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## On the origin of glycocoll in the animal body.

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The various forms of protein, with the exception of casein and gelatin, contain about four per cent. of their N in the form of preformed glycocoll N. On giving benzoic acid or its salts to animals, they have the power of detoxicating it by combining it with glycocoll and forming hippuric acid.

About eleven years ago, Parker and Lusk employed this fact in an attempt to determine the maximum amount of hippuric acid that rabbits can produce. They studied the relationship between the total N in the urine and the glycocoll N eliminated as hippuric acid, HN/N. They found that for every 100 grams of total N excreted in the urine, an average of about 4 grams of N was eliminated in the glycocoll radical of the hippuric acid. After administering the first large dose of lithium benzoate to the animals, they invariably obtained a much higher HN/N ratio, 9.01 per cent. in experiment III., 7.14 per cent. in experiment IV., and 7.87 per cent. in experiment VI. They regarded this as a "sweeping out" of surplus glycocoll.

Since then, Wiechowski and Magnus-Levy have studied the same problem. Wiechowski obtained HN/N ratios of 45.4, 55, 50 and in one case, even as much as 64 per cent. Magnus-Levy found in his rabbits a maximum ratio of 25 and 28 per cent., in his sheep 27.8 per cent.

To investigate the cause of these discrepancies, Professor Lusk kindly suggested that I continue the study of this problem.

### EXPERIMENT I.

A goat weighing 42.3 kg. was employed. In Table I., the results of this experiment are summarized. It shows that the animal was able to eliminate in its urine a good deal more glycocoll than is found preformed in the proteins of its tissues. The hippuric acid formation, *i. e.*, the glycocoll elimination does not depend upon the amount of protein catabolized, but within certain

## TABLE I.

| Date, 1910. | Period. | Weight. | Total N, Gr. | Hippuric Acid, Gr. | Hippuric Acid Nitrogen, Gr. | Hippuric Acid N % / Total N | A Benzoic Acid Fed. | B Benzoic Acid Excreted as Hippuric Acid. | A/B Per Cent. | Hippuric Acid per Kg. Weight. | Remarks. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| February 25 | I. | —— | 5.441 | —— | —— | —— | —— | —— | —— | —— | —— |
| February 26 | II. | —— | 6.39 | —— | —— | —— | —— | —— | —— | —— | —— |
| February 27 | III. | —— | 5.027 | —— | —— | —— | —— | —— | —— | —— | —— |
| February 28 | I. | 42.3 | 4.303 | 10.19 | 0.805 | 18.7 | 8.47 | 6.95 | 82.04 | 0.247 | 250 gm. hay, 100 gm. oats. |
| March 1 | II. | —— | Urine Lost | | | 23.06 | 16.94 | —— | —— | —— | 88 gm. hay, 195 gm. white bread, 190 gm. milk. |
| March 2 | III. | 41.25 | 7.23 | 19.46 | 1.537 | 21.26 | 16.94 | 13.27 | 78.32 | —— | 200 gm. white bread, 150 gm. hay. |
| March 3 | IV. | —— | 9.08 | 27.75 | 2.193 | 24.14 | 21.18 | 18.93 | 89.39 | —— | 100 gm. bread, 100 gm. cabbage, 160 gm. carrots. |
| March 4 | V. | 40.1 | 6.45 | 11.06 | 0.874 | 13.54 | 8.47 | 7.54 | 89.06 | —— | Ate what was left from previous day, no more. |
| March 5 | VI. | —— | 6.36 | 30.93 | 2.443 | 38.41 | 25.42 | 21.10 | 83.05 | 0.786 | Starving. |
| March 6 | VII. | 39.35 | 8.06 | 28.28 | 2.234 | 27.72 | 25.42 | 19.03 | 74.86 | —— | Starving. |
| March 7 | VIII. | —— | 7.81 | 15.59 | 1.230 | 15.77 | 25.42 | 10.63 | 41.83 | —— | Starving. All benzoate one dose. |
| | | | | | Intermission of sixteen days. | | | | | | |
| March 23 | IX. | —— | 8.12 | 19.96 | 1.577 | 19.41 | 42.36 | 13.61 | 32.15 | —— | Starving. |

limits runs parallel to the amount of benzoic acid fed. In period VI., it reached its maximum. 38.4 per cent. of the total N was eliminated as glycocoll N in the hippuric acid.

Where do these enormous quantities of glycocoll originate? It might be argued that the source of the glycocoll found in the system lies in the different vegetable foods which are known to contain rather large quantities of free amino-bodies. But after giving 8 grams of sodium benzoate to a calf two weeks old which had had no other form of food but milk, the protein of which contains no glycocoll, it was found that it was able to form and eliminate hippuric acid glycocoll as readily as the adult goat.

Ingestion of glycolic or glyoxylic acid with very large quantities of sodium benzoate in rabbits, does not increase the quantity of glycocoll formed as indicated by the amount of hippuric acid eliminated. This might have been possible from their chemical relationship to glycocoll. (A detailed account of these experiments will be given in the final report.)

On careful consideration of the nitrogen metabolism in animals during the benzoate period, a possible explanation of the origin of glycocoll suggests itself. The goat during the three days of the foreperiod, excreted an average of 5.6 grams of N. Excepting the first day, which may be due to a sudden change in the quantity of food, there is a marked rise in the protein metabolism throughout the course of the benzoate period. This was observed in all the experiments and in all the varieties of animals that have been experimented upon. Furthermore, the increase in the protein destruction, *i. e.*, that increase in the N elimination above the normal, or above a previous day of a smaller benzoate dose, is always two to three times greater than the amount of nitrogen that has been eliminated as glycocoll in the hippuric acid molecule.

In Table II., the results of experiments on two rabbits are recorded. These show that the amount of urea N plus ammonia N during the benzoate period does not differ from normal days, and also that the extra N catabolized is much greater than the amount of N that was eliminated in the form of hippuric acid.

All these facts suggest the possibility that the glycocoll excreted as hippuric acid does not come from the fraction of protein that would have been metabolized had no benzoate been given,

but entirely from the extra protein which is destroyed, due to the presence of the toxic substance. We cannot state with any degree of certainty, what the character of the intermediary processes is, but that it is specific and peculiar seems very probable, for none of the extra N destroyed goes over into urea. It is all eliminated either as glycocoll or as undetermined N.

TABLE II.

*Rabbit No. 6.*

| Date, 1911. | Period. | Weight. | Total N. | Urea N. | Per Cent. of Total N. | $NH_3N$. | Per Cent. of Total N. | Hippuric Acid, N. | Per Cent. of Total N. | Benzoic Acid Fed. |
|---|---|---|---|---|---|---|---|---|---|---|
| March 12 | I. | 1.8 | 0.802 | 0.7024 | 87.6 | 0.232 | 2.89 | — | — | — |
| March 13 | II. | 1.72 | 1.147 | 0.796 | 69.4 | 0.36 | 3.177 | 0.088 | 7.7 | 1.7 |
| March 14 | III. | 1.60 | 0.913 | 0.782 | 85.67 | 0.166 | 1.82 | — | — | — |

*Rabbit No. 7.*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| March 23 | I.[1] | 1.96 | 0.596 | 0.487 | 81.68 | 0.043 | 7.23 | — | — | — |
| March 24 | II. | 1.71 | 1.369 | 0.9673 | 70.66 | 0.1127 | 8.23 | 0.082 | 6.0 | 1.7 |
| March 25 | III. | 1.68 | 1.199 | 1.0898[2] | | | | | | |

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## Experiments on the diffusibility of alkaloids through rubber.[3]

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Rosenbloom and Gies have found that various ether-soluble substances, when dissolved in ether and placed in rubber bags immersed in ether, readily pass through the rubber membranes

[1] Period of about 12 hours.

[2] Urea + $NH_3N$ = 90.9 per cent.

[3] This study is one of a projected series on *physico-chemical conditions in the cell*, which in turn constitutes a section of a comprehensive plan of research on the composition of protoplasm as well as the structural and dynamic relationships of cell constituents and products. These investigations are now in progress in the Laboratory of Biological Chemistry of Columbia University, at the College of Physicians and Surgeons, and under the auspices of the George Crocker Special Research Fund.