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SENSORY IRRITATION AND INDOOR AIR QUALITY

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Abstract

Sensory irritation, an aspect of the common chemical sense (CCS), figures prominently among the varied complaints brought about by indoor air pollution. Studies of persons lacking a functional sense of smell (anosmics) offer a simple and unbiased means to understand the functional characteristics of the nasal CCS. Testing anosmics for their ability to detect series of chemically related (e.g., homologous) substances should allow construction of quantitative structure-activity models for human pungency (irritation) perception.

Introduction

Although scientists wish to link complaints regarding indoor air pollution to specific chemical causes, various sources of uncertainty plague the effort. First, the mere variety of the complaints engenders uncertainty. How should we count them? Should we aggregate complaints of fatigue, lassitude, and memory loss with those of eye irritation or should we keep the complaints separate and seek a different cause for each? Does one complaint drive another? Does irritation cause lassitude? Second, people often experience the symptoms of concern outside problem buildings, as well as inside them. There is therefore little control over whether the symptoms, even if valid, arise strictly from exposure to agents in any particular building. Third, we can rarely validate the symptoms objectively. Without such means, we will always have the potential problem of over-reporting and embellishment. Although one person may seem more sensitive than another, the difference may lie in a greater proclivity to complain.

Although the varied complaints about indoor pollution may resist aggregation, sensory irritation figures prominently among them and even forms a common denominator. Irritation lends itself to measurement psychophysically in humans and animals, functionally in animals, and, when severe, clinically in humans. Because of its prominence and scientific accessibility, irritation can provide the focus for both basic and applied research on reactions to indoor contaminants. Only when the mechanism for irritation becomes known will we have the tools to avert irritative symptoms of indoor pollution completely. If irritation in buildings came about only from substances known as frank irritants, such as formaldehyde, we could avoid or eliminate the problem quickly. It appears instead that irritation from indoor pollution must arise from the aggregate effect of low concentrations of materials not normally considered irritants. Volatile organic compounds (VOCs), such as the ingredients in common solvents, ubiquitous in the indoor environment, are prime candidates.

Almost all airborne organic substances can stimulate both the olfactory sense and the irritation sense, and aspect of the common chemical sense (CCS). In everyday life, we often fail to notice that a smell may have a little sharpness that implies co-activation of the CCS as well as olfaction. Personal products and cleaning products, for example, will sometimes signal their efficacy by a sharp "clean" or "refreshing" aroma that results from a CCS component. Commonly in psychophysical experiments, participants may be asked to assess the odorous and pungent attributes of a given stimulus separately [3, 4, 7, 8]. In a few studies, the use of subjects with unilateral destruction of the trigeminal nerve [2] or of subjects without olfactory function, i.e., anosmics (e.g., [5, 6]), have permitted a more direct look at the independent functioning of the nasal CCS.

In studies shown below, we will compare the irritating and olfactory potency of various volatile organic compounds that appear in indoor air in anosmic and normosmic persons, respectively, and will illustrate the lawfulness of what makes one substance more potent than another.

Thresholds

For those substances with capacity to stimulate both olfaction and the CCS, the odor threshold typically falls below the pungency threshold . Until our use of anosmic subjects, it has been impossible to establish true nasal CCS thresholds. Anosmic persons lack the sense of smell either congenitally or secondary to another cause (e.g., head trauma, nasal sinus disease), so their only way to detect airborne chemicals is through the CCS.

We have charted how well normal, i.e., normosmic, and anosmic participants can detect homologous series of aliphatic alcohols and acetate esters [5, 6]. Figure 1 depicts thresholds for odor (normosmics), nasal pungency (anosmics), and eye irritation (obtained from a third, normosmic, group). Clearly, the thresholds decline with carbon chain-length. The eight-carbon molecule, for example, is a thousand or more times more effective than the one-carbon molecule, irrespective of the sense organ. Such a basic observation says much about the physicochemical basis for all three chemosensory reactions. The figure reveals as well a striking similarity in the absolute values of the thresholds for corresponding sensations in the acetate and alcohol series. The gap between odor and pungency, however, varies from about one order of magnitude to about four orders. Within the acetates series, eye irritation thresholds fell close to those for nasal pungency.

The thresholds in Figure 1 refer to vapor phase concentration. In order to reach the appropriate receptors, the stimuli must penetrate the mucus layer and then reach the lipid bilayer of the receptive membrane. The mucus comprises both viscous and watery layers [11]. The effective concentration at the receptors will therefore reflect the net effect of partitioning between air and viscous mucus, between the viscous mucus and watery mucus, and between the watery mucus and the lipid membrane. The filtering effect will vary from very water soluble molecules - such as methanol or methyl acetate - to lipid soluble molecules - such as 1-octanol or dodecyl acetate.

Both the odor and pungency thresholds change logarithmically with carbon chain-length as do thresholds for narcosis [1, 9] and various toxic phenomena [10, 12]. The relative thresholds for such phenomena seem to result from an equilibrium between heterogeneous phases - reflecting water solubility, vapor pressure, surface activity, and partition coefficients - and are largely determined by a distribution equilibrium between an external phase and a susceptible biophase. In such cases, the thermodynamic activity of the stimulus is the same in all phases involved in such equilibrium - air, mucus, lipid membrane - while concentration can differ vastly from one phase to another.

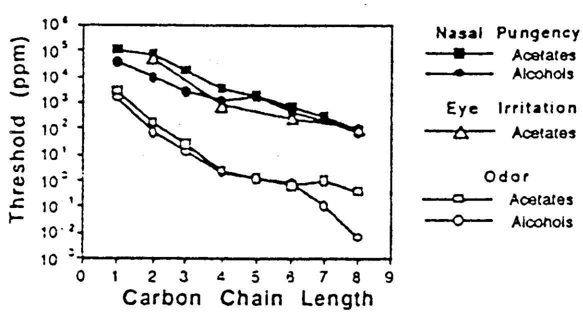


Figure 1. Comparison between two homologous series: a) normal aliphatic alcohols from 1 = methanol to 8 = 1-octanol and b) acetates from 1 = methyl acetate to 8 = octyl acetate in terms of their ability to provoke threshold nasal pungency in an anosmic group, and threshold odor in a normosmic group. Eye irritation thresholds - measured in another group - are also shown for selected acetates. From Cometto-Muñiz and Cain [6].

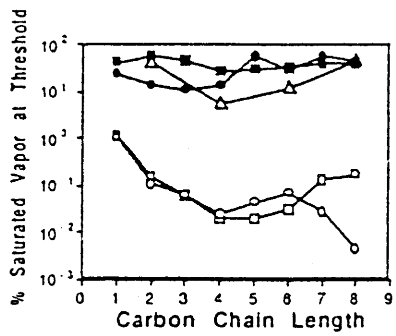
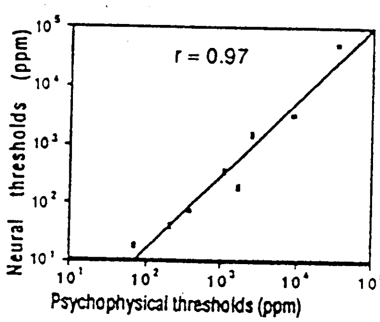


Figure 2. Comparison between the homologous series in terms of thermodynamic activity at threshold odor from normosmics, at threshold nasal pungency from anosmics, and at threshold eye irritation. Thermodynamic activity was calculated as the ratio between vapor concentration at threshold odor, nasal pungency, or eye irritation, over saturated vapor concentration, multiplied by 100. From Cometto-Muñiz and Cain [6].

The ratio of partial vapor pressure at a threshold effect - e.g., threshold of pungency or narcosis or toxicity - to saturated vapor pressure provides an index of thermodynamic activity. Figure 2 shows the odor, nasal pungency, and eye irritation thresholds expressed as percentage of saturated vapor at threshold. The thresholds for nasal pungency, unlike odor thresholds, are elicited at a fairly constant percentage of saturated vapor irrespective of molecular size or functional group. Eye irritation thresholds roughly coincide with those for nasal pungency, although there was slightly higher relative sensitivity for the middle acetates. In view of the strong role played by thermodynamic activity, it appears that the pungency evoked by these relatively nonreactive chemicals arises from a nonspecific, physical interaction between the stimuli and susceptible mucosal target sites.

Studies of anosmic persons offer a simple means to understand the functional characteristics of the nasal CCS. Studies of additional chemical series in such subjects should eventually allow construction of quantitative structure-activity models for human pungency perception. The human data can be compared with relevant animal data when possible. Figure 3 shows the association between our nasal pungency thresholds and thresholds for the integrated trigeminal nerve response from rats (see [13]). The level of agreement encourages further comparisons.

Figure 3. Comparison of human psychophysical thresholds obtained from anosmic subjects [5] and rat neural (trigeminal nerve) thresholds [13] for aliphatic alcohols from methanol (upper right) to 1-octanol (lower left).



Studies of the rules of additivity of pungency in mixtures should also stand high on the agenda. Regarding the possible role of VOCs in the creation of irritation, we need to ask whether subthreshold levels add up or even amplify each other to produce noticeable irritation. Do repetitive or continuous exposures to subthreshold concentrations increase sensitivity to those substances, so that they evoke pungency when they otherwise would not? Do the various mucosae - ocular, nasal, throat - differ in their sensitivity?

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