TABLE 1.

Experiment	Concentration of paraoxon in the bath fluid	
	2½ hr after setting up the diaphragm	6 hr after setting up the diaphragm
(ii) Diaphragm-nerve holder immersed in the bath fluid containing 2×10^{-6}M paraoxon	$1{\cdot}75 \times 10^{-8}$M	not measured
(iii) As above but holder not immersed in fluid	4×10^{-9}M	2×10^{-9}M
(iv) Dummy holder made of Perspex in one piece immersed in bath fluid containing 2×10^{-6}M paraoxon	$2{\cdot}5 \times 10^{-9}$M	1×10^{-9}M
(v) As expt (iii) but no diaphragm set up after washing	5×10^{-9}M	$4{\cdot}3 \times 10^{-9}$M

It is therefore suggested that the diaphragm-nerve holder be constructed of solid Perspex or glass, so that drugs cannot diffuse into the cavities containing the electrode connections.

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Disulfiram and the effect of catecholamines on neuroleptic-induced catalepsy in mice and rats

SIR,—We have found that chlorpromazine- or haloperidol-induced catalepsy in mice and rats could be reversed by dopa or monoamine oxidase- and catechol-*O*-methyltransferase inhibitors or both (Maj & Zebrowska, 1966a,b). We therefore wished to know whether noradrenaline or dopamine was involved in this anticataleptic action. For this purpose we used disulfiram which inhibits the β-hydroxylation of dopamine to noradrenaline in various tissues (Goldstein, Anagnoste, Lauber & McKereghan, 1964; Musacchio, Goldstein, Anagnoste, Poch & Kopin, 1966).

Catalepsy was examined in white mice according to Zetler & Moog (1958) and in Wistar rats according to Courvoisier, Ducrot & Julou (1957). In mice, reserpine was given intraperitoneally 3·5 hr, chlorpromazine and haloperidol subcutaneously 1·5 hr, disulfiram intraperitoneally 2 hr and DL-dopa, intraperitoneally 0·5 hr before the experiment. Rats were given reserpine intraperitoneally 3·5 hr, chlorpromazine and haloperidol subcutaneously 1 hr and disulfiram intraperitoneally 2 hr and DL-dopa intraperitoneally immediately before the test. Nialamide was injected in both species 18 hr before the experiment. Observations were made at 5 min intervals for 1 hr (13 observations) in mice and at 10 min intervals (7 observations) in rats. The number of cataleptic animals and the number of cataleptic responses were recorded. The animal was considered to be cataleptic after 7 or more positive responses in mice, or 4 or more in rats.

Dopa and nialamide were not antagonistic towards reserpine-chlorpromazine or haloperidol-induced catalepsy in mice pretreated with disulfiram (Table 1). In experiments with chlorpromazine catalepsy was not seen after disulfiram, since in 5 mice the righting reflex had been abolished.

In rats (Table 2) the administration of dopa and nialamide counteracted the cataleptic action of reserpine and haloperidol. Only in animals receiving

TABLE 1. EFFECT OF DOPA, NIALAMIDE AND DISULFIRAM ON THE NEUROLEPTIC-INDUCED CATALEPSY IN GROUPS OF 10 MICE

Group No.	Compound and dose (mg/kg)				Number of cataleptic mice	Number of cataleptic responses	
	Neuroleptic	Dopa	Nialamide	Disulfiram		Mean	P
I	Reserpine	—	—	—	8	9·0 (±1·2)	—
II	1	200	10	—	1	1·7 (±0·9)	<0·001 (I:II)
III		200	10	400	7	8·4 (±1·0)	<0·001 (II:III)
IV	Chlor-	—	—	—	10	11·3 (±0·4)	—
V	prom-	200	10	—	2	3·5 (±1·2)	<0·001 (IV:V)
VI	azine 3	200	10	400	*	— —	—
VII	Haloperi-	—	—	—	9	10·3 (±0·9)	—
VIII	dol 1	200	10	—	2	3·9 (±1·1)	<0·001 (VII:VIII)
IX		200	10	400	8	9·1 (±1·3)	<0·01 (VIII:IX)

* 4 mice were cataleptic, in 5 mice was the righting reflex abolished.

TABLE 2. EFFECT OF DOPA, NIALAMIDE AND DISULFIRAM ON THE NEUROLEPTIC-INDUCED CATALEPSY IN GROUPS OF 8 RATS

Group No.	Compound and dose (mg/kg)				Number of cataleptic rats	Number of cataleptic responses	
	Neuroleptic	Dopa	Nialamide	Disulfiram		Mean	P
I	Reser-	—	—	—	8	5·8 (±0·4)	—
II	pine 7·5	200	20	—	1	1·8 (±0·6)	<0·001 (I:II)
III		200	20	400	6	4·6 (±0·8)	<0·02 (II:III)
IV	Chlor-	—	—	—	6	4·4 (±0·7)	—
V	prom-	200	10	—	3	3·5 (±0·7)	>0·4 (IV:V)
VI	azine 10	200	10	400	7	6·3 (±0·8)	<0·02 (V:VI)
VII	Haloperi-	—	—	—	7	5·9 (±0·5)	—
VIII	dol 3	200	10	—	3	3·5 (±0·9)	<0·05 (VII:VIII)
IX		200	10	400	8	6·9 (±0·1)	<0·01 (VIII:IX)

chlorpromazine was the difference not statistically significant. We did not observe this anticataleptic effect in rats treated with disulfiram. In the control mice and rats, when injections of disulfiram alone or with dopa or with dopa and nialamide, but without neuroleptics, catalepsy was not seen.

Disulfiram has been found to decrease the noradrenaline level and to increase the dopamine level in the brains of mice injected with dopa (Hashimoto, Ohi & Imaizumi, 1965), as well as in the brains (or some structures of them), of rats treated with catecholamine releasers and dopa (Goldstein & Nakajima, 1966). Similar changes in the catecholamine content were obtained in normal rats after diethyldithiocarbamate, the active metabolite of disulfiram (Carlsson, Lindquist, Fuxe & Hökfelt, 1966). Therefore our results seem to indicate that the anticataleptic effect of dopa and nialamide could be ascribed to an increase in the brain noradrenaline level but not to an increase in the dopamine level, as may be assumed, at least in reserpinized animals, on the basis of facts known from literature.

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The effect of purgative drugs on the intestinal absorption of glucose

SIR,—We have examined the effects of several purgatives on the *in vivo* absorption of glucose by the small intestine of the rat. In control experiments 20 ml of 0·9% saline containing 0·1% D-glucose and 5·0% ethanol was perfused through the lumen of the proximal 60 cm of the small intestine of an anaesthetized rat for 20 min. At the end of the experiment the rat was killed, the perfusate collected, its volume measured and the glucose concentration determined. The drugs were dissolved in the perfusion fluid, with ethanol as solvent.

The results (Table 1) show that inhibition of glucose absorption occurred with low concentration of all the purgatives except the anthraquinone derivatives. Oxyphenisatin produced the greatest inhibition and was more active than phloridzin which was included as a reference drug. Dioctyl was included because of the known inhibitory activity of other surface-active agents on the absorption of nutrients (Nissim, 1960).

TABLE 1. EFFECT OF PURGATIVES ON THE ABSORPTION OF GLUCOSE

Compound		Conc.	No. of rats	Absorption %	P value
Chemical name	Name			Mean ± s.e.	
Controls			10	87·28 ± 1·76	
	Sennoside "A"	10^{-4}	4	87·37 ± 1·43	<0·98
1,3,8-Trihydroxy-6-methylanthraquinone	Emodin	10^{-4}	4	83·72 ± 4·21	<0·4
1,8-Dihydroxyanthraquinone	Danthron	10^{-4}	4	90·92 ± 1·19	<0·3
2,3-Indolinedione	Isatin	10^{-4}	4	76·70 ± 1·41	<0·005
Dioxyphenylisatin	Oxyphenisatin	10^{-4}	6	20·50 ± 0·80	<0·001
Di-(4-acetoxyphenyl)-2-pyridylmethane	Bisacodyl	10^{-4}	4	49·38 ± 2·44	<0·001
2,2-Di(*p*-hydroxyphenyl)phthalide	Phenolphthalein	10^{-4}	4	61·45 ± 1·45	<0·001
Phloretin-2′-β-glucoside	Phloridzin	10^{-4}	4	40·24 ± 3·53	<0·001
Di-(2-ethylhexyl) sodium sulphosuccinate	Dioctyl sodium sulphosuccinate	$2 \cdot 10^{-3}$	4	62·42 ± 1·36	<0·001

The inhibition observed with phenolphthalein confirms the results of Hand, Sanford & Smyth (1966) who demonstrated inhibition of glucose transport in an *in vitro* preparation of rat small intestine. Bisacodyl has been reported to be without action in the small intestine (Macgregor, 1960) but the significant inhibition of glucose absorption obtained in the present study confirms the report by Forth, Baldauf & Rummel (1963) that this drug is capable of blocking nutrient absorption.

The observation that certain purgatives are capable of blocking glucose absorption in the small intestine raises two questions. Firstly, how do these drugs affect glucose absorption and will their study be of value in the elucidation of the transport mechanism? Secondly, of what significance is this activity in the normal purgative action of these drugs?