

Dualistic Thiourea Moiety Taste Response of Methimazole

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Determination of the taste responses to phenylthiourea, to propylthiouracil, and to 1-methyl-2-mercaptoimidazole (methimazole) using impregnated filter paper strips on a group of 191 individuals showed that methimazole, contrary to its literature description of "almost no taste," is quite bitter to 30 per cent of the population studied, and does possess a dualistic taste similar to the other two compounds tested.

INDIVIDUALS differ in their ability to taste substances containing the thioureyne, —NHCS—NH— , or thiocarbonyl, —NHC(S)— groups. Phenylthiourea and the cyclic thioureyne, propylthiouracil, taste bitter to a considerable portion of the population, and tasteless to the rest; the inability to taste is apparently a recessive, inherited Mendelian characteristic (1-3). Structures of representative compounds, with their taste responses, are given in Figs. 1-3.

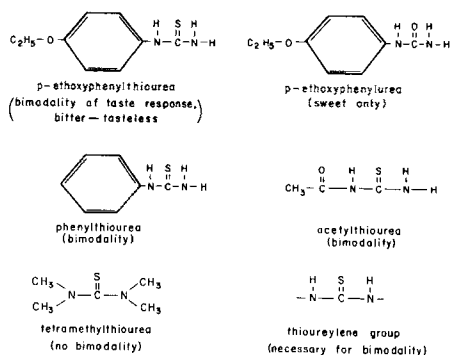


Fig. 1—Thiourea derivatives with taste responses.

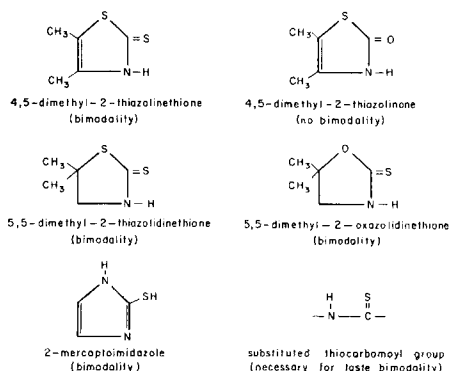


Fig. 2—Thiourea derivatives with taste responses.

The antithyroid substances, L-5-vinyl-2-oxazolidinethione (goitrin) (4, 5), 2-mercaptoimidazole (2), and propylthiouracil (2) possess the dualistic taste response. Harris, Kalmus, and Trotter found that nontasters of phenylthiourea were slightly more prone to develop adenomatous goiter than tasters (6). This finding has been confirmed by Kitchin *et al.*, who also found that toxic diffuse goiter is more prevalent among tasters (7). Shepard and Gartler

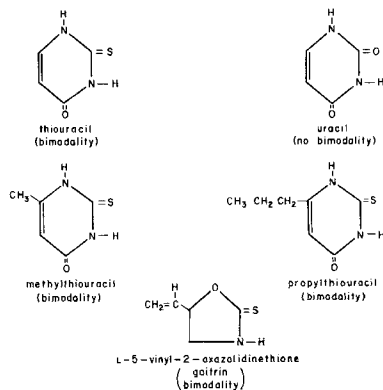


Fig. 3—Thiourea derivatives with taste responses.

reported an increased incidence of nontasters of phenylthiourea among congenital athyreotic cretins (8).

This study extends the determination of the taste response to the antithyroid drug, 1-methyl-2-mercaptoimidazole (methimazole). The propylthiouracil taste response and the phenylthiourea taste threshold were also determined. In order to contribute data to help in possible correlation of taste and thyroid disease, the phenylthiourea taste threshold was also ascertained on a group of thyroid patients. The three compounds in this study are shown in Fig. 4.

EXPERIMENTAL

Serial Dilutions Method—The phenylthiourea taste threshold was determined by the serial dilutions method of Harris and Kalmus (2). A control

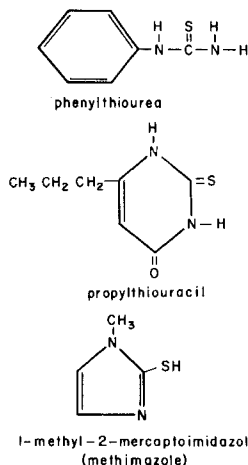


Fig. 4—Structures of compounds studied.

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TABLE I—SUMMARY OF TASTE RESPONSES TO MEDICATED PAPER STRIPS

Impregnating Soln. Concn. Gm./100 ml.	Drug	Total	Tasters	Nontasters	Percentage of Nontasters
0.040	Phenylthiourea	191	97	94	49.2
0.040	Propylthiouracil	191	92	99	51.8
0.040	Methimazole	191	56	135	70.6
		Strong			
1.0	Phenylthiourea	279	246	33	11.8
1.0	Propylthiouracil	279	240	39	13.9

group of 171 individuals¹ were tested with 14 concentrations of phenylthiourea. Dilution No. 1 contains 1300 mg./L., and each subsequent number dilution is one-half the strength of the preceding concentration. The threshold is the weakest concentration at which the individual is able to differentiate four cups of distilled water from four cups of the test concentration. The people tested were then divided into two groups; tasters are persons who can distinguish phenylthiourea solutions numbered 5 (81.25 mg./L.) or higher, and nontasters are those who can taste only solutions numbered 4 (162.5 mg./L.) or lower. The phenylthiourea taste threshold was also determined on a group of 148 thyroid patients.²

Filter Paper Strip Method—The paper strip method of Parr (9) was used to obtain the relative taste response of persons to phenylthiourea, propylthiouracil, and methimazole,³ and to establish a correlation between this and the serial dilutions method. Two types of filter paper strips were used for phenylthiourea and propylthiouracil. One type was prepared by soaking the paper strips in a 1% solution of the drug, so that each strip contained approximately 2.5 mg. of compound, which is nearly equal to the 2.6 mg. found in 8 ml. of solution No. 3 in the serial dilutions method. A weaker concentration paper strip was prepared by immersing the strips in a 0.04% solution of the substance in acetone, so that each strip contained about 0.1 mg. of drug, corresponding to the 0.08 mg. present in 8 ml. of the serial dilutions No. 8. Only the more weakly medicated strips of methimazole were prepared.

In the procedure of tasting, the persons were asked to put the weaker of the two strips on the back of the tongue, where sensitivity to bitter taste is pronounced. When a taste sensation was ob-

served, a blank strip was given in order to check the result. If the strip with weak medication did not produce a sensation, the stronger was administered (except in the case of methimazole).

Using the serial dilutions method, the percentage of nontasters found in the white control group of 134 students was 21.6; while that found in 37 Mongolian students was 8.1. Preliminary data obtained by similar performance of the phenylthiourea threshold on a group of 148 thyroid patients indicates a relatively high percentage of nontasters in euthyroid patients and in male thyroid patients, with a low percentage of nontasters in hyperthyroid individuals.

Table I shows that methimazole, like phenylthiourea and propylthiouracil, exhibits the dualistic taste response; and contrary to its literature description of "almost no taste" (10), it is quite bitter to almost 30% of the population. Nontaster percentages found for filter paper strips weakly medicated with phenylthiourea, propylthiouracil, and methimazole were 49.2, 51.8, and 70.6, respectively. Therefore, taste sensitivity to phenylthiourea was the strongest, followed closely by propylthiouracil, whereas sensitivity to methimazole was lower. A similar correlation was observed with strongly medicated phenylthiourea and propylthiouracil paper strips, the percentage of nontasters being, respectively, 11.8 and 13.9.

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¹ Consisting mainly of first year students at the School of Pharmacy, University of Southern California, Los Angeles.

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