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Permalink
https://escholarship.org/uc/item/1612x20t

Journal
Physiology & Behavior, 67(2)

ISSN
00319384

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Publication Date
1999-08-01

DOI
10.1016/S0031-9384(99)00074-8

Data Availability
The data associated with this publication are within the manuscript.

Peer reviewed
Chemosensory detectability of 1-butanol and 2-heptanone singly and in binary mixtures

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Running head: Chemosensory detectability of mixtures
Abstract

Using 1-butanol and 2-heptanone as stimuli we measured detectability (i.e., psychometric) functions for the odor, nasal pungency, and eye irritation of these two substances alone and in binary mixtures. Nasal pungency responses were tested in subjects lacking olfaction (i.e., anosmics) for whom odors do not interfere. Eye irritation responses were tested in normosmics and anosmics and found to be similar in both groups so their results were pooled. When all stimuli — single and mixtures — were transformed into concentration units of one (or the other) chemical, a single function could fit all data from the same sensory endpoint with a correlation coefficient of 0.91 or higher. The outcome lends support, as a first approximation, to the notion of chemosensory agonism, in the sense of dose additivity, between the members of binary mixtures presented at perithreshold levels.

Keywords: Olfaction – Chemosensory irritation – Odor – Nasal pungency – Eye irritation – Odor mixtures – Irritant mixtures – Anosmics – 1-Butanol – 2-Heptanone – Psychometric functions
Introduction

Studies of the functional properties of the olfactory and trigeminal chemosensory systems in humans have focused often on threshold measurement of a single point on a detectability function (e.g., (14)) or on suprathreshold functions over a range of concentrations (e.g., (31)). Relatively fewer investigations have approached the topic via measurement of psychometric or detectability functions spanning the range from chance detection to virtually perfect detection (e.g., (6, 10, 30)). Odor and “chemesthetic” (see (21)) detectability functions provide a means to compare olfactory and trigeminal functioning as both chemosensory systems cross the boundary between threshold and suprathreshold responses.

In addition, detectability functions can provide information on how the senses of smell and chemesthesis process mixtures of compounds. The topic of chemosensory responses to mixtures has relevance not only to the basic understanding of the chemosenses but also to a wide variety of applied topics such as food aromas or air quality issues (11). Many studies addressing the human perception of chemical mixtures have focused on olfaction and on the suprathreshold range, expressing results in terms of the response (that is, perceived sensory intensity of the chemicals). Within this context, the terms hypoadditivity, complete additivity, and hyperadditivity refer to cases where the chemosensory response to a mixture is — respectively — less than, equal to, or more than the sum of the responses to the individual components. These studies have concluded that the perceived odor intensity of a mixture is less than the sum of the perceived odor intensities of the components (i.e., hypoadditivity) (e.g., (7)). When the type and concentration of the mixed chemicals appeals not only to the olfactory but also to the nasal trigeminal system, the degree of additivity grows larger (18). A perceptual dissection of the overall chemosensory response into “odor” and “nasal
pungency” revealed that the chemesthetic response, as opposed to the olfactory response, showed complete additivity and, even, hyperadditivity (19).

The relatively fewer studies of mixtures at the threshold level have, as a rule, focused exclusively on olfaction, and have expressed the results in terms of the stimulus (that is, concentration of the chemical). Within this context — and taking the example of a binary mixture — partial agonism, complete agonism, and synergistic agonism represent cases where each of the two components needs to be at a concentration that is — respectively — higher than, equal to, or lower than one-half of its individual threshold concentration for the mixture to achieve threshold. The outcome of studies of odor mixtures at threshold has suggested complete stimulus agonism (e.g., (29)) with some cases of synergistic stimulus agonism, as number of components increased (e.g., (23)). A recent investigation addressed measurement of thresholds for nasal and ocular chemesthesis, labeled respectively nasal pungency and eye irritation, in addition to odor thresholds (17). The results for odor implied various degrees of partial agonism, including complete agonism for one of the five mixtures of varying number and type of components. The results for chemesthesis implied a stronger degree of agonism than that for odor, particularly in the case of eye irritation where there was significant synergistic agonism for the mixture with the higher number of components (9 substances) and the mixture having the most lipophilic components (a 6 substance-mixture).

This previous work included important features, both regarding the stimulus and regarding the response. Regarding the stimulus: 1) It covered fairly complex mixtures having 3, 6, or 9 components. 2) It included compounds selected within and across homologous series according to gradually changing physicochemical properties. 3) It included vapor-phase measurement of all stimuli, mixtures and single chemicals. Regarding the response: 1) It entailed separation of nasal pungency from the possibly
confounding effects of odor via tests of subjects with no olfaction (i.e., anosmics). 2) It included presentation of the components of the mixtures at equisensory potency, as calculated from previous results. 3) It tested the single chemicals under the same procedure and for the same subjects as the mixtures. Still, all mixtures were targeted to include components present at only one, and the same, fixed ratio referenced to their individual thresholds, e.g., 1/3, 1/6, or 1/9, and multiples or submultiples of them.

In the present investigation we thought to complement the previous approach by performing a detailed study of an example of the simplest of all mixtures, the binary case, but where the two components vary systematically in their relative ratios in the mixture referenced to their individual probabilities of detection. In this way, we planned to: 1) measure complete detectability functions for each component alone, 2) use the data to create mixtures where the individual detectability of the components has been measured and 3) measure detectability functions for such mixtures. The same subjects will be tested throughout the process. Within the context of testing the mixtures we repeated testing of the single components to strengthen the comparability of the results.

The previous approach focused on measuring thresholds for single chemicals and mixtures according to a fixed criterion of performance. The present strategy measures complete detectability functions, ranging from chance detection to virtually perfect detection. In addition, the present investigation involves testing detectability of mixtures under varying proportions of its individual components. The new strategy, focusing on a wider perceptual range and on varying proportions of components, is crucial to understand the rules governing combined effects of chemicals.

**Materials and Methods**
**Subjects.** An initial group of 4 normosmics — i.e., participants with normal olfaction — provided psychometric functions for odor and eye irritation from the two single substances. The group included one male, aged 54 years, and three females, aged 24, 28, and 37 years. Once the odor functions for the single substances were obtained, we prepared the mixtures as described under “Procedure” and tested odor detection on these same 4 normosmics plus an additional 14 normosmics (median age: 22 years, range: 18 to 39 years, 8 males and 6 females).

An initial group of 4 anosmics — i.e., participants lacking olfaction — provided psychometric functions for nasal pungency and eye irritation from the two single substances. The group included one male, aged 59 years, and three females, aged 28, 32, and 40 years. All these subjects were congenital anosmics. Once the nasal pungency functions for the single substances were obtained, we prepared the mixtures as described under “Procedure” and tested pungency detection on 3 of these anosmics plus 3 additional anosmics (two males: a 38 year-old head-trauma anosmic and a 43 year-old idiopathic anosmic; one female: a 43 year-old congenital anosmic).

Prior to participation, olfactory sensitivity was assessed in all subjects by means of a clinical olfactory test (9). All participants were nonsmokers. The study protocol was approved by the Human Subjects Committee of the University of California, San Diego. All subjects gave written informed consent on forms approved by the Committee.

**Stimuli and Equipment.** The compounds tested were 1-butanol (99.8% purity) and 2-heptanone (98% purity). Mineral oil (light, Food Chemical Codex quality) served as solvent.

Concentration of each chemical in the headspace of every bottle was measured by gas chromatography (flame ionization detector) via a gas sampling valve (1 ml
sampling loop). We used a 5890 Hewlett-Packard Gas Chromatograph and a DB-1, 30 m × 0.53 mm i.d., 5.0 µm film thickness column purchased from J&W Scientific, Folsom, CA. Chromatographic readings were taken right after preparation of the stimuli, concomitantly with testing, and after all subjects had been tested, to confirm stability. Figure 1 shows the average vapor-phase concentration (±SD) that corresponds to each liquid dilution of butanol and heptanone, singly or in mixture. The headspace of bottles containing undiluted chemical (100% v/v) was assumed to be saturated with the chemical at room temperature (≈23°C). Such saturated vapor concentration (in ppm) was taken from handbooks or databases on vapor pressure. Vapor concentration in all other bottles was referenced to the concentration of saturated vapor.

Procedure. To obtain the stimulus-response (psychometric) functions for individual compounds, a series of twofold dilution-steps of the undiluted chemical (100% v/v, labeled dilution step 0) was prepared, i.e., 50%, 25%, 12.5%, 6.25%, etc., v/v, labeled dilution steps 1, 2, 3, 4, etc. Once the psychometric function for the group of subjects was obtained for each substance, we interpolated the concentrations producing probabilities of detection corrected for chance, p, of 0.20, 0.40, 0.60, and 0.80. Then, we prepared binary mixtures of 1-butanol and 2-heptanone to form a 4 × 4 (=16 stimuli) matrix where each level, i.e., p, of one chemical was combined with each level of the other. We also included ten single stimuli: 1-butanol at p = 0.00, 0.20, 0.40, 0.60, and 0.80, 2-heptanone at p = 0.00, 0.20, 0.40, 0.60, and 0.80, and one mixture where butanol and heptanone were both at p = 0.00. This amounted to 27 (16 + 10 + 1) stimuli. Using this set, we again measured psychometric functions for single stimuli and mixtures.
A different set of 27 stimuli was prepared for each of the three sensory endpoints studied: odor, nasal pungency, and eye irritation. All sets — single compounds and mixtures — were prepared in duplicate. Stimuli were delivered as vapors from cylindrical, squeezable, high-density polyethylene bottles (270-ml capacity) containing 25 ml of liquid. For nasal testing (odor and pungency) the bottles had a cap with a pop-up spout that allowed separate testing of each nostril (9). For ocular testing, the bottles had a cap of the sort used in variable-volume dispensers, leading to a 25-ml, roughly conical, reservoir, the rim of which was placed around the eye, allowing separate testing of each eye upon squeezing of the bottle (12).

All psychometric functions were obtained via a two-alternative, forced-choice procedure with presentation of ascending concentrations. Participants presented the stimuli to themselves by either inserting the pop-up spout inside the designated nostril or placing the rim of the conical reservoir around the designated eye, and squeezing the bottle. Each trial involved presentation of two stimuli and the subject had to choose the one that delivered the stronger sensation. One stimulus was always a blank (i.e., mineral oil) and the other a dilution step of the chemical(s), starting with the lowest concentration (i.e., the highest dilution step). Over a session with single chemicals, and in ascending order of concentration, each dilution step was presented paired with a blank a total of eight times (half with each nostril/eye). In the case of single chemicals, testing for each nostril/eye stopped when the subject chose the stimulus over the blank eight times in a row — four for each of two consecutive dilution steps. This performance was considered 100% detection. In the case of the sets of 27 stimuli the ascension through the matrix followed a path of expected probabilities of detection until all stimuli were tested.

To obtain the initial nasal and ocular psychometric functions for 1-butanol and 2-heptanone, each subject participated in four sessions. In each session, the subject
provided two complete functions — one nasal, one ocular — for one chemical. The chemicals were tested in irregular order. The data from the two sessions per chemical were averaged within individuals and across individuals of the same group, i.e., normosmic or anosmic. These averaged psychometric functions constituted the source for preparing the sets of 27 stimuli based on probability of detection corrected for chance, p, as described under Stimuli. For computation of the psychometric functions for odor from the corresponding set of 27 stimuli, 18 normosmics (the original 4 plus 14 more) provided a total of 332 two-alternative forced-choice judgments (half with each nostril) per stimulus. For computation of the psychometric functions for nasal pungency from the corresponding set of 27 stimuli, six anosmics (three of the original four plus three more) provided a total of 144 two-alternative forced-choice judgments (half with each nostril) per stimulus. For computation of the psychometric functions for eye irritation from the corresponding set of 27 stimuli, 8 subjects (the original 4 normosmics and 4 anosmics) provided a total of 128 two-alternative forced-choice judgments (half with each eye) per stimulus.

Data analysis. Plots of detection probability corrected for chance (ranging from 0.0, that is, chance detection, to 1.0, that is, perfect detection) as a function of stimulus concentration (in ppm by volume) summarize the outcome. Analysis of variance (ANOVA) with reported p values corrected (Huynh-Feldt correction) served to compare statistically detectability functions for single chemicals and mixtures.

Results

Figure 2 shows that psychometric functions for the odor of 1-butanol and 2-heptanone lie at concentrations about three orders of magnitude lower than the corresponding functions for their nasal pungency. For both sensory endpoints, 2-heptanone evokes any fixed level of detection, e.g., p=0.50, at a concentration about
half an order of magnitude lower than that of 1-butanol. Over the range where odor functions for 1-butanol and 2-heptanone, respectively, are linear, both have slopes of 0.5. Over the range where pungency functions for 1-butanol and 2-heptanone, respectively, are linear, both have slopes of 0.7, higher than the slopes for odor. These results agree with the described functional properties of the senses of olfaction and chemesthesia at threshold and suprathreshold levels (13, 15).

Insert Figure 2 about here

Figure 3 reveals that normosmics and anosmics do not differ in their sensitivity to eye irritation for either chemical, an outcome in agreement with previous findings (16). Based on this result the data for eye irritation from normosmics and anosmics were pooled. The pooled function for eye irritation from 1-butanol and that for 2-heptanone were compared to the corresponding nasal pungency functions as illustrated in Figure 4. In the case of 1-butanol, nasal pungency and eye irritation functions show considerable overlap. In the case of 2-heptanone, the ocular mucosa seemed more sensitive than the nasal mucosa — regarding chemesthesia — although the difference always fell below half an order of magnitude. Over the range where the functions for eye irritation (combined results of normosmics and anosmics) for 1-butanol and 2-heptanone are linear, the slopes had values between 0.7 and 0.8, respectively, falling into register with the slopes for nasal pungency.

Insert Figures 3 and 4 about here

As described under “Stimuli” in the “Materials and Methods” section, the psychometric functions for 1-butanol and 2-heptanone presented in Figures 2 to 4 served to define the concentrations of the components in the binary mixtures to be tested. Also, five selected concentrations of each of the two single compounds (those
corresponding to $p = 0.00, 0.20, 0.40, 0.60, \text{ and } 0.80$) were also tested interspersed with the mixtures in the same session. This allowed a direct comparison of the detectability of all stimuli, single and mixed. Figure 5 (upper part) presents the psychometric function for the odor of 2-heptanone alone and mixed with increasing concentrations of 1-butanol. Similarly, Figure 5 (lower part) presents the psychometric function for the odor of 1-butanol alone and mixed with increasing concentrations of 2-heptanone. An analysis of variance (ANOVA) performed on these data (Figure 5) revealed significant effects for the factors heptanone ($F[3, 51]=29.48, p<0.0001$) and butanol ($F[4, 68]=24.91, p<0.0001$) concentrations, as well as for their interaction ($F[12, 204]=2.68, p<0.05$). This provides statistical support to the increased odor detectability observed with the addition of increasing concentrations of the second chemical.

![Insert Figure 5 about here](image)

Figure 6 presents analogous psychometric functions to those of Figure 5 but for nasal pungency. Similar trends to those observed for odor are evident here. An ANOVA performed on these data (Figure 6) revealed significant effects for the factors heptanone ($F[3, 15]=8.92, p<0.005$) and butanol ($F[4, 20]=21.34, p<0.0001$) concentrations, but not for their interaction ($F[12, 204]=2.68, p<0.05$).

![Insert Figure 6 about here](image)

Figure 7 show psychometric functions for eye irritation from 2-heptanone and 1-butanol. An ANOVA performed on these data (Figure 7) revealed significant effects for the factors heptanone ($F[3, 21]=34.38, p<0.0001$) and butanol ($F[4, 28]=41.51, p<0.0001$) concentrations, as well as for their interaction ($F[12, 84]=3.26, p<0.005$).
It is clear from the results presented in Figures 5 through 7 that, as a rule, the addition of increasing amounts of a second compound progressively enhances the probability of detection of the (now mixed) stimulus across the entire range of detection probability levels, i.e., from \( p = 0.0 \) to \( p = 1.0 \). This effect holds for all three sensory endpoints: odor, nasal pungency, and eye irritation. A question of interest is whether such increase in detection probability can be uniformly accounted for by transforming the added concentrations of the second chemical into sensory-equivalent concentrations of the first chemical. If this is so, a common stimulus-response function should be able to describe the sensory detection of all stimuli, single and mixed, as long as the mixtures are expressed entirely as equivalent-concentrations of one (or the other) component.

To address this question we converted each set of four concentrations of butanol added to heptanone as illustrated in the upper part of Figures 5, 6, and 7 into corresponding detection probabilities using the “Butanol alone” functions shown in the lower part of Figures 5, 6, and 7 for odor, nasal pungency, and eye irritation, respectively. Then, using these detection probabilities, we interpolated on the “Heptanone alone” function of Figures 5 (for odor), 6 (for nasal pungency), and 7 (for eye irritation) and found the concentration-equivalents of each set of four levels of butanol, now expressed in terms of heptanone concentration units.

An analogous procedure was used to convert each set of four concentrations of heptanone added to butanol as illustrated in the lower part of Figures 5 (odor), 6 (nasal pungency), and 7 (eye irritation) into detection probabilities and, ultimately, into concentration-equivalents expressed in terms of butanol concentration units.
These transformations allowed us to express sensory detection of single and mixed stimuli as a function of concentration units of just heptanone, or as a function of concentration units of just butanol. The outcome of such graphs for odor detection is presented in Figure 8 (upper part) using exclusively heptanone concentration units, and in Figure 8 (lower part) using exclusively butanol concentration units. An ordinate expressed as p in Figure 8 portrays the results almost identically to an ordinate expressed as normal deviate units, z, the theoretically better justified unit for a linear fit. The use of p in Figure 8, as well as in Figures 9 and 10, maintains consistency with the units of the previous figures. The use of a straight line to fit the data expressed as p implies no attempt to create new psychophysical theory. Both parts of Figure 8 reveal that all stimuli (single and mixed) fall along a single odor detectability function with a statistically significant correlation coefficient (r>0.98, p<<0.01) and slope around 0.5. This implies that the odor detectability of these binary mixtures follows a straightforward rule of “dose addition” whereby introduction of a second component can be simply seen as introduction of more of the first component.

Insert Figure 8 about here

Similarly, the next figure presents the results for nasal pungency detection plotted as a function of heptanone concentration units (Figure 9, upper part) or as a function of butanol concentration units (Figure 9, lower part). Here also there is a tendency for single and mixed stimuli to fall along the same nasal pungency detectability function, whether expressed as concentration units of one compound or the other. Both pungency functions show significant correlation coefficients (r>0.90, p<<0.01) with slopes around 0.7–0.8.

Insert Figure 9 about here
Finally, Figure 10 shows eye irritation detectability functions in terms of heptanone (upper part) and butanol (lower part) concentrations. Again, single and mixed stimuli fall closely along the same function with significant correlation coefficients ($r=0.96$, $p<<0.01$) and slopes around 0.7–0.8.

Discussion

The topic of olfactory perception of chemical mixtures has received attention in both animal and human studies. The animals used were crustaceans (e.g., (26)), fish (e.g., (22)), and mammals (e.g., (5)), including primates (e.g., (24)). These investigations, done at the behavioral (i.e., whole-animal) or cellular level, have addressed principally the issue of olfactory discrimination of mixtures and their components, and the issue of types of electrophysiological cellular responses — i.e., excitatory, inhibitory, or no response — to mixtures and their components. The studies have not addressed threshold response to single substances vis-à-vis threshold response to their mixtures.

Human studies of odor mixtures have largely focused on suprathreshold intensity (e.g., (8, 28)) and quality discrimination (e.g., (25)). Considerably less attention has been paid to studies of thresholds for mixtures and for their components (see, for example, (17)). The novelty of our present approach consisted in testing mixtures where the constituents varied systematically in their relative proportions, and in measuring complete psychometric functions as opposed to thresholds according to some fixed criterion of performance.
The present results provide additional support to the existence of stimulus agonism (17, 29) in the detection of chemical mixtures at perithreshold levels. This holds for all three sensory endpoints: odor, nasal pungency, and eye irritation. The present data for smell, seen in the context of the commonly observed hypoadditivity of responses at suprathreshold levels, suggests that peri-threshold stimulation might elicit little or no mutual inhibition between components of a mixture (11, 28). At levels progressively above threshold, an inhibitory interaction appears to grow. From a pharmacological point of view, at very low concentrations of an odorant binary mixture (as near the odor threshold) there might be negligible competition between components for binding to olfactory receptors, resulting in large sensory agonism. As the concentration of the two odorants increases so does the competition for binding to olfactory receptors, resulting in decreased sensory agonism. The structural similarity between odorants in a mixture, and thus their ability to bind to a smaller or larger overlapping family of receptors, becomes then a crucial factor as shown in a recent study with spiny lobsters (20).

The finding of stimulus agonism in the chemesthetic modalities also falls into register with the finding that a combination of no more than five general physicochemical properties in a solvation equation does quite well at describing and predicting nasal pungency (2, 3) and eye irritation thresholds (4) for volatile organic compounds (VOCs) in humans. If simple physicochemical “transport” processes (e.g., distribution of the VOC among biophases or rate of transfer of the VOC from one biophase to another) largely govern the chemesthetic potency of these stimuli, then stimulus agonism is to be expected. The latest update of the equation for human nasal pungency thresholds (NPT, expressed in ppm by volume) reads as follows (3):

\[
\log \left( \frac{1}{NPT} \right) = -8.519 + 2.154 \pi^H_2 + 3.522 \sum \alpha^H_\ell + 1.397 \sum \beta^H_\ell + 0.860 \log L^{16}
\]
where the physicochemical descriptors are: dipolarity/polarizability ($\pi_2^H$), overall or effective hydrogen-bond acidity ($\Sigma\alpha_2^H$), overall or effective hydrogen-bond basicity ($\Sigma\beta_2^H$), and gas–liquid partition coefficient on hexadecane at 298K ($L_1^6$). Also, n is the number of data points (VOCs), $r$ is the correlation coefficient, $sd$ is the standard deviation in log 1/NPT, and $F$ is the F-statistic.

In turn, the equation for eye irritation thresholds (EIT, expressed in ppm by volume) reads as follows (4):

$$\log (1/EIT) = -7.918 - 0.482R_2 + 1.420\pi_2^H + 4.025\Sigma\alpha_2^H + 1.219\Sigma\beta_2^H + 0.853\log L_1^6$$

where the only descriptor not defined before is an excess molar refraction ($R_2$).

Despite the relatively large differences in odor quality between 1-butanol and 2-heptanone, particularly at suprathreshold levels, the molecular structure of both VOCs might still be similar enough to result in dose addition at perithreshold odor levels (i.e., low doses). Only a systematic study of a number of binary mixtures where the components differ from one another in a graded fashion can answer the question of whether an increasing degree of molecular difference between components reduces the degree of agonism in mixtures to produce odor detection. Our lab is planning to address the issue in future studies. So far, the solvation equation referred above has not been as successful with odor thresholds as with nasal pungency and eye irritation thresholds (1). This suggests that the key step in odor detection involves a mechanism more finely tuned to other properties of the stimulating molecule (e.g., a specific shape, size, and/or
orientation) than to the less specific “transport” processes that seem to suffice to explain chemesthetic thresholds.

The present approach of studying chemosensory detection of mixtures vis-à-vis detection of the separate components via detectability functions is a typical “bottom up” approach. Without a means for generalization and modeling, this strategy might consume enormous time and effort before providing data directly relevant to real situations where mixtures are composed of dozens of chemicals. Nevertheless, combined with the solvation equation strategy that has worked so well for individual VOCs — at least regarding chemesthesis — they provide the potential for understanding the chemosensory impact of mixtures of VOCs in the not-so-distant future.
Acknowledgments

The work described in this article was supported by research grant number R29 DC 02741 from the National Institute on Deafness and Other Communication Disorders, National Institutes of Health, and by the Center for Indoor Air Research. Thanks are due to René Loya for excellent technical assistance. Thanks are also due to J.P. Lu and Regina Meijninger for their help in running the experiments.
References


**Figure Legends**

**Figure 1.** Average and variability (standard deviation) of vapor-phase concentrations of all stimuli, single and mixed, as measured by gas chromatography (FID detector). Presence of a second chemical produced no systematic variation in the vapor-phase concentration of the first chemical. Empty squares represent 1-butanol, and filled squares represent 2-heptanone. Bars indicating standard deviations are sometimes hidden by the symbols.

**Figure 2.** Detectability functions for the odor and nasal pungency of 2-heptanone and 1-butanol. Each point represents the result of 64 trials made by four subjects. Detection probabilities here and in all following figures are corrected for chance (27).

**Figure 3.** Detectability functions for the eye irritation of 2-heptanone and 1-butanol in normosmics and anosmics. Each point represents the result of 64 trials made by four subjects.

**Figure 4.** Comparison of the detectability functions for nasal pungency and for eye irritation of 2-heptanone and 1-butanol. For nasal pungency, each point represents the result of 64 trials made by four subjects. For eye irritation, each point represents the result of 128 trials made by eight subjects.

**Figure 5.** (Upper part). Odor detectability functions for 2-heptanone alone and mixed with each of four concentrations of 1-butanol (the parameter). These four concentrations corresponded to the levels of butanol capable of producing odor detection at probabilities (p) 0.20, 0.40, 0.60, and 0.80 according to the results presented in Figure 2. (Lower part). Similar to upper part (odor detectability) but
plotted as a function of 1-butanol with 2-heptanone as the parameter. For both parts, each point represents the results of 332 trials made by a total of 18 normosmics.

Figure 6. (Upper part). Nasal pungency detectability functions for 2-heptanone alone and mixed with each of four concentrations of 1-butanol (the parameter). These four concentrations corresponded to the levels of butanol capable of producing nasal pungency detection at probabilities (p) 0.20, 0.40, 0.60, and 0.80 according to the results presented in Figure 2. (Lower part). Similar to upper part (nasal pungency detectability) but plotted as a function of 1-butanol with 2-heptanone as the parameter. For both parts, each point represents the results of 144 trials made by a total of 6 anosmics.

Figure 7. (Upper part). Eye irritation detectability functions for 2-heptanone alone and mixed with each of four concentrations of 1-butanol (the parameter). These four concentrations corresponded to the levels of butanol capable of producing eye irritation detection at probabilities (p) 0.20, 0.40, 0.60, and 0.80 according to the results presented in Figure 4 (combined data of normosmics and anosmics). (Lower part). Similar to upper part (eye irritation detectability) but plotted as a function of 1-butanol with 2-heptanone as the parameter. For both parts, each point represents the results of 128 trials made by a total of 8 subjects.

Figure 8. (Upper part). Odor detectability function for all stimuli (2-heptanone alone, 1-butanol alone, and all mixtures) expressed as heptanone concentrations (see text). (Lower part). Same, but with all stimuli expressed as butanol concentrations (see text).

Figure 9. (Upper part). Nasal pungency detectability function for all stimuli (2-heptanone alone, 1-butanol alone, and all mixtures) expressed as heptanone concentrations (see text).
text). (Lower part). Same, but with all stimuli expressed as butanol concentrations (see text).

**Figure 10.** (Upper part). Eye irritation detectability function for all stimuli (2-heptanone alone, 1-butanol alone, and all mixtures) expressed as heptanone concentrations (see text). (Lower part). Same, but with all stimuli expressed as butanol concentrations (see text).
FIGURE 1

Gas Chromatography data

Vapor-phase concentration (log ppm)

Liquid-phase concentration (log %v/v)

1-Butanol
2-Heptanone
FIGURE 2

Detection probability ($p$)

Concentration (log ppm)

2-Heptanone
- O - Odor
- - Pungency

1-Butanol
- O - Odor
- - Pungency

Detection probability ($p$)

Concentration (log ppm)
FIGURE 3

EYE IRRITATION

2-Heptanone

- Normosmics
- Anosmics

1-Butanol

- Normosmics
- Anosmics

Detection probability (p)

Concentration (log ppm)
FIGURE 4

Detection probability (p)

Concentration (log ppm)

Nasal Pungency

Eye Irritation

2-Heptanone

1-Butanol

Detection probability (p)

Concentration (log ppm)
FIGURE 5

Odor

2-Heptanone (log ppm)

Detection probability (p)

Butanol alone (p)
+ 0.20 (p) Butanol
+ 0.40 (p) Butanol
+ 0.60 (p) Butanol
+ 0.80 (p) Butanol

1-Butanol (log ppm)

Butanol alone (p)
+ 0.20 (p) Heptanone
+ 0.40 (p) Heptanone
+ 0.60 (p) Heptanone
+ 0.80 (p) Heptanone
FIGURE 6

Nasal Pungency

Detection probability (p)

2-Heptanone (log ppm)

+ 0.80 (p) Butanol
+ 0.60 (p) Butanol
+ 0.40 (p) Butanol
+ 0.20 (p) Butanol
Butanol alone (p)

1-Butanol (log ppm)

+ 0.80 (p) Heptanone
+ 0.60 (p) Heptanone
+ 0.40 (p) Heptanone
+ 0.20 (p) Heptanone
Heptanone alone (p)
FIGURE 7

EYE IRRITATION

Detection probability (p)

- Eye Irritation Heptanone (p)
- + 0.20 (p) Butanol
- + 0.40 (p) Butanol
- + 0.60 (p) Butanol
- + 0.80 (p) Butanol

Detection probability (p)

- Eye Irritation Butanol (p)
- + 0.20 (p) Heptanone
- + 0.40 (p) Heptanone
- + 0.60 (p) Heptanone
- + 0.80 (p) Heptanone

2-Heptanone (log ppm)

1-Butanol (log ppm)
FIGURE 8

Detection probability (p)

Heptanone concentration (log ppm)

y = 0.470x + 0.959  r = 0.983

Butanol concentration (log ppm)

y = 0.509x + 0.512  r = 0.982
FIGURE 9

Nasal Pungency

Detection probability ($p$)

Heptanone concentration (log ppm)

y = 0.659x - 1.295  r = 0.935

Butanol concentration (log ppm)

y = 0.786x - 2.038  r = 0.907
FIGURE 10

Eye Irritation

Detection probability (p)

Heptanone concentration (log ppm)

\[ y = 0.658x - 0.854 \quad r = 0.965 \]

Butanol concentration (log ppm)

\[ y = 0.790x - 1.769 \quad r = 0.960 \]