Bianchi (1961) has shown that caffeine increases intracellular calcium ions in skeletal muscle, but increasing the concentration of Ca<sup>2+</sup> in the perfusion fluid from 1.5 mm, by varying amounts, up to 4.5 mm only increased the amplitude of the heart beat. It did not affect the response induced by phenylephrine.

Since the concentrations of theophylline and iminazole used have been shown to inhibit and activate phosphodiesterase respectively (Butcher & Sutherland, 1962), the results described here indicate that the potentiation of the inotropic effects of phenylephrine by theophylline is mediated by its action on phosphodiesterase and indirectly support the hypothesis that adenylcyclase is part of the β-effector system (Robison, Butcher & Sutherland, 1967).

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## A reinvestigation of the substrate specificity of pig kidney diamine oxidase

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Pig kidney diamine oxidase (Histaminase, E.C. No. 1.4.3.6) was purified 600-fold and the substrate pattern was reinvestigated using known substrates and several other compounds. All substrates used were purified as hydrochlorides by recrystallization until homogeneous by thin layer chromatography, and pure as judged by melting point. Satisfactory infrared and proton magnetic resonance spectra were recorded for all compounds synthesized. The oxidation of substrates was followed manometrically and the results did not always agree with those previously reported (Blaschko & Chrušciel, 1959; Zeller, Fouts, Carbon, Lazana & Voegtli (1956). The differences are probably attributable to the use of more highly purified materials. Oxidation was expressed as a percentage of the rate for cadaverine as measured concurrently.

Ortho- and para-isomers of bis(aminomethyl) benzene were synthesized. The rate of oxidation of the para-isomer was found to be 50% of that of cadaverine, whereas the ortho- and meta-isomers were not substrates but were good inhibitors of cadaverine oxidation.

Ortho-, meta- and para-isomers of bis(2-aminoethyl) benzene were also synthesized. The ortho- and para-isomers were not oxidized and the meta-isomer was a poor substrate (7%).

The oxidation of diamino alkanes from 1,2-diaminoethane to 1,8-diaminooctane was broadly in agreement with that reported. Dimethylaminoalkylamines were also oxidized; 3-dimethylaminopropylamine (5%); 4-dimethylaminobutylamine (32%); 5-dimethylaminoamylamine (43%) and 6-dimethylaminohexylamine (8%).

Meta- and para-isomers of bis(methylaminomethyl) benzene and bis(dimethylaminoethyl) benzene were synthesized, and were shown to be neither substrates nor inhibitors of cadaverine oxidation.

A series of monoamines was oxidized thus: propylamine (8%); butylamine (10%); amylamine (less than 5%); benzylamine (0); 2-phenylethylamine (0); 3-phenylpropylamine (0); 4-phenylbutylamine (0); tyramine (0); mescaline (0); noradrenaline (0) and tryptamine (0).

Alpha, omega amino acids (3-aminopropionic and to 6-aminocaproic acid) were not oxidized, and showed no inhibitory potency. Ortho-, meta- and para- isomers of aminomethylbenzoic acids were prepared and behaved in a similar way.

The oxidation of both cadaverine and of para-bis(aminomethyl) benzene by the enzyme preparation was inhibited strongly by KCN  $(10^{-3}\text{M})$ ; sodium diethyl dithiocarbamate  $(10^{-3}\text{M})$ ; and hydrazine  $(10^{-5}\text{M})$ ; semicarbazide  $(10^{-5}\text{M})$  and hydroxylamine  $(10^{-3}\text{M})$ , thus establishing that the oxidation of both these compounds was effected by the same enzyme.

A scheme for the interaction between enzyme and substrate, based upon these observations, is proposed.

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## An apparatus for measuring passive resistance to movement of the forearm in man

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Basically the apparatus (Fig. 1) consists of an armboard (A) supported on bearings (X). Mounted beneath the board is a strain gauge (B) (Ether UFI 908 g load range).

Attached to the gauge are wires (W) leading over pulleys to a winding drum linked by suitable gearing to the shaft of a constant speed reversible motor.

On operating the motor, the armboard can be moved by a pull through the wire on to the strain gauge. This distorts the gauge and a record of output from the gauge, after suitable amplification, is recorded on a Devices pen-recorder. The board pivots about point (P) through an arc of a circle and there is a photocell or microswitch arrangement (Ph) which cuts off the motor after the desired arc has has been transversed.

A subject places his arm so that the elbow is resting above point P with hand resting on board. The apparatus is then switched on and force required now to move hand and board noted. The experiment is repeated a number of times and mean force (in arbitrary units), required to move arm can be calculated.