TABLE 1. EFFECT OF HYDROCORTISONE AND SALICYLIC ACID CONGENERS ON FORMALDEHYDE-INDUCED ARTHRITIS IN RATS

	Dose mg/100 g i.p.	Initial diameter mm	Average ten day diameter mm	% anti-inflammatory effect	P
Control	—	6·1 ± 0·07	7·53 ± 0·04	—	—
Hydrocortisone	0·5	6·04 ± 0·09	7·1 ± 0·09	30·7	<0·001
2,4-Diacetoxybenzoic acid	2·0	6·1 ± 0·05	7·08 ± 0·08	31·5	<0·001
m-Cresotinic acid	2·0	6·15 ± 0·06	7·22 ± 0·09	21·7	0·02–0·01
5-Ethyl-2-hydroxybenzoic acid	2·0	5·92 ± 0·06	7·11 ± 0·08	29·3	<0·001

The drugs showed potent anti-inflammatory activity similar to that of hydrocortisone. Quantitatively, *m*-cresotinic acid was found to be a less potent anti-inflammatory agent (21·7%) than 2,4-diacetoxybenzoic acid (31·5%) and 5-ethyl-2-hydroxybenzoic acid (29·3%).

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Anti-erythemic effectiveness of some metabolic inhibitors in guinea-pigs

SIR,—Among the methods applied to the measurement of the anti-inflammatory activity of nonsteroid compounds is the inhibition of ultra-violet light-induced erythema in guinea-pigs. The advantages of the method are its sensitivity and specificity and the close relation between clinical and anti-erythemic doses. Having subjected more than a hundred compounds to careful analysis, Winder (1958) concluded that only the well known antiphlogistics used clinically have a significant anti-erythemic effect.

The existence of a correlation of the antiphlogistic and metabolism-inhibiting (uncoupling) effect of nonsteroid agents is becoming an accepted hypothesis (Whitehouse, 1963). Thus, to clarify the role of the major energy producing processes—glycolysis and oxidation—in the development of ultra-violet-induced erythema we examined the influence of some enzyme inhibitors, of known biological mechanisms of action, in guinea-pigs. The effect of these compounds has not been investigated in this way before.

Our method was identical with that of Winder (1958). The depilated skin of the guinea-pig's back was irradiated with a 1000 W mercury lamp. Heat rays were filtered by cold water in a quartz tube. Each spot was irradiated for 80 sec. The spots were scored by marks 0, 0·5 and 1, the maximum score for the total of the three spots irradiated being 3 per animal. If the effect scored was below or equal to 1·5 in an animal, this was considered as an inhibition.

Table 1 shows that the substances when administered in non-toxic doses, intensely inhibited the appearance of erythema. 2-Deoxyglucose inhibits

TABLE 1. EFFECT OF SOME METABOLIC INHIBITORS ON ULTRA-VIOLET ERYTHEMA IN GUINEA-PIGS

Inhibitor	Dose* mg/kg	Anti-erythemic effect (animals scored $\leq$ 1·5) (total animals)				Effective dose (ED50) mg/kg
		Control	Hr after exposure 2	3	4	
Monoiodoacetic acid	15 (s.c.)	0/7	2/7	1/7	1/7	21
	25 (s.c.)	0/8	4/8	3/8	1/8	
	75 (s.c.)	0/8	8/8	8/8	7/8	
Sodium fluoride	25 (s.c.)	0/8	2/8	0/8	0/8	40
	50 (s.c.)	0/11	7/11	5/11	3/11	
2-Deoxyglucose	25 (i.p.)	0/6	1/6	0/6	0/6	47
	50 (i.p.)	0/8	5/8	3/8	2/8	
	100 (i.p.)	0/16	13/16	10/16	1/16	
	300 (i.p.)	0/7	7/7	5/7	5/7	
2-Deoxyglucose†	100 (i.p.)	0/9	1/9	1/9	0/9	
Arsenate	2 (i.p.)	0/5	2/5	2/5	0/5	2·4
	5 (i.p.)	0/8	7/8	3/8	2/8	

* 30 min before the ultraviolet exposure.
† All animals received 4 U/100 g insulin (protamine-zinc) by the subcutaneous route simultaneously with 2-deoxyglucose.

glucolysis far beyond the glucose-6-phosphate level (Sols & Crane, 1954). The effect of 2-deoxyglucose in inhibiting the release of histamine *in vitro* (Chakravarty, 1962) and of dextran oedema *in vivo* (Goth, 1959) is generally known. The effect of 2-deoxyglucose in inhibiting oedema produced by dextran can be prevented by insulin (Goth, 1959). Monoiodoacetic acid stops glycolysis primarily by the inhibition of phosphoglycerinealdehyde dehydrogenase; fluoride suspends it by inhibiting the enolase. It is well-known that arsenate causes "arsenolysis" which results in the suspension of the oxidative phosphorylation. Strenger (1959), has found monoiodoacetic acid and fluoride to have an inhibiting effect upon the dextran and formalin oedema in rats.

The dextran oedema-inhibiting effect of fluoride and arsenate was discussed in our previous paper (Görög & Szporny, 1964). The results of our present experiments permit us also to attribute an important role to increasing glycolysis and oxidation in the mechanism of the development of ultra-violet-induced erythema. The present experiments show such erythema in guinea-pigs to be inhibited by compounds which have an inhibitory effect upon the metabolism and which are not applied in therapy. The effectiveness of nonsteroid antiphlogistics in this test, (Winder, 1958) may also be attributed to their inhibition of metabolism and adenosine triphosphate synthesis.

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