4].

In previous studies performed in the CSGA of Dijon [5-7], we investigated the perception of a mixture of 6 components: vanillin, oxanone (4-(4-hydroxyphenyl)butan-2-one), isoamyl acetate, beta-ionone, ethyl acetate, and beta-damascenone. We have shown that, at specific proportions, this mixture is configurally processed and perceived as different from its components and carries the specific odor of red cordial (blending RC mixture).

Assuming that combinations of activated ORs encode odor qualities [8, 9], we used Common Feature Pharmacophore Generation protocol (Discovery Studio 4.1, Biovia) to generate pharmacophore hypotheses [10]. The purpose is to identify whether molecular characteristics may be common to the molecules of the mixture, which would highlight that configural perception is linked to overlapping patterns of OR. In our study, the pharmacophoric features considered are hydrogen bond acceptors (HBA) and hydrophobic regions (HY); the maximum number of generated hypothesis for each run was set to 10.

The pharmacophores obtained by using the six molecules are built up of one HY and one HBA; this seems not very meaningful despite a satisfactory alignment of the molecular structures. Besides, we generated the pharmacophores for each molecule using its conformers as individual molecules (maximum 250 conformers in energy range 20kcal/mol). By comparing the pharmacophores two by two, we identified a pair of molecules, vanillin and oxanone, whose pharmacophores possess some common characteristics 2 HBA located 8 Å from each other and 1 HY between those two. Interestingly, the basis of RC consists of a mixture of vanilla and red berries, while vanillin and oxanone carry respectively the notes "vanilla" and "raspberry". These results suggest that a similar binding site could exist for at least the two molecules likely sharing key odor notes of the blending mixture. It thus supports the hypothesis that molecules involved in a mixture that elicits an emergent odor recognize a common set of ORs.

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