Table 1. ATHEROSCLEROTIC SCORE IN THE AORTAE AND CEREBRAL ARTERIES OF CHICKENS FED AN ATHEROGENIC OR NON-ATHEROGENIC DIET FOR 2 YEARS

Sex	Mean atherosclerotic score ± S.E.* Atherogenic diet No. of birds	T.A.	A.A.	C.A.	Non-atherogenic diet No. of birds	T.A.	A.A.	C.A.
Males	5	34 ± 7	400 ± 0	Trace (2) Normal (3)	7	2 ± 0	43 ± 9	Trace (2) Normal (5)
Females	8	107 ± 31	363 ± 20	Trace (1) Normal (7)	9	9 ± 6	107 ± 42	Trace (1) Normal (8)

* Atherosclerotic score ± standard error, severity (1–4) times area involved (per cent).
T.A., Thoracic aorta; A.A., abdominal aorta; C.A., cerebral arteries (the lesions were too small to warrant special grading). White Leghorn chickens were used.

small as to warrant no special grading. When present, these lesions could not have given rise to any circulatory disturbance, and they are probably best considered as insignificant.

The results are interesting in that they point out the difference that exists between arterial vessels in the chicken. The cerebral arteries of a chicken fed an atherogenic diet appear to be resistant to the development of atherosclerosis, but the aorta and the coronary arteries, as previously reported, are susceptible to the disease. The reason for this resistance is difficult to explain. In the intimal layer of the cerebral artery, however, there may exist a barrier to the diffusion of cholesterol and other lipids through the arterial wall to the brain. This suggested explanation finds support from the evidence that birds fed an atherogenic diet containing cholesterol did not show an increase in concentration of brain cholesterol, whereas other body tissues showed significant increases in cholesterol level[4,5]. An answer to the question whether the cerebral artery in the chicken does not develop atherosclerosis is as important as whether the aorta and coronary vessels do become atherosclerotic; this information is necessary for a proper understanding of the aetiology of atherosclerosis.

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BIOCHEMISTRY

Metabolism of Propranolol ('Inderal'*), a Potent, Specific β-Adrenergic Receptor Blocking Agent

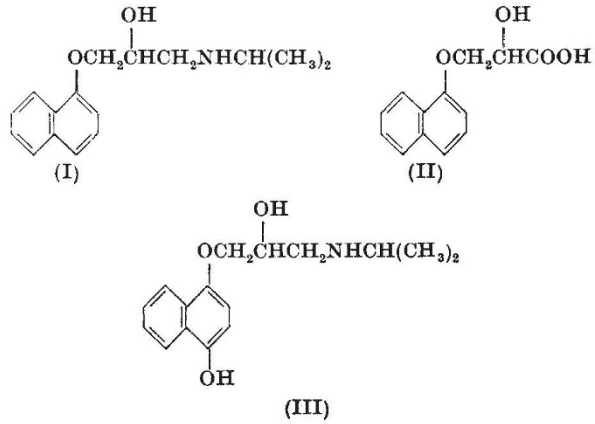
THIS is a preliminary report on the metabolism of propranolol[1] (I) in several species, including man.

When propranolol labelled with carbon-14 at C-1 in the naphthalene ring was injected subcutaneously into the rat, mouse, guinea-pig or rabbit at a dose of 1 mg/kg, the majority of the radioactivity was excreted in the urine, mainly during the first 24 h after the injection. In the case of the rat, half the administered radioactivity appeared in the urine during the 24 h immediately after dosing, and only traces of radioactivity were detected in the expired air.

The radioactive metabolites were separated by electrophoresis of the rat urine in 0·05 molar sodium dihydrogen phosphate. There were two main groups, namely, acidic (approximately 30 per cent) and amphoteric (approximately 70 per cent) compounds; only small amounts of basic compounds were found.

A pure acidic metabolite was isolated from the urine of injected rabbits by ion exchange chromatography and counter-current distribution. It was shown to be identical with a synthetic sample[2] of 2-hydroxy-3-(1′-naphthyloxy)-propionic acid (II) by melting point and mixed melting point determinations, ultra-violet and infra-red spectroscopy, and thin layer chromatography in two systems.

Two amphoteric compounds were also separated from the urine of injected rats, mice and rabbits by ion exchange and gel filtration chromatography. These compounds were shown to be glucuronides of propranolol (I) and its 4-hydroxy derivative (III). The nature of these was demonstrated by the acidic hydrolysis of the former to propranolol and enzymatic hydrolysis (using β-glucuronidase taken from *Helix pomatia*) of the latter, to a compound shown to be identical with a synthetic sample[3] of 1-(4′-hydroxy-1′-naphthyloxy)-3-isopropylamino-2-propanol (III) in infra-red and ultra-violet spectroscopy and thin layer and paper chromatography. The two glucuronides were also excreted in the bile of the rat and guinea-pig. Small amounts of propranolol and its 4-hydroxy derivative were detected in the urine of all the species examined.



The same metabolites were obtained after administering propranolol to mice, rats, guinea-pigs, rabbits and man. The main pathways of the metabolism of propranolol are thus demonstrated to be (*a*) hydroxylation (followed by conjugation with D-glucuronic acid) and (*b*) side-chain oxidation.

Work on further aspects of this problem including the absorption, distribution, metabolism, excretion and the possible entero-hepatic circulation of propranolol, together with the possibly differing metabolism of its two optical isomers, is in progress and will be reported separately.

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* The term 'Inderal' is a registered trade mark, the property of Imperial Chemical Industries, Ltd.

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