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On the decomposition of caffeine in the liver.[1]

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The earlier workers on the metabolism of caffeine and theobromine maintained that these substances may undergo partial or complete transformation in the body with the loss of one or more of the methyl groups. Investigations carried out recently seemed to indicate that this was due to specific enzymes. Schittenhelm, Brugsch and Pincussohn[2] claimed to have found an enzyme in the lungs of the horse capable of splitting off the methyl groups of caffeine. Kotake[3] came to similar conclusions as a result of studies on the decomposition of caffeine in beef livers. He added varying amounts of caffeine to aqueous extracts of the liver which he allowed to digest under antiseptic precautions at body temperature in the thermostat for four days. Liver extracts without caffeine, similarly treated, were used as controls. At the end of each period the purin bodies were precipitated and total nitrogen determined. He found in every case much larger amounts of total nitrogen in the extract containing caffeine than in the control, from which he concluded that the increase of purin substances was due to the reduction of caffeine to non-methyllated purins.

The work of Fuijitani[4] has shown that caffeine stimulates peptic digestion *in vitro*. The possibility of a stimulating action of caffeine on intra-cellular enzymes is therefore not to be excluded, and might explain the results of Kotake. Moreover, in Kotake's experiments no separation of the alkaloid was attempted.

We therefore carried out a series of experiments in which the caffeine as well as the purin nitrogen was determined. Finely minced fresh beef livers were allowed to stand twenty four hours in the presence of 5 c.c. toluol and were filtered through paper.

[1] Published by permission of the secretary.

[2] *Cent. f. d. ges. Physiol. u. Path. des Stoffewechs*, 1908, ix, 290.

[3] *Arch. internat. d. pharm. et de ther.*, 1905, xiv, 21.

[4] *Zeit. f. physiol. Chem.*, 1908, lix, 378.

Half a gram of caffeine was added to a portion of the extract thus obtained, and kept in the thermostat at body temperature for from two to ten days. An equal quantity of the extract without adding caffeine, similarly treated, was used as a control. As indicated in the accompanying table, practically the entire amounts of caffeine were regained. The total quantities of nitrogen found in the precipitated purins were approximately equal save in two experiments in which the amounts of total nitrogen were from 13 to 19 per cent. greater when caffeine was added than in the controls.

Digestion of liver extracts with and without caffeine in the presence of hydrogen peroxide likewise failed to indicate the presence of a specific enzyme capable of splitting off the methyl group in caffeine.

EXPERIMENTS.

Series No.	Experiment No.	Liver extract in c.c.	Duration of digestion in days.	Caffeine added.	Nitrogen.[1]	Caffeine regained.
I.	1	250	Two.	0.5	0.0699	0.4935
		250	Two.	—	0.0704	—
	2	250	Four.	0.5	0.0660	0.4921
		250	Four.	—	0.0581	—
	3	250	Eight.	0.5	0.0531	0.4915
		250	Eight.	—	0.0522	—
II.	1	300	Five.	0.5	0.0511	0.4918
		300	Five.	—	0.0499	—
	2	300	Ten.	0.5	0.0604	0.4799
		300	Ten.	—	0.0496	—
III.	1	250	Four and one half.	0.5	0.0345	0.4897
		250	Four and one half.	—	0.0370	—
IV.	1	500+ 5 c.cm. H_2O_2	Four and one half.	0.5	0.0416	0.4951
		500+ 5 c.cm. H_2O_2	Four and one half.	—	0.0441	—
V.	1	300	Four.	0.5	0.0478	0.4931
		300	Four.	0.5	0.0432	0.4952
		300	Four.	—	0.0444	—

[1] Total nitrogen was determined by E. C. Trescott.