to several other pathological conditions. Under such altered conditions OX-Dapro could exert its central effects, eventually resulting in the observed clinical condition of "neurolathyrism".

Department of Biochemistry,
Indian Institute of Science,
Bangalore 12,
India

S. L. N. RAO
P. S. SARMA

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Effects of salicylate congeners on glucose metabolism in the human red cell

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SALICYLATE and 2:6-dihydroxybenzoate have been shown to inhibit glycolytic reactions and the pentose phosphate pathway in mature erythrocytes.[1] The present report shows that these actions are shared to a varying degree by a number of related mono- and dihydroxybenzoates. An exception is 2:5-dihydroxybenzoate which caused stimulation of the pentose phosphate pathway. The incorporation of radioactivity from ^{14}C-labelled glucose into soluble metabolic intermediates and into $^{14}CO_2$ in the human red cell suspensions and the effects of the salicylate congeners were studied by the techniques described previously.[1]

The results in Table 1 show the amounts of ^{14}C from [^{14}C] glucose incorporated into the separated soluble intermediates in the presence or in the absence of 5 mM and 20 mM concentrations of the congeners. All the congeners resembled salicylate and 2:6-dihydroxybenzoate in causing diminished utilization of the labelled substrate and an increased formation of labelled pyruvate. However, at the 5 mM level, 3-hydroxy-, 4-hydroxy- and 3:4-dihydroxybenzoates were the only compounds to cause

an accumulation of radioactivity in the hexose monophosphate fraction. The magnitude of this effect roughly paralleled the ability of each of these substances to inhibit glucose utilization. At the 20 mM level, these three compounds, plus 2:4-dihydroxy- and 2:6-dihydroxybenzoates, caused an increased formation of the radioactive hexose monophosphates. These results are explicable in terms of all the compounds tested resembling salicylate and 2:6-dihydroxybenzoate in inhibiting hexokinase and lactate dehydrogenase activities at both concentrations used.[1] In addition, they suggest that 3-hydroxy-, 4-hydroxy- and 3:4-dihydroxybenzoate are more powerful inhibitors of phosphofructokinase activity than is 2:6-dihydroxybenzoate since they cause an accumulation of hexose monophosphates at the 5 mM level whereas this effect only occurred with 20 mM 2:6-dihydroxybenzoate.

The results in Table 2 show that all the congeners decrease the utilization of [1-^{14}C] glucose, thus confirming the results with the [^{14}C] glucose (Table 1). They also show that all the compounds, with

TABLE 1. EFFECTS OF SALICYLATE CONGENERS ON THE INCORPORATION OF RADIOCARBON FROM [^{14}C] GLUCOSE INTO THE SOLUBLE METABOLIC INTERMEDIATES OF HUMAN RED CELLS

	Concn (mM)	Hexose monophosphates	Fructose diphosphate	Diphosphoglycerate	Monophosphoglycerates	Pyruvate	Lactate	6-Phosphogluconate	Uridine diphospho-glucose	α-Glycerophosphate	Residual glucose	Inhibition of glucose utilized %
Control		1·5	6·1	22·5	2·8	4·4	17·6	0·4	2·1	1·3	4·2	—
2-Hydroxybenzoate	5	0·9	4·3	15·9	2·0	7·9	15·1	0·4	1·2	1·3	10·3	7
	20	0·8	4·3	11·4	1·7	7·0	13·1	0·3	0·7	1·4	18·1	18
3-Hydroxybenzoate	5	6·1	8·0	13·9	1·2	4·9	10·2	0·4	2·6	0·4	24·0	25
	20	10·6	4·9	12·4	0·6	1·6	4·1	0	2·0	0·4	34·3	38
4-Hydroxybenzoate	5	7·8	10·9	11·5	1·5	4·9	10·5	0	1·9	0·3	20·0	20
	20	7·5	7·5	11·5	0·6	1·0	2·8	0	1·2	0	36·4	41
2,4-Dihydroxybenzoate	5	1·0	4·9	15·9	2·5	7·4	12·2	0·5	1·3	1·2	12·2	10
	20	7·1	6·2	14·3	2·1	6·0	7·0	0·4	3·0	1·0	21·2	22
2,5-Dihydroxybenzoate	5	1·0	3·8	17·9	2·2	8·9	12·5	0·4	1·3	1·8	8·7	6
	20	1·1	4·5	17·5	2·3	6·8	8·6	0·3	0·8	2·6	14·8	14
2,6-Dihydroxybenzoate	5	1·8	3·8	16·7	2·1	8·0	12·1	0·6	1·9	1·2	13·7	12
	20	15·5	8·4	4·3	2·4	3·3	3·8	0	3·4	0·7	29·0	32
3,4-Dihydroxybenzoate	5	8·4	5·8	10·8	1·9	5·8	7·9	0	1·7	0·3	24·1	25
	20	9·7	6·4	6·2	0·6	0·9	2·0	0	3·3	0·5	41·2	47

The total radioactivity in the [^{14}C] glucose initially present in each experiment was 82·6 counts/min $\times 10^{-3}$.

* The results are expressed as counts/min $\times 10^{-3}$ of ^{14}C and represent the mean of two experiments.

the exception of 2:5-dihydroxybenzoate, reduce the amounts of $^{14}CO_2$ produced from the labelled substrate. 2:5-Dihydroxybenzoate is readily oxidised to its corresponding para-quinone (2-carboxy-1,4-benzoquinone) and the two compounds could form an oxidation-reduction system, similar to that of hydroquinone and quinone. It has been suggested[2] that this latter system may function like methylene blue, which acts as an electron acceptor to facilitate the oxidation of $NADPH_2$ by molecular oxygen, thus increasing the proportion of glucose metabolized by the pentose phosphate pathway in the red cell.[3] This stimulation of the pentose phosphate pathway by 2:5-dihydroxybenzoate is also reflected in the increased percentage of the [1-^{14}C] glucose converted to $^{14}CO_2$. 2:4-Dihydroxy- and 3:4-dihydroxybenzoate gave values for the percentage of [1-^{14}C] glucose converted to $^{14}CO_2$ greater than the value for the corresponding control experiment showing that these congeners inhibited the pentose phosphate pathway to a lesser extent than glycolysis whereas the remaining congeners showed the reverse effect.

TABLE 2. EFFECTS OF SALICYLATE CONGENERS ON THE RESPIRATION OF HUMAN RED CELLS

	Conc (mM)	Glucose utilized dis/min × 10^{-3}	$^{14}CO_2$ Produced dis/min × 10^{-3}	% [1-^{14}C] Glucose converted to $^{14}CO_2$
Control		406 ± 8	22·0 ± 0·3	5·4 ± 0·2
2-Hydroxybenzoate	5	404 ± 3	20·7 ± 0·5	5·1 ± 0·1
	20	349 ± 3	12·0 ± 0·3	3·4 ± 0·1
3-Hydroxybenzoate	5	384 ± 6	21·0 ± 0·4	5·5 ± 0·1
	20	376 ± 11	16·1 ± 0·6	4·3 ± 0·3
4-Hydroxybenzoate	5	380 ± 14	17·3 ± 0·6	4·6 ± 0·3
	20	312 ± 9	13·7 ± 0·8	4·4 ± 0·4
2,4-Dihydroxybenzoate	5	344 ± 7	20·5 ± 1·0	6·0 ± 0·5
	20	216 ± 12	16·3 ± 0·7	7·5 ± 0·5
2,5-Dihydroxybenzoate	5	328 ± 10	28·8 ± 1·7	8·8 ± 0·8
	20	208 ± 15	35·6 ± 2·5	17·1 ± 1·3
2,6-Dihydroxybenzoate	5	334 ± 7	14·5 ± 0·7	4·4 ± 0·1
	20	220 ± 4	6·3 ± 0·2	2·9 ± 0·1
3,4-Dihydroxybenzoate	5	328 ± 10	18·2 ± 0·6	5·5 ± 0·3
	20	280 ± 14	19·4 ± 0·5	6·9 ± 0·6

* Each observation represents the mean of eight estimations ± S.D. Radioactivity is expressed as dis/min × 10^{-3}.

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Arthritis and Rheumatism Council Research Unit,
King's College Hospital Medical School,
Denmark Hill,
London, S.E.5

J. A. STURMAN
M. J. H. SMITH

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Effects of monoamine oxidase inhibitors on 5-hydroxytryptamine content in different anatomical areas of dog brain

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ADMINISTRATION of monoamine oxidase inhibitors has been shown to result in the increase of the levels of certain brain amines including 5-hydroxytryptamine, adrenaline, and noradrenaline.[1–5] So far such studies have mostly been conducted on the determination of 5-hydroxytryptamine and