In a typical run 4 mg 1,6-dimethanesulphonyl-D-mannitol were introduced into the thermostatted vessel and dissolved in 10 ml 0·2 M aqueous KCl and the apparatus was set to maintain the required pH by the continuous addition of 0·1 N NaOH. The use of 0·2 M KCl was necessary to provide a solution of sufficient ionic strength to ensure accurate pH control by the instrument.

Percentage conversion of polyol derivatives into epoxides

A typical run was carried out as follows: 430 mg 1,6-dimethanesulphonyl-D-mannitol were dissolved in 10 ml water and kept at 37°. 9·5 ml 0·1 N NaOH were required to keep the pH at 7·5 during a 130 min period. After this time the addition of about 5 g sodium thiosulphate caused a rapid development of alkalinity and this was titrated with 0·1 N HCl keeping the pH at 7·5. In 10 min 7·0 ml acid had been added and no further alkalinity was being developed. Thus the extent of hydrolysis was 37·4 per cent and of epoxide formation was 27·6 per cent, that is, 73 per cent of the reaction led to epoxide formation.

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Inhibition of glutamate decarboxylase by salicylate congeners

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SALICYLATE has been reported to inhibit *E. coli* glutamate decarboxylase activity *in vitro*. The present report shows that this inhibitory action is shared by a number of related compounds. The estimation of the enzyme activity and the effects of the salicylate congeners were studied by the techniques described previously[1] and the results are given in Table 1.

TABLE 1. INHIBITION OF GLUTAMATE DECARBOXYLASE ACTIVITY BY SALICYLATE CONGENERS AT A CONCENTRATION OF 20 mM

(The results, which are expressed as percentage inhibitions, represent the means of six different observations Analysis of the results by the t-test showed that P wa less than 0·05 in each case).

Congener	% Inhibition
Salicylic[1] (2-Hydroxybenzoic)	22
Benzoic	14
Hexahydrobenzoic	40
3-Hydroxybenzoic	11
4-Hydroxybenzoic	20
3-Hydroxysalicylic	11
3-Methylsalicylic	40
3-*Cyclo*hexylsalicylic (sat. soln.)	98
4-Hydroxysalicylic	16
5-Hydroxysalicylic	7
5-Nitrosalicylic	61
6-Hydroxysalicylic	42

The inhibitory effects of the congeners were not removed when the inhibited enzyme preparations were dialysed but were reduced by preincubation of the enzyme with pyridoxal phosphate. Thus they resembled salicylate in causing an irreversible reaction with the enzyme protein which was modified by preincubation of the glutamate decarboxylase preparation with its coenzyme.[1]

In general there was a reasonable correlation between inhibitory activity against both glutamate decarboxylase and rat serum glutamate–pyruvate transaminase amongst salicylate congeners.[2] The compounds such as 3-*cyclo*hexyl- and 5-nitrosalicylate, which were the most active against the one enzyme were also against the other. However, the structural requirements for inhibitory activity

TABLE 2. COMPARISON OF INHIBITORY ACTIVITIES OF HYDROXYSALICYLIC ACIDS AGAINST GLUTAMATE DECARBOXYLASE AND GLUTAMATE–PYRUVATE TRANSAMINASE ACTIVITIES

Congener	% Inhibition of Glutamate Decarboxylase by 20 mM conc.	% Inhibition of Glutamate–Pyruvate Transaminase by 5 mM conc.[2]
Salicylic	22	26
3-Hydroxysalicylic	11	43
4-Hydroxysalicylic	16	32
5-Hydroxysalicylic	7	35
6-Hydroxysalicylic	42	54

with respect to the decarboxylase appeared to be much less precise since phenol, benzoate and hexahydrobenzoate all showed activity. A further point of difference was that the introduction of an extra hydroxyl group into the salicylate molecule enhanced inhibitory activity against the transaminase whereas only the 6-hydroxysalicylate showed an increased inhibition, relative to salicylate, of the decarboxylase (Table 2).

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