The absence of lead nephropathy or renal tumors in TEL-treated mice is of interest, in contrast to the induction of these effects in rats following prolonged administration of high levels of lead salts[5,6]. The relatively low toxicity of TEL, administered parenterally, to neonatal mice is noteworthy; the LD_{50} on day 1 of life is between 50 and 100 mg/kg, in contrast to an LD_{50} of between 16 and 24 mg/kg following oral administration in adult rats[1]. Possibly, the relative resistance of neonatal mice to TEL is due to immaturity in their microsomal liver enzymes with consequent failure to dealkylate TEL to its stable triethyl derivative, known to be more toxic[2]. At a total TEL dosage of 0.6 mg, one of limited toxicity, a weak carcinogenic effect is apparent. It should, however, be noted that the TEL-induced lymphomas occurred late in life, in contrast to the general tendency to earlier development of such tumors following administration of strong carcinogens to neonatal mice.

Zusammenfassung. Ein vermehrtes Vorkommen von Lymphomas zeigte sich bei mit Tetraäthylblei behandelten weiblichen Mäusen (12%) im Gegensatz zu den entsprechenden Kontrollen (0%). Die carcinogene Wirkung von Tetraäthylblei wurde durch parenterale Administration einer totalen Dosis von 0.6 mg an neugeborenen Schweizer Mäusen gezeigt.

S. S. Epstein[7] and N. Mantel

Laboratories of Carcinogenesis and Toxicology, Children's Cancer Research Foundation Inc., and Department of Pathology, Harvard Medical School, Boston (Mass.); National Cancer Institute, Bethesda (Maryland, USA), 15 December 1967.

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Anti-Inflammatory Action of a Benzyl Glucofuranoside Applied Topically

It has previously been demonstrated that 3,5,6-tri-*O*-benzyl-D-glucofuranoside[1] (henceforth referred to as benzyl glucofuranoside) displays anti-inflammatory actions following systemic (oral or parenteral) administration in a variety of experimental inflammatory reactions in the laboratory animal as well as in man[2-5]. In view of the pronounced lipophilic character of benzyl glucofuranoside, it seemed likely that the compound might easily be absorbed by the skin. The following account shows that benzyl glucofuranoside inhibits an inflammatory reaction of the skin when applied topically to the area in which this reaction is elicited. The procedure adopted was a slight modification of the method described by Tonelli et al.[6] by which the topical antiphlogistic effect of steroids can be assessed. With this method an acute inflammatory response is elicited by applying croton oil with an appropriate vehicle to the rat ear, and then quantitating it gravimetrically by comparison with the contralateral untreated ear. Co-application of an active compound results in a reduction of the weight increase.

The main modification consisted in the use of: (a) male mice of a body weight of 22–27 g instead of immature female rats, and (b) a reading time of 4 instead of 6 h following the application of the irritant.

The benzyl glucofuranoside was incorporated in graded concentrations in the vehicle containing the irritant. The effects of benzyl glucofuranoside were compared with those of a well-established antiphlogistic corticosteroid, hydrocortisone.

As may be seen from Table I, benzyl glucofuranoside is capable of reducing the increase in weight provoked in the mouse ear by topical application of croton oil. This anti-inflammatory effect of the compound shows a clear-cut dose-dependent behaviour, a concentration of 30 mg/ml producing a weight reduction which is already highly significant statistically. The ED_{50} determined graphically is 70 mg/ml.

In order to ascertain that the anti-inflammatory effect of benzyl glucofuranoside is not due to a non-specific

Table I.

Preparation	No.	Concentration (mg/ml)	Weight increase of the ear mg	± S.E.[a]	P[a]	Inhibitory effect (%)
Controls	15	–	27.2	1.6	–	–
Benzyl glucofuranoside	10	10	27.8	1.9	–	0
	10	30	19.3	1.5	< 0.001	29
	10	100	12.0	2.0	< 0.001	56
	10	300	3.8	0.8	< 0.001	86
Hydrocortisone	5	0.3	22.8	3.1	< 0.01	16
	10	1.0	14.1	1.5	< 0.001	48
	10	3.0	11.3	1.1	< 0.001	58
	10	10.0	5.7	0.9	< 0.001	79

[a] Mean ± S.E., and *P* calculated according to Lord.

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action resulting from its highly lipophilic nature (e.g. retention of croton oil on the surface of the ear skin), a control experiment was run in which paraffin oil (Paraffinum liquidum Ph. H.V) was incorporated in the irritant and tested simultaneously with benzyl glucofuranoside. From the data presented in Table II it is evident that paraffin oil is slightly inhibitory at concentrations starting from 30 mg/ml. A statistically significant reduction of the ear oedema, however, is only obtained with the oil at a concentration of 300 mg/ml, its effect then being roughly equal to that of benzyl glucofuranoside at a concentration 10 times lower. The anti-inflammatory effect of benzyl glucofuranoside at concentrations of 100 and 300 mg/ml is highly different from that of paraffin oil at the same concentrations ($P < 0.001$). It can therefore safely be concluded that the inhibitory actions of benzyl glucofuranoside at concentrations of 30 and 100 mg/ml are entirely due to the compound, and that some non-specific effect contributes only minimally to the decrease in the inflammatory reaction observed with benzyl glucofuranoside at a concentration of 300 mg/ml.

Table II.

Preparation	No.	Concentration (mg/ml)	Weight increase of the ear mg ± S.E.[a]		P[a]	Inhibitory effect (%) I[b]	II[c]
Controls	5	–	37.8	2.3	–	–	–
Paraffinum liquidum Ph. H.V.	5	30	33.7	2.0	0.1	11	–
	5	100	32.7	3.4	0.1	14	–
	5	300	26.1	4.3	0.05	31	–
Benzyl glucofuranoside	5	100	13.8	1.8	0.001	64	58
	5	300	4.4	1.8	0.001	89	83

[a] Mean ± S.E., and P calculated according to LORD. [b] As compared with control ears treated with irritant in vehicle described by TONELLI et al.[5]. [c] As compared with ears treated with irritant as above containing identical amounts of paraffin oil instead of benzyl glucofuranoside.

Hydrocortisone, on the other hand, exerts an inhibitory action at concentrations starting from 0.3 mg/ml. At concentrations of 1 and 3 mg/ml hydrocortisone is roughly comparable with benzyl glucofuranoside at concentrations of 30 and 100 mg/ml respectively. Graphical determination of the ED_{50} for hydrocortisone yields a figure of 2 mg/ml, i.e. the corticosteroid is some 30–35 times more active than benzyl glucofuranoside. This quantitative inferiority of benzyl glucofuranoside is largely offset by qualitative advantages, i.e. a complete absence of undesirable effects on the thymus and adrenals even following prolonged administration at very high daily doses[3]. On the other hand, it seems worth noting that the anti-inflammatory action of hydrocortisone as determined by the mouse ear assay outlined here compares favourably with that established for the same corticosteroid in the rat by TONELLI et al.[6], i.e. the mouse ear assay would seem equally suitable as a means of assessing the activity of anti-inflammatory agents applied topically.

Zusammenfassung. Es wird gezeigt, dass Äthyl-3,5,6-tri-*O*-benzyl-D-glucofuranosid (CIBA 21401-Ba, Glyvenol®) eine am Mausohr erzeugte Entzündung bei topikaler (epikutaner) Applikation zu hemmen vermag.

L. RIESTERER and R. JAQUES

Research Laboratories of the Pharmaceutical Department of CIBA Limited, 4000 Basel 7 (Switzerland), 19 February 1968.

A Pharmacological Investigation of the Influence of Suxamethonium on Cardiac Function in the Horse

A number of investigators have reported on the use of suxamethonium as a casting agent in large animals, particularly in the horse[1–9]. The events following i.v. injection of the drug consist of the onset of muscular fasciculations within 10–40 sec, rapidly followed by muscular paralysis, the animal gently falling to the ground. This phase is associated with a period of apnoea of 0.5–3 min duration. The horse is usually able to stand again within 4–7 min of administration of the drug. Other untoward effects observed when suxamethonium is administered for this purpose, consist of changes in cardiac rate and rhythm. HOFMEYR[3], NEAL and WRIGHT[5] and TAVERNOR[8,9] observed a marked acceleration of heart rate, with values exceeding 150 beats/min in many cases. Since the average normal heart rate in horses at rest is of the order of 30–40 beats/min, these responses involve a three- to six-fold increase in rate. Moreover, serious disturbances of cardiac rhythm have been reported and some investigators[3,8,9] have recorded deaths from primary cardiac arrest.

In the present experiments we have attempted to analyse further the changes in cardiac function that occur

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