URIC ACID METABOLISM IN RABBITS

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In previous experiments¹ an attempt was made, by perfusing the surviving liver of the dog with sodium urate solutions, to ascertain whether allantoin was the sole end product of uric acid metabolism, or whether some fraction went by another line of decomposition to urea. The results obtained were inconclusive, for although no urea could be isolated, the amount of uric acid which disappeared was considerably greater than could be accounted for by the quantity of allantoin obtained, and it was shown that this was not due to a further destruction of allantoin.

Bezzola, Izar and Preti² have shown that, when diluted defibrinated blood containing uric acid is perfused through a dog's liver with a plentiful supply of oxygen, a considerable amount of the uric acid disappears, but that if the fluid be then saturated with carbon dioxide, and the perfusion continued, part of the uric acid previously destroyed is re-formed.

Further, Ascoli and Izar,³ in attempts to ascertain the nature of the chemical substances which were thus synthesised into uric acid, showed that by incubating liver extracts (ox) kept saturated with carbon dioxide with urea and dialuric acid a synthesis of uric acid could be brought about, but not when the added substances were allantoin or allantoin and urea. It seems likely, therefore, that the uric acid first destroyed in the perfusion experiments was not converted entirely into allantoin, or it would have been impossible to re-form any of the uric acid. This agrees with my own observations that the uric acid destroyed by the dog's liver is only partially converted into allantoin.

Similar observations to those already carried out on dogs¹ have now been made with rabbits. The excised livers of large rabbits have been perfused with saline solution containing sodium urate; the uric acid was estimated before and after the perfusion, and the amount of allantoin produced determined. The methods employed were identical with those used in the previous experiments.

As in the case of the dog, it was found that when a surviving liver is perfused with Ringer's solution alone a small quantity of allantoin is produced from the liver. In rabbits, owing to the much smaller size of the liver, this is very small, not exceeding 2 mgm. per cent. of the fluid, even in a five hours' perfusion.

Experiment I. The liver of a rabbit weighing 3,650 g. was perfused for two hours with Ringer's solution. At the end of the experiment the perfusion fluid contained 1.2 mg. of allantoin per cent. This melted at 231° C.; mixed with an equal quantity of Merck's allantoin it melted at 231.5° C. It had the crystalline form of allantoin, was readily soluble in hot water, with difficulty in cold, and was almost insoluble in alcohol. Boiled with sodium hydrate it gave the glyoxylic reaction, its solution gave no precipitate with silver nitrate alone but a flocculent one on the addition of a trace of ammonium hydrate which redissolved with excess.

Experiment II. The liver of a rabbit weighing 4,300 g. was perfused with Ringer's solution for five hours. At the end of the experiment the perfusion fluid contained 2 mg. of allantoin per cent. This melted at 226° C.; mixed with an equal part of Merck's allantoin and using the same thermometer the melting point was unchanged. It had the crystalline form and physical and chemical properties of allantoin.

When sodium urate was added to the perfusion fluid a considerable amount of the uric acid disappeared, even in such a short time as two hours, while in five hours only traces of uric acid may be left. The uricolytic power of rabbit's liver seems to be much greater, weight for weight, than that of a dog. The allantoin isolated from the fluid after perfusion corresponded to 85 per cent. to 100 per cent. of the uric acid which had disappeared. Under the conditions of these experiments, therefore, uric acid is converted quantitatively into allantoin by rabbit's liver, and it is most unlikely that any other substance is produced or that any allantoin is further destroyed.

Experiment III. The liver of a rabbit weighing 3,150 g. was perfused for two hours with Ringer's solution containing 48.8 mg. per cent. of uric acid as sodium urate. At the end of the experiment the fluid contained 30.6 mg. per cent. of uric acid and 19 mg. per cent. of allantoin. This melted at 231° C., and had the crystalline form and chemical and physical properties of allantoin. The percentage of nitrogen determined by Kjeldahl's method was 35.6 (theoretical 35.44).

In this experiment, allowing for 1.2 mgm. of allantoin produced from the liver itself (Exp. I), the whole of the uric acid destroyed was recovered as allantoin.

Experiment IV. The liver of a rabbit weighing 4,300 g. was perfused for two hours with Ringer's solution containing 33 mg. per cent. of uric acid as sodium urate. At the end of the experiment the fluid contained 6.9 mg. per cent. of uric acid and 22 mg. per cent. of allantoin. This had a melting point of 231° C. which remained unchanged when mixed with an equal part of Merck's allantoin. It had the crystalline form and physical and chemical properties of allantoin.

In this experiment, allowing a correction of 1.2 mgm. per cent., 85 per cent. of the uric acid destroyed was recovered as allantoin.

Experiment V. The liver of a rabbit weighing 3,220 g. was perfused for five hours with Ringer's solution containing 31.9 mg. per cent. of uric acid as sodium urate. At the end of the experiment the fluid contained 4.2 mg. per cent. of uric acid and 26.3 mg. per cent. of allantoin. This melted at 231° C. and the melting point remained unchanged when mixed with Merck's allantoin. It had the crystalline form and physical and chemical properties of allantoin.

In this experiment, allowing for a correction of 2 mgm. per cent. (Exp. II) of allantoin produced in five hours from the liver itself, 93.2 per cent. of the uric acid destroyed was recovered as allantoin.

Experiment VI. The liver of a rabbit weighing 2,800 g. was perfused for five hours with Ringer's solution containing 29 mg. per cent. of uric acid as sodium urate. At the end of the experiment the fluid contained 11.5 mg. per cent. of uric acid and 17 mg. per cent. of allantoin. This melted at 231°C. when mixed with an equal part of Merck's allantoin it melted at 230°C. It had the crystalline form and solubilities and gave the chemical reactions of allantoin.

In this experiment, allowing a correction of 2 mgm. per cent., 91.4 per cent. of the uric acid destroyed was recovered as allantoin.

CONCLUSIONS

The excised liver of a rabbit, when perfused with Ringer's solution, produces a small quantity of allantoin. Sodium urate, added to the perfusion fluid, is converted quantitatively into allantoin. None of the allantoin so produced is further destroyed.

REFERENCES.

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3. Ascoli and Izar, *Zeitsch. physiol. Chem.*, Vol. LXII, p. 347, 1909.

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