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Fatigue in a Fluid-filled Pulsating Elastic Tube

EXPERIMENTS with the 'oscillator' described by me¹ have shown that fatigue affects the elastic tube, after it has been pulsating for several hours.

Aneurysmal-like bulges may occur. Alternatively, a small hole forms at the end close to the rigid outlet tube, presumably due to cavitation occurring in contact with the wall. Fluid may escape from this hole, or air be sucked in, at each pulse.

A remarkable effect is obtained by the application of cedar wood oil. Within a few minutes, the distal segment of the elastic tube, when so treated, becomes permanently stretched into a sigmoid shape and develops periodic constrictions and dilatations, affecting the system of short wave-length, that is in the range 1-2 cm.

These figures resemble the shapes of arteries in atherosclerosis.

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PHARMACOLOGY

Alleged Anticomplementary Effect of Aspirin

VAN OSS *et al.*¹ recently reported that aspirin at concentrations of 2.2×10^{-3} M (40 mgm./100 ml.) inhibited the lysis of red cells in a simple complement-haemolysis reaction, but that sodium salicylate was inactive. This was interesting in view of the therapeutic action of aspirin against diseases such as the rheumatic disorders which are thought to involve immunological phenomena². Two other related compounds, salicylaldehyde and salicylaldehyde, were earlier reported³ to inhibit red cell lysis in a similar reaction. I therefore investigated the complement-haemolysis technique since it might usefully predict anti-rheumatic activity in other salicylate derivatives.

Sheep erythrocytes (E), anti-sheep erythrocyte serum prepared in the rabbit (A) and complement (C') were standard serological reagents obtained from the Commonwealth Serum Laboratories, Melbourne. Complement was received as ampoules of freeze-dried guinea pig serum which was reconstituted with distilled water and stored at 4°C. It gave results identical with fresh guinea pig serum prepared in these laboratories. Barbital buffer, pH 7.4 and containing added Mg^{++} and Ca^{++} , was prepared according to Mayer *et al.*⁴ and diluted 1 in 5 with distilled water on the day of use. All reagents were

diluted in barbital buffer. When 0.1 ml. of a 2 per cent suspension of washed erythrocytes was sensitized with 0.1 ml. of antiserum 1/1,000, the addition of 0.5 ml. of guinea pig serum 1/200 caused complete haemolysis of the erythrocytes within 30 min. at 37°C. The effect of added substances on the progress of the C' haemolysis was determined by placing 0.25 ml. of guinea pig serum 1/100 into haemolysis tubes and adding 0.25 ml. of a solution of the compound in barbital buffer. The latter solution was replaced by buffer alone in control tubes. The diluted antiserum and red blood cells were then added and the tubes incubated at 37°C. for 30 min. The pH of the solutions prior to incubation was determined with a glass electrode in duplicate tubes, which were prepared for each concentration of the compound under test.

The substances I have investigated and the concentrations that caused an approximate 50 per cent inhibition of haemolysis in our procedure are shown in Table 1. All the acids decreased the pH of the final mixture proportional to their concentration, and the pH range at the concentrations where haemolysis was inhibited are shown in column 2. Where applicable I have included the inhibitory concentrations reported by other workers for comparison.

Table 1. SUBSTANCES WHICH INHIBITED COMPLEMENT-HAEMOLYSIS AND THEIR EFFECT ON THE pH OF THE REACTION MIXTURE

Compound	Concentrations (molar) giving 50 per cent inhibition of haemolysis in 30 min.	pH ranges of the reaction mixtures at the inhibitory concentrations	Concentrations (molar) elsewhere reported to inhibit complement-haemolysis	Ref. No.
Aspirin	$2-3 \times 10^{-3}$	5.8-6.4	2.2×10^{-3}	1
Salicylic acid	$2-3 \times 10^{-3}$	5.8-6.4	10 per cent inhibition 3.3×10^{-3}	—
Sodium salicylate	No inhibition	7.4	No inhibition	1
Fumaric acid	$2-3 \times 10^{-3}$	5.8-6.2	—	—
Hydrochloric acid	$2-3 \times 10^{-3}$	5.8-6.4	—	—
Salicylaldehyde	8×10^{-4}	7.5	5×10^{-4}	3
Salicylaldehyde	8×10^{-4} - 10^{-3}	7.3	2.5×10^{-4}	3

Several important points emerge from Table 1. The capacity of the diluted Mayer solution was clearly inadequate to buffer the effects of the acidic compounds on the pH of the haemolytic reaction. Furthermore, it seemed strange that while salicylic acid inhibited haemolysis, sodium salicylate at similar concentration was inactive—yet at pH values above 5, both compounds would be in solution in identical form as salicylate ions. Finally all the acids tested inhibited my haemolytic reaction at approximately the same molar concentration ($2-3 \times 10^{-3}$), hydrochloric acid being just as effective as the organic acids. At this concentration they reduced the pH of the reaction from 7.4 to about 6. It appeared likely therefore that inhibition of haemolysis was due in some manner to the pH shift rather than a specific anticomplementary action. This explanation was further justified when the above experiments were repeated using undiluted Mayer buffer, the tonicity of which was adjusted by omitting some of the sodium chloride. Under these conditions haemolysis was complete within 30 min. in the absence of a test compound and was inhibited by salicylaldehyde and salicylaldehyde at the same concentrations as in the dilute buffer. However, none of the other substances in Table 1 lowered the pH of the final mixture below 7.0 or caused any inhibition of complement-induced