mal cells is mentioned by Nettleship *et al.*[9] in urethane treated mice. Paterson *et al.*[3] reported fibrosis in the bone marrow, liver and spleen of urethane treated leukemia patients and the authors have noted excess fibroplasia in excised sections of urethane treated wounds.

It is conceivable that the induction of a degree of vascular dilation and excess fibroblastic proliferation would be beneficial in the treatment of healing wounds.

Although the evidence is insufficient to exclude a direct action of urethane on liver cells, it was productive of comparatively slight hepatic and renal damage even when given in lethal doses. These changes are apparently causally dependent upon vascular injury which is reversible.

Conclusions. (1) Doses of urethane simulating those used in the topical treatment of infected wounds in man are not productive of toxic parenchymal changes in the organs of guinea pigs subjected to prolonged daily subcutaneous injections. The animals remained healthy and gained weight.

(2) A marked mesenchymal cell reaction was consistently seen in the lungs and to a lesser extent in the liver and myocardium of urethane treated animals.

[9] Nettleship, A., Henshaw, P. S., and Meyer, H. L., *J. Nat. Cancer Inst.*, 1943, **4**, 309.

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17159. Anticonvulsant Action of 2-Substituted-1,3-Propanediols.

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3-(o-Toloxy)-1,2-propanediol, called myanesin, possesses two important pharmacological properties: it causes transient paralysis of skeletal muscles and has an anticonvulsant action.[1] The pharmacological examination of numerous related ethers of glycerol has shown that there was no simple relationship between their paralysing and anticonvulsant activities. The observation that nuclear substitution of 3-phenoxy-1,2-propanediol markedly affected paralysing activity but did not have any influence on anticonvulsant action[2] suggested the examination of the anticonvulsant properties of 2-substituted-1,3-propanediols.†

The anticonvulsant action of the compounds was determined in male, white mice, weighing 18 to 22 g. Metrazol 100 mg per kg, which caused convulsions and deaths in 99% of the animals, was injected intraperitoneally together with graded doses of the compound under test. Ten mice were used at each dose level. The animals were observed for 90 minutes following the injection and the incidence of convulsions and deaths noted. The relative efficacy of the substances was evaluated by finding graphically the dose protecting one half of the animals from convulsions and deaths. This mean protective dose of 13 experimental compounds and of phenobarbital and myanesin is given in Table I. Several of the investigated substances had anticonvulsant properties of a similar order as myanesin (No. 3, 6, 7, 9). Compounds containing butyl radicals (No. 4 and 8) were inactive. When a phenyl or phenoxy group was a substituent, activity was decreased or lost (No. 11, 12, 13). 2,2-Diethyl-1,3-propanediol, called DEP, possessed outstanding anticonvulsant properties. A short description of its pharmacological properties appears to be of interest.

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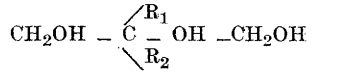
[1] Berger, F. M., and Bradley, W., *Brit. J. Pharmacol.*, 1946, **1**, 265.

[2] Berger, F. M., *J. Pharm. and Exp. Therap.*, 1948, **93**, 470.

† I am obliged to Mr. W. A. Lott of the Squibb Institute for Medical Research for supplying me with some of these compounds.

TABLE I.

Antagonistic Action of 2-substituted-1,3-propanediols to the Lethal Effects of Metrazol 100 mg per kg. Metrazol and one of the other drugs were given simultaneously by intraperitoneal injection to white mice.



No.	R_1	R_2	Mean protective dose in mg per kg
1	methyl	methyl	>250
2	ethyl	ethyl	40
3	n-propyl	n-propyl	88
4	n-butyl	n-butyl	>250
5	methyl	ethyl	135
6	,,	n-propyl	70
7	,,	iso-propyl	88
8	,,	n-butyl	210
9	ethyl	iso-propyl	77
10	,,	ethoxy	>250
11	phenyl	H	>250
12	,,	ethyl	120
13	phenoxy	,,	>250
14	phenobarbital		39
15	myanesin		80

DEP resembled myanesin in causing transient paralysis of skeletal muscles. The paralysing activity of DEP was, however, of a lower order than that of myanesin, the doses causing loss of the righting reflex in 50% of mice after intraperitoneal administration being 390 mg per kg and 180 mg per kg, respectively. In small doses not causing paralysis DEP somewhat increased the spontaneous activity of the animals whereas myanesin had a sedative effect. The acute toxicity of DEP was very low. The mean lethal dose in mice on intraperitoneal administration was 1400 mg per kg. Doses as high as 30 mg per kg given intravenously to anesthetized cats did not affect blood pressure and respiration. Similar doses did not alter normal electroencephalographic patterns in cats and did not influence spinal reflexes. On a weight for weight basis DEP was as active as phenobarbital in preventing the occurrence of convulsions and deaths from lethal doses of metrazol. It was more effective than myanesin, phenobarbital or other drugs in antagonizing the lethal and convulsant effects of strychnine.

DEP was more effective against convulsions induced by chemical agents than against those induced by electric current. It abolished the tonic extensor component of supramaximal electroshock seizures in mice and rabbits but was in this respect about 6 times weaker than phenobarbital. The duration of the effect was also much shorter with DEP than with phenobarbital.

Myanesin is known to abolish abnormal electroencephalographic patterns in cases of true petit mal.[3] Because of the qualitatively similar anticonvulsant effect of DEP and myanesin, the stronger anticonvulsant action of DEP may be of value in the treatment of petit mal and of other disorders in which myanesin has been tried.

Summary. 2,2-Diethyl-1,3-propanediol and certain other substituted 1,3-propanediols possess qualitatively similar pharmacological properties as myanesin. These compounds differ from myanesin in having a weaker paralysing action and a more powerful anticonvulsant action.

[3] Gammon, G. D., and Churchill, J. A., *Am. J. Med. Sci.*, 1949, **217**, 143.

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