culture media were used; control medium, mainly composed of baker's yeast and sucrose, and treated medium in which formaldehyde (Panreac) was added to the control medium to obtain a concentration of 0.2% (v/v). Control or treated food was poured into vials (10 × 2.5 cm), using 10 ml per vial.

Virgin males and females were taken from each population and introduced into plastic cylinders (3.60 × 7.80 cm) containing control medium. In these receptacles females laid eggs for 24 h. Eggs were transferred to the vials by using a lancet (50 eggs/vial). Adult males and females from these vials were counted, and the overall lethality (100 minus (adults/eggs) × 100) and induced lethality[8,9] computed. All experiments were performed at 21 °C.

Results and discussion. The table shows that in all populations formaldehyde induced a high percentage of lethality. For each population, the difference between the number of adults from control and treated samples was analyzed by means of 2 × 2 contingency table, and the differences were always highly significant ($p < 0.001$). In addition to this, relevant results appeared when comparing on the one hand the overall lethality percentages from the 4 control samples with each other, and on the other hand the corresponding percentages from the 4 treated samples. The comparisons were carried out by homogeneity analysis of proportion through a chi-square[10]. The result for the control samples was: Naranco > Teverga–Oviedo > Felguera with a $\chi^2 = 88.60$; and for the treated samples: Felguera–Oviedo–Teverga > Naranco with a $\chi^2 = 71.00$ (the Felguera and Teverga populations showed significant difference at the 5% level). Thus, it was not possible to establish any connection between the natural environment of populations and the overall lethality, since no significant difference was shown between the Teverga and Oviedo populations. However, the Naranco population, showing the highest control lethality, was at the same time the least sensitive to the formaldehyde. In contrast to this, the Felguera population with the lowest control lethality was the most sensitive to the toxic.

Other methods of formaldehyde treatment, analysis of other traits and a larger number of populations, will help to clarify the possible existence of any specific adaptation.

Overall and induced lethality by formaldehyde food in 4 populations of *D. melanogaster*

Populations		Eggs	Adults	Overall lethality ± SE (%)	Induced lethality (%)
Teverga	Control	500	385	23.00 ± 1.88	–
	Treated	500	74	85.20 ± 1.58	80.78
Felguera	Control	1000	869	13.10 ± 1.06	–
	Treated	1000	99	90.10 ± 0.94	88.60
Oviedo	Control	1000	794	20.60 ± 1.27	–
	Treated	1000	111	88.90 ± 0.99	86.02
Naranco	Control	1000	697	30.30 ± 1.45	–
	Treated	1000	219	78.10 ± 1.30	68.57

1 Moutschen, J., Introduction à la toxicologie génétique, p. 48. Masson, Paris 1979.
2 Perera, F., and Petito, C., Science *216* (1982) 1285.
3 Slizynska, H., Proc. Roy. Soc. Edinburgh *666* (1957) 288.
4 Auerbach, C., A. Rev. Genet. *5* (1971) 187.
5 Dickey, F. H., Cleland, G. H., and Lotz, C., Genetics *35* (1949) 581.
6 Nishioka, H., Mutat. Res. *17* (1973) 261.
7 Chanet, R., Mutat. Res. *62* (1979) 239.
8 Abbott, W. S., J. econ. Ent. *18* (1925) 265.
9 Graf, U., and Würgler, F. E., Mutat. Res. *34* (1976) 251.
10 Snedecor, G. W., and Cochran, W. G., Métodos Estadísticos, p. 285. C.E.C.S.A., 1975.

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Beta$_1$-adrenoceptor mediated salivary gland enlargement in the rat[1]

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Summary. In the rat, prolonged activation of β_1-adrenoceptors causes a gain in salivary gland weight, whereas prolonged blockade of these receptors causes a reduction in weight.

Prolonged treatment with the nonselective beta-adrenoceptor agonist isoprenaline causes the parotid and submaxillary glands of the rat to increase markedly in weight[2]. In the rat, isoprenaline also evokes a flow of saliva from these glands; that from the parotid gland is rich in amylase[3]. The beta-adrenoceptors that are responsible for mediating secretion of fluid from the parotid and submaxillary glands of the rat belong to the β_1-subtype[4-6], and this is also the case for those mediating secretion of amylase from the parotid gland[7]. Treatment with dobutamine, a β_1-adrenoceptor selective agonist, but not with terbutaline, a β_2-adrenoceptor selective agonist, has been found to cause a gain in weight of the rat submaxillary gland[8]. However, terbutaline has also been reported to cause an increase in the weight of the rat parotid gland[9,10]. In the present study the effects on the weight of the 3 major salivary glands of the rat of prolonged treatment with the β_1-adrenoceptor selective agonist prenalterol, terbutaline and the β_1-adrenoceptor selective antagonist metoprolol were examined.

Materials and methods. Adult female rats, weighing about 225 g, of a Sprague-Dawley strain were used. There were 3 experimental groups. The rats of each group were litter-mates. The groups were as follows: 1. control (7 animals) and prenalterol-treated animals (7); 2. control (8) and terbutaline-treated animals (8); 3. control (5), metoprolol-treated (5) and metoprolol + terbutaline-treated animals (5). The drugs were given twice daily, dissolved in 0.2 ml saline, over a period of 14 days. Prenalterol HCl (AB Hässle) 3.5 mg (15.5 mg/kg) and terbutaline sulphate (AB Draco) 3.7 mg (16 mg/kg) were given s.c., while metoprolol tartrate (AB Hässle) 5 mg (22 mg/kg) was given i.p.; when metoprolol and terbutaline treatments were combined, the former drug was given 20 min in advance. At the end of the experiment the animals were killed by inhalation of ether; the parotid, submaxillary and sublingual glands were removed and weighed (wet weight). The glands were then heated at 110 °C for at least 3 days (dry weight). Gland weights (mg) were expressed in relation to body-weight (g). Student's t-test for unpaired data was used.

Results and discussion. The body-weights of treated animals did not differ from those of the respective controls.

Prenalterol, β_1-selective agonist, increased both wet (by 30%) and dry (by 21%) weights of the parotid glands (fig. 1), but not significantly those of the submaxillary glands (fig. 2). Terbu-

taline, β_2-selective agonist, increased both the weights of the parotid glands (wet weight by 44%; dry weight by 43%) and those of the submaxillary glands (wet weight by 18%; dry weight by 12%). Metoprolol, β_1-selective antagonist, decreased the dry weight of the parotid glands (by 15%), and both wet (by 8%) and dry weights (by 16%) of the submaxillary glands. Metoprolol prevented the terbutaline-induced enlargement of both glands. After this combined treatment the dry weight of the parotid gland was (22%) lower than the controls, while the wet and dry weights of the submaxillary glands were (15 and 26%) lower than their controls; there was no significant difference in gland weights between rats treated only with metoprolol and those treated with metoprolol + terbutaline. The weights of the sublingual glands were unaffected by the treatment with either prenalterol, terbutaline or metoprolol.

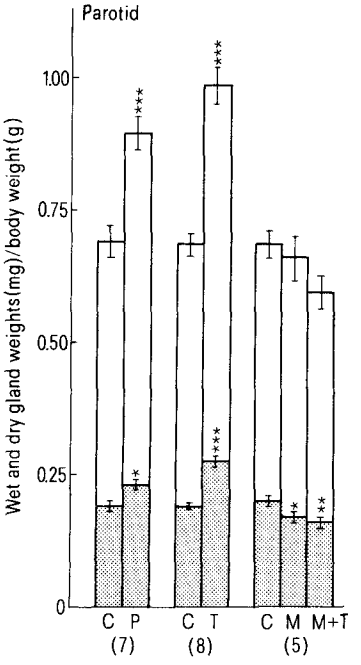

Figure 1. Parotid glands. The effect on wet (open columns) and dry weights (hatched columns) of 14-day treatment with prenalterol (P), terbutaline (T), metoprolol (M) or a combination of metoprolol and terbutaline (M+T). Within each group the number of control animals (C), indicated in brackets, was the same as that of animals exposed to respective treatment; the glands of both sides were used. Gland weights (mg) are related to body-weight (g). Columns indicate mean and vertical bars ± SE. *p < 0.05, **p < 0.01 and ***p < 0.001, when comparisons were made with controls.

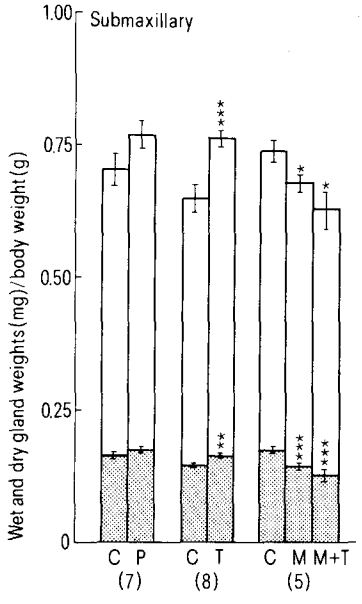

Figure 2. Submaxillary glands. For details see legend of figure 1.

Dry weights are usually considered more reliable than wet weights, particularly when the glands have been secreting[11]. In the present study the animals were killed by inhalation of ether, which evokes secretion of saliva by a reflex[12]. The increase in weight of the parotid gland in response to treatment with prenalterol and the decrease in weight of this gland and the submaxillary gland in response to metoprolol indicate that β_1-adrenoceptors are involved in the regulation of salivary gland size. Terbutaline caused an increase in the weight of both parotid and submaxillary glands. However, metoprolol prevented this effect of terbutaline, demonstrating that gland enlargement due to terbutaline is mediated via β_1-adrenoceptors. This suggests that with the dose of terbutaline used the drug has lost its selectivity for only β_2-adrenoceptors. The weight of the sublingual glands was not changed by the different treatments. This is not surprising, since in this gland there is a scarcity of β-adrenoceptors. The parotid gland responded better than the submaxillary gland to prenalterol and terbutaline. In response to isoprenaline treatment the increase in weight of the parotid gland has been found to be about twice that of the submaxillary gland[2,15]. The decrease in weight following metoprolol treatment was in the same range as that found after sympathetic denervation of the glands[13,14].

Human salivary glands seem to be supplied with β_1-adrenoceptors[16]. Patients suffering from asthma are often treated with terbutaline and those suffering from hypertension with nonselective β-adrenoceptor blockers or with β_1-selective adrenoceptor blockers like metoprolol. It may perhaps be of interest to take into consideration that prolonged treatment with these drugs in man may affect salivary secretory activity and salivary gland size[17].

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2 Schneyer, C.A., Am. J. Physiol. *203* (1962) 232.
3 Emmelin, N., Schneyer, C.A., and Schneyer, L.H., in: International Encyclopedia of Pharmacology and Therapeutics, Sec. 39A, vol. 1, p. 1. Ed. P. Holton, Pergamon, Oxford and New York 1973.
4 Ekström, J., Experientia *25* (1969) 372.
5 Ekström, J., Acta pharmac. toxic. *45* (1979) 325.
6 Thulin, A., Experientia *28* (1972) 420.
7 Carlsöö, B., Danielsson, Å, and Henriksson, R., Br. J. Pharmac. *62* (1978) 364.
8 Brenner, G.H., and Wulf, E.G., J. Pharmac. exp. Ther. *218* (1981) 608.
9 Sodicoff, M.S., Sinesi, M.S., and Pratt, N.E., Archs oral Biol. *25* (1980) 781.
10 Henriksson, R., Bloom, G.D., Carlsöö, B., Danielsson, A., and Magnusson, N.G., Adv. physiol. Sci. *28* (1980) 153.
11 Ohlin, P., Q. J: exp. Physiol. *50* (1965) 446.
12 Robbins, D., J. Pharmac. exp. Ther. *54* (1935) 426.
13 Ekström, J., Acta physiol. scand. *108* (1980) 253.
14 Ekström, J., and Malmberg, L., Acta physiol. scand. *113* (1981) 103.
15 Ekström, J., Acta physiol. scand. *92* (1974) 272.
16 Arglebe, C., Chilla, R., and Witzemann, V., Adv. physiol. Sci. *28* (1981) 335.
17 The drugs were kindly supplied by AB Hässle, Mölndal, and AB Draco, Lund, Sweden.

0014-4754/84/080862-02$1.50 + 0.20/0