Viscosity of air at 23° C

Author	Date	Method	Comments	$\eta_{23} \times 10^7$	Claimed uncertainty* $\times 10^7$	Reference
Gilchrist	1913	R.C.		1825·6	3·6	10
Rapp	1913	C.F.		1823·1	1·8	11
Markwell	1916	C.F.	Repeat of Rapp experiment	1827·3		12
Harrington	1916	R.C.	Same apparatus as Gilchrist	1822·6	1·8	13
Kellström	1937	R.C.		1835·0	3·0	2
Houston	1937	R.C.	Apparatus designed by Millikan and Day	1829·13	4·5	2
Bond	1937	C.F.		1834·34	0·8	2
Rigden	1938	C.F.	Completion of Bond's preliminary investigation	1829·96	0·7	2
Banerjea and Plattanaik	1938	C.F.		1833·75	2·2	2
Bearden	1939	R.C.		1833·79	0·06	2
				Derived values		
Millikan	1917	F.D.	No allowance made for slight density variation	1830·0	1·2	1
Bäcklin and Flemberg	1936	F.D.	Small apparatus. Correction for hole uncertain and likely to be important	<1830·4		3
Ishida, Fukushima and Suetsugu	1937	F.D.	Similar apparatus to Millikan. Corrected for density variation	1820·0	0·8	4
Hopper and Laby	1941	F.D.	Small apparatus. Vertical plates. Wall correction uncertain	<1824·6		5
Ishida, Fukushima and Suetsugu	(1948)		Voltage correction applied to their previous result (unpublished)	1833·6		
Ishida, Suetsugu and Matsui	(1948)	F.D.	New determination. Corrected for density variation (unpublished). (Uncorrected for density variation)	1830·4 (1829·2)		
Present investigation	(1948)	F.D.	Small apparatus. A decrease <0·04 per cent may be necessary owing to the Oseen correction	1826·5	0·6	

R.C. Rotating cylinder method.
C.F. Capillary flow method.
} (Viscosities have been corrected for temperature using Sutherland's formula.)
F.D. Falling drop method, assuming $e = 4{\cdot}8024 \times 10^{-10}$ E.S.U. (see ref. 14).
* Inconsistent methods of estimation of errors used.

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ACTION OF SURAMIN ON ENZYMES

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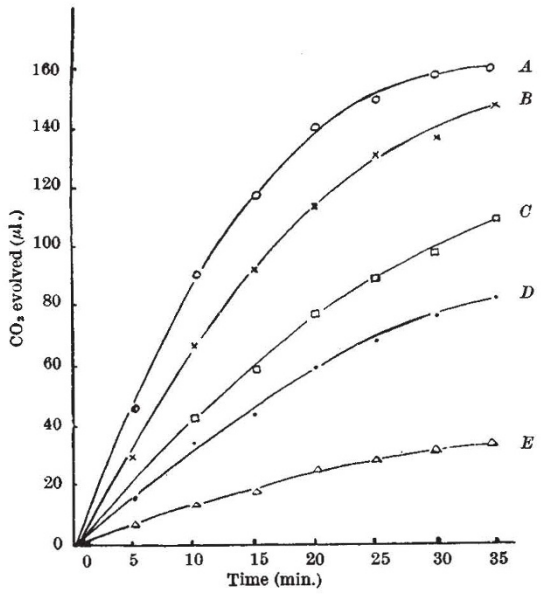
WHEN injected intravenously, suramin (synonyms: 'Antrypol': Bayer 205; 'Germanin': Fourneau 309) quickly effects the removal of trypanosomes from the blood and tissues of man and other animals suffering from sleeping sickness due to *Trypanosoma gambiense* or *T. rhodesiense* infections, if the infection is not too far advanced. The precise way in which suramin exerts its specific action on the trypanosome or on the defence mechanisms of the host or on both is still unknown, although several theories have been advanced[1].

One possible explanation is that the drug combines with or otherwise inhibits enzymes in the trypanosome which are necessary for the normal metabolic changes in that organism. Trypanosomes consume considerable quantities of carbohydrates; it was found, for example, that trypanosomes can be kept alive *in vitro* much longer if glucose is added to the medium[2]. The rapid utilization of oxygen by the trypanosomes can easily be demonstrated by manometric methods, or more simply by keeping small samples of citrated blood from infected sleeping sickness patients and suitable controls out of contact with oxygen for a short time; the trypanosome-containing blood often becomes noticeably darker than the controls, owing to deoxygenation of the oxyhæmoglobin by the trypanosomes.

Any inhibition of this comparatively vigorous oxidative metabolism in the trypanosome might be expected to reduce its reproductive capacity and/or its resistance to the attack of the body defence mechanisms, and a knowledge of the action of trypanocidal drugs on enzymes might prove very useful. We are therefore studying the action of suramin on various enzyme systems, including those of the trypanosome, to determine whether concentrations of the drug similar to those reached in the blood of injected animals, or inside the trypanosome, are likely to prove toxic to any particular enzymes. So far we have largely confined our tests to the yeast enzymes concerned with carbohydrate metabolism and some other enzymes selected for particular reasons.

Previous investigators have studied the action of suramin on a few enzymes. In relatively high concentrations (0·007 *M*, that is, 1 per cent) the drug inhibits trypsin[3], and in $1{\cdot}75 \times 10^{-4}$ *M* concentrations it was found to be toxic to the enzyme fumarase but not to urease[4]. Acceleration of post-mortem lactic acid production in muscle and liver has been reported[5], but retardation of blood glucolysis[6]. Hyaluronidase

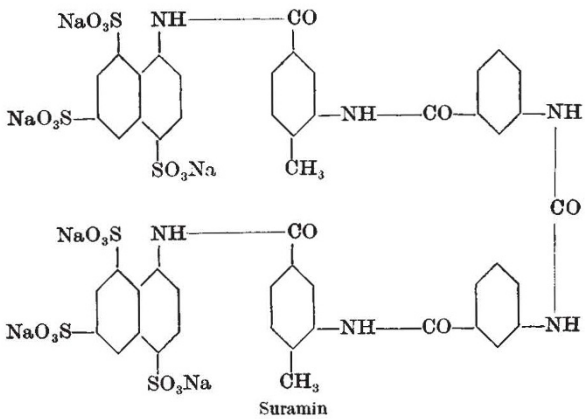


Inhibition of urease by suramin at *p*H 5·0. (Soya bean urease; $2·3 \times 10^{-3}$ *M* urea; enzyme and drug in contact for 30 min. before suramin added)

A, no suramin; *B*, *M*/15,000 suramin; *C*, *M*/7,500 ,, ; *D*, *M*/5,000 suramin; *E*, *M*/3,000 ,,

has very recently[7] been found to be remarkably sensitive to the drug; 85 per cent inhibition of the enzyme is effected by 7×10^{-5} *M* suramin and 15 per cent by 7×10^{-7} *M*.

In our experiments we have found that although suramin has no inhibitory action on urease at *p*H 7·5 (thus confirming previous work[4]), marked inhibition occurs at *p*H 5; at this latter *p*H a final concentration of $3·3 \times 10^{-4}$ *M* suramin gives 90 per cent inhibition, and 7×10^{-5} *M* suramin inhibits to the extent of 25–65 per cent (varying with the time of contact of drug and enzyme). A few typical results of these experiments are shown in the accompanying graph. The mechanism of this inhibition is still under investigation; but our results suggest that the suramin acts by competitive inhibition. This may be related to the presence of a urea structure in suramin, but it is also possible that the action of the drug on urease and other enzymes, like the combination with serum and other proteins[8], and the persistence of the drug in the animal body[9], is largely determined by the sulphonic acid groups of suramin.



Suramin

Very recently we learned that Dr. Madinaveitia, of Imperial Chemical Industries, Ltd., has also been carrying out investigations with suramin and urease, and that he has obtained results similar to our own.

Suramin combines with a variety of proteins[10], particularly at *p*H 5 or in more acid solutions[8]. It might be expected, therefore, that most enzymes would be inhibited by suramin in acid solution, but this is not so. The hydrolysis of plasma proteins by pepsin at *p*H 2 is not inhibited by 0·001 *M* suramin; the fact that in precisely the same buffer solution at *p*H 5 urease is strongly inhibited by suramin, whereas invertase is unaffected by the drug, is indicative of the specificity of the inhibition. Furthermore, we have found that there are many enzymes which are not significantly inhibited by suramin.

In our experiments, trypsin (Harrington Bros., Ltd.) has been found to be much more sensitive to the drug than was previously[3] reported; for example, 0·001 *M* concentrations of suramin gave 30 per cent inhibition of the hydrolysis of casein, and 0·0005 *M* suramin gave 20 per cent inhibition at *p*H 8·9 and 30°. Inhibition of this enzyme may be due to the similarity between the —NH—CO—NH— structure of suramin and the peptide linkage of proteins, but further work will be needed before this is fully established. Tests are now being carried out to determine the effect, on urease, trypsin and other enzymes, of several suramin analogues and similar compounds.

Since the metabolism of trypanosomes is largely concerned with carbohydrates, we decided to study, by manometric methods, the action of suramin on the carbohydrate-metabolizing enzymes of yeast. We have found that the drug strongly inhibits the fermentation of glucose by yeast juice, concentrations greater than $2·0 \times 10^{-5}$ *M* giving 100 per cent inhibition. This concentration is considerably less than that which is maintained in the plasma of a rabbit for several hours or days after the injection of an amount of the drug equivalent to that used clinically; even after four days, for example, the level may still be 3·5 mgm. of suramin/100 ml. of plasma (equivalent to $2·5 \times 10^{-5}$ *M*)[11]. Our study of the effect of the drug on the individual enzymes of yeast is not yet complete, but it is hoped that it will provide a clue to the enzymes in the trypanosome which are likely to be affected by the drug.

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