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Effect of Methylhistamine and Hydroxyethylglyoxaline on Gastric Secretion and Blood Pressure in the Dog.

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Prior to the work reported in this paper histamine (0.5-1.0 mg.), pilocarpine (5-10 mg.), and iso-pilocarpine (10 mg.) were the only imidazoles out of 10 examined that stimulated gastric secretion.^{1, 2}

Through the courtesy of Dr. Pyman of the Boots Pure Drug Company of Nottingham, England, samples of 2 other imidazoles, namely, methylhistamine (4.5 methylaminoethylglyoxaline dihydrochloride) and 4,5 hydroxyethylglyoxaline, were supplied to us for physiological investigation.

With a recently devised method Pyman has succeeded in the synthesis of methylhistamine which has properties altogether different from those reported by him and Fargher³ for this supposed formerly synthesized compound. The oxytocic activity of methylhistamine on the isolated guinea pig uterus, instead of being about 1% of that of histamine, as recorded in their original paper, was now found by them to be almost as great as that of histamine itself.

We have studied the effect of these 2 imidazoles upon gastric secretion and the blood pressure in the dog. It was found that subcutaneous injections of doses of histamine and methylhistamine, which contained equivalent quantities of base, caused a definitely parallel response in the stimulation of gastric secretion and acidity in Pavlov pouch dogs. (Table I.) Methylhistamine likewise caused a drop in the blood pressure of the dog quantitatively

TABLE I.
Effect of Histamine, Methylhistamine and Hydroxyethylglyoxaline on Gastric Secretion in Pavlov Pouch Dog.*

Dog	Histamine		Methylhistamine		Hydroxyethylglyoxaline	
	Vol. of G Sec. (cc) Mean	Total HCl Output (mg.)	Vol. of G Sec. (cc) Mean	Total HCl Output (mg.)	Vol. of G Sec. (cc) Mean	Total HCl Output (mg.)
1	28.2	130.24	29.0	114.05	0	0
2	12.4	62.75	11.7	40.50	0	0

* Only secretion above basal recorded in this table.

¹ Sacks, Ivy, Burgess and Vandolah, *Am. J. Physiol.*, 1932, **101**, 334.

² Burgess and Ivy, *PROC. SOC. EXP. BIOL. AND MED.*, 1930, **28**, 115.

³ Pyman and Fargher, *J. C. S.*, 1921, 731.

similar to that caused by histamine. Hydroxyethylglyoxaline showed no stimulation of gastric secretion nor did it affect the blood pressure in the dog. This is apparently due to the absence of either the methyl or ethyl-amino group from this compound.

Conclusions. (1) Methylhistamine and histamine are equally potent in stimulating the gastric glands to secrete acid. (2) Methylhistamine and histamine cause a similar fall in the blood pressure in the dog. (3) Hydroxyethylglyoxaline has no effect upon gastric secretion and blood pressure in the dog.

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Body Temperature Changes Produced by Sodium Salts of Some Aromatic Acids.*

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Concerning the relations between the chemical constitution of the nitrophenols and their specific action on cellular metabolism Heymans¹ makes the following statements:

"In the dinitrophenol the stimulating action on metabolism is associated with position 1 to 4 of one of the NO₂ radicles, the greater the distance between the two NO₂ radicles the greater is the hyperthermic action. The introduction of one or more aliphatic CH chains up to the pentyl chain, progressively increases the specific action of the dinitro-derivatives as catalyzers of cellular respiration. The stimulating action on cellular metabolism is decreased by the addition of an NH₂ radicle to the benzyl chain and is abolished by the addition of an HSO₃ radicle."

3-5 dinitrosalicylic acid which has the two NO₂ groups in the desired positions relative to each other and hydroxyl group offers the opportunity to study the effect on body temperature when a COOH group is substituted into a dinitrophenol.

Sodium 3,5 dinitrosalicylate injected intramuscularly into pigeons and subcutaneously, intramuscularly or intraperitoneally into rats, in the range dosage 25 to 133 mg. per kilo body weight, does not produce a rise in body temperature, but on the contrary

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¹ Heymans, C., *J. Pharm. and Exp. Therap.*, 1934, **51**, 144.