since they possess the ability to convert phenylalanine to tyrosine and have, consequently, a higher absolute turnover-rate than phenylketonuric patients.

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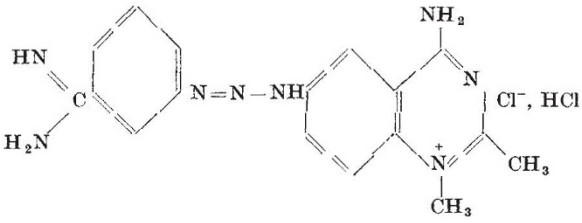
[1] Stein, W. H., Paladini, A. C., Hirs, C. W. H., and Moore, S., *J. Amer. Chem. Soc.*, **76**, 2848 (1954).
[2] Armstrong, M. D., Chao, F.-C., Parker, V. J., and Wall, P. E., *Proc. Soc. Exp. Biol. and Med.*, **90**, 675 (1955).
[3] Bruns, F. H., Haberland, G. L., and Altman, K. I., *Biochem. Z.*, **331**, 446 (1959).
[4] Bernhard, K., Vuilleumier, J. P., and Brubacher, G., *Helv. Chim. Acta*, **38**, 1438 (1955).
[5] Schreier, K., Altman, K. I., and Hempelmann, L. H., *Proc. Soc. Exp. Biol. and Med.*, **87**, 61 (1954).
[6] Grümer, H.-D., Koblet, H., and Woodard, C., *Fed. Proc.*, **19**, No. 1, 193 (1960).
[7] Ishii, K., *Japan. J. Clin. Path.*, **5**, 167 (1957).

6-(*m*-Amidinophenyldiazoamino)-4-amino-1,2-dimethylquinazolinium Chloride Hydrochloride: a New Drug active against *Babesia canis*

As part of a study of diamidines which has extended over many years, we have recently screened for trypanocidal and babesicidal activity a number of compounds in which one of the amidine groups has been replaced by a cyclic amidine group. One of the most active of these is 6-(*m*-amidinophenyldiazoamino)-4-amino-1,2-dimethylquinazolinium chloride hydrochloride[1]:



(I)

(M. and B. 4986) (I). This compound, which contains the *m*-amidinophenyldiazoamino linkage present in the very active trypanocidal drug, *iso*metamidium[2], has babesicidal properties and is markedly active against *Babesia canis* in dogs.

The approximate maximum tolerated dose (subcutaneous) of M. and B. 4986 in healthy puppies was 25 mgm./kgm. body-weight, though marked tachycardia, accompanied by diarrhœa and vomiting, followed this dose, and persisted for about 1 hr. Fourteen days after a subcutaneous dose of 20 mgm./kgm. body-weight of M. and B. 4986 in adult dogs, there was no loss in weight, and no macroscopic signs of toxicity, apart from slight local skin thickening at the injection site, were observed on autopsy.

In therapeutic tests, a total of 46 puppies experimentally infected with *Babesia canis* were treated with doses of M. and B. 4986 between 0·5 and 10 mgm./kgm. body-weight. All the 12 infected puppies which received a subcutaneous dose of 2·5 mgm./kgm. survived, 3 were parasitologically negative within 24 hr., and all within 72 hr., 8 remained free of parasites for at least 30 days and 4 developed a parasitological relapse.

M. and B. 4986 (I) was prepared by coupling *m*-amidinobenzenediazonium chloride with 4,6-diamino-1,2-dimethylquinazolinium chloride. It was obtained as an orange crystalline solid, which decomposes at 237–238° C. (Found: N, 24·6; Cl, 15·3; H_2O, 11·4. $C_{17}H_{19}N_8^+,Cl^-,HCl,3H_2O$ requires N, 24·4; Cl, 15·4; H_2O, 11·7 per cent). It is approximately 0·5 per cent w/v soluble in water. In order to present a more soluble salt for field investigations the corresponding methanesulphonate (M. and B. 4986*A*) has been prepared as orange crystals, decomposing at 205–208° C. (Found: N, 20·6; S, 12·0; H_2O, 3·4. $C_{17}H_{19}N_8^+,CH_3SO_3^-,CH_3SO_3H,H_2O$ requires N, 20·6; S, 11·7; H_2O, 3·3 per cent); it is approximately 25 per cent w/v soluble in water.

Further details, including a report on the field investigations, will be published in due course.

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[1] May and Baker, Ltd., and Berg, S. S., Brit. Pat. App. 19267/58.
[2] Berg, S. S., *Nature*, **188**, 1106 (1960).

PHYSIOLOGY

Excretion of Tryptophan Metabolites after Physical Effort

It has been shown that muscular effort is accompanied by the increased urinary excretion of one of the metabolites of tryptophan, namely, indoleacetic acid[1]. Pelikán and co-workers[2] have proved that there is increased excretion of another tryptophan metabolite, xanthurenic acid, after muscular effort.

Another tryptophan metabolite, 5-hydroxyindoleacetic acid, was then studied. The close relation between 5-hydroxytryptamine and the central nervous system is well known, and I wished to find out whether there is an increased urinary excretion of 5-hydroxyindoleacetic acid after muscular effort which is, moreover, often accompanied by considerable nervous tension.

5-Hydroxyindoleacetic acid is formed from 5-hydroxytryptamine by oxidase, and Sjoerdsma[3], Ressel[4], Udenfriend[5], de Gennes[6] and others state that its excretion is relatively constant. The normal urinary excretion of 5-hydroxyindoleacetic acid in men varies from 2 to 9 mgm./day[7]. Using a modification of Udenfriend's reaction, Schön and co-workers[8] recently found 1–6 mgm. (average 2·53 mgm./day). In the case of food only, the consumption of bananas results in increased excretion of this substance[9,10].

The urinary excretion of 5-hydroxyindoleacetic acid in men after various degrees of stress during athletics was followed. It was estimated in samples