The injections of phenylbutanolamine hydrochloride and phenylhexanolamine hydrochloride seem to indicate that their actions are hyperglycemic. The introduction of the methyl into the aromatic nucleus, as in *p*-tolylpropanolamine hydrochloride, produces marked hyperglycemic activity when injected intravenously. These results indicate that possibly an interesting relationship between hyperglycemic activity and homology might be revealed by a more comprehensive study of the compounds of this series, and such a study will be undertaken in these laboratories.

SUMMARY.

1. The action of phenylpropanolamine hydrochloride upon the blood sugar level of rabbits has been studied intravenously, subcutaneously and orally.

2. The action of certain homologs of phenylpropanolamine has been studied intravenously.

BIBLIOGRAPHY.

(1) F. Blum, *Deut. Arch. klin. Med.*, 71 (1901), 146.
(2) T. Sollman, "Manuel Pharmacology," page 442, Saunders & Co., Philadelphia, Pa.
(3) C. F. Cori and G. T. Cori, *J. Biol. Chem.*, 74 (1928), 321.
(4) K. K. Chen and C. F. Schmidt, *J. Pharmacol. and Exptl. Therap.*, 34 (1925), 339.
(5) J. A. Wilson, *Ibid.*, 30 (1927), 209.
(6) A. Nagel, *Arch. exptl. Pharmacol.*, 110 (1925), 129; through Wilson.
(7) W. H. Hartung and J. C. Munch, *J. Am. Chem. Soc.*, 51 (1929), 2261.
(8) K. K. Chen, Chang-Keng Wu and E. Henrikson, *J. Pharmacol. and Exptl. Therap.*, 36 (1929), 363.
(9) Shaffer and Hartmann, *J. Biol. Chem.*, 45 (1921), 349.

RESEARCH LABORATORIES,
SHARP & DOHME.

PHYTOCHEMICAL NOTES.*,**

NO. 105. MONARDA PUNCTATA, L.†

BY A. A. HARWOOD.

For the purpose of supplementing earlier chemical work on this species, it seemed desirable to subject the several parts of the plant to a preliminary chemical examination. More particularly did it seem important to acquire some understanding of the inorganic constituents because of the possible relation these may have to the thymol-carvacrol isomerism of the two species *M. punctata* and *M. fistulosa*.

The Root.—Two moisture determinations yielded 4.0 p. c. and 4.5 p. c., respectively, in the air-dried material when determined by the xylene method. The same material yielded the following amounts of ash in two determinations.

	I.	II.
Water-soluble ash	0.96 p. c.	1.03 p. c.
Water-insoluble ash	6.67 " "	4.71 " "
Total ash	7.63 " "	5.74 " "

* Part of a thesis submitted for the degree of Doctor of Philosophy, University of Wisconsin.
** From the laboratory of Edward Kremers.
† See also THIS JOURNAL, 18 (1929), 228; 19 (1930), 1171.

The water-insoluble ash resolved itself into:

Acid soluble	1.52 p. c.	1.31 p. c.
Acid insoluble	5.15 " "	3.40 " "

Upon analysis, the ash revealed the presence of the following elements and groups, the percentage, as above, being computed with reference to the air-dried material from which the ash had been obtained:

	I.	II.		I.	II.
Ca	0.25 p. c.	0.24 p. c.	CO_3	0.21 p. c.	0.22 p. c.
Mg	0.02 " "	0.02 " "	SO_4	0.132 " "	0.144 " "
Fe	0.044 " "	0.045 " "	SiO_3	5.18 " "	5.42 " "
Al	0.06 " "	0.065 " "	Undeter-		
Cl	0.015 " "	0.014 " "	mined	1.72 " "	1.46 " "

Tests for K and Na gave positive results.

The preliminary analysis with selective solvents, according to the Dragendorff Method, yielded the following amounts of extractive on two 100-Gm. samples.

Solvent.	I.	II.
Petroleum ether	1.2 p. c.	1.6 p. c.
Ether	1.0 " "	1.0 " "
Alcohol	3.7 " "	3.0 " "
Water	2.1 " "	1.9 " "
Aqueous alkali (2 p. c. KOH)	8.6 " "	8.8 " "
Aqueous acid (1 p. c. HCl)	3.6 " "	3.6 " "
Marc	80.0 " "	82.0 " "
Total	100.2 " "	101.9 " "

The Stem.—The moisture content, when determined by the xylene method, was shown to be 5.4 p. c. and 5.6 p. c., respectively.

Two ash determinations yielded the following results:

	I.	II.
Water-insoluble ash	3.90 p. c.	3.78 p. c.
Water-soluble ash	2.18 " "	2.33 " "
Total ash	6.08 " "	6.11 " "

The water-insoluble ash contained:

Acid-insoluble ash	1.61 p. c.	1.54 p. c.
Acid-soluble ash	2.29 " "	2.24 " "

Of the more common constituents, the following were determined quantitatively:

	I.	II.		I.	II.
Mg	0.029 p. c.	0.026 p. c.	CO_3	0.59 p. c.	0.61 p. c.
Ca	0.430 " "	0.430 " "	SO_4	0.31 " "	0.29 " "
Fe	0.085 " "	0.085 " "	SiO_3	1.68 " "	1.61 " "
Al	0.11 " "	0.11 " "	Undeter-		
Cl	0.032 " "	0.039 " "	mined	2.84 " "	2.91 " "

The preliminary analysis with selective solvents, according to the Dragendorff Method, yielded the following amounts of extractive on two 100-Gm. samples:

Solvent.	I.	II.
Petroleum ether	0.6 p. c.	0.8 p. c.
Ether	0.3 " "	0.3 " "
Alcohol	3.2 " "	4.0 " "
Water	4.7 " "	6.6 " "
Aqueous alkali (2 p. c. KOH)	7.8 " "	7.6 " "
Aqueous acid (1 p. c. HCl)	5.0 " "	4.6 " "
Marc	80.0 " "	78.0 " "
Total	101.6 " "	101.9 " "

Aside from minor experimental errors the excess in "total" over 100 p. c. is due to the alkali introduced through one of the solvents.

The Leaf.—Two moisture determinations yielded 8.0 p. c. and 7.6 p. c., respectively.

Ash determinations of the air-dried material yielded the following results:

	I.	II.
Water-insoluble ash	10.99 p. c.	10.52 p. c.
Water-soluble ash	2.38 " "	2.77 " "
Total ash	13.37 " "	13.29 " "
The water-insoluble ash resolved itself into:		
Acid-insoluble ash	4.77 p. c.	4.54 p. c.
Acid-soluble ash	6.22 " "	6.03 " "

The following quantitative determinations of ash constituents are computed with reference to air-dried material:

	I.	II.		I.	II.
Mg	0.173 p. c.	0.171 p. c.	CO_3	0.75 p. c.	0.74 p. c.
Ca	1.19 " "	1.14 " "	SO_4	0.25 " "	0.26 " "
Fe	0.14 " "	0.14 " "	SiO_2	5.78 " "	5.77 " "
Al	0.24 " "	0.23 " "	Undetermined	4.78 " "	4.85 " "
Cl	0.027 " "	0.032 " "			

The preliminary analysis with selective solvents yielded the following amount of extractive on two 100-Gm. samples:

Solvent.	I.	II.
Petroleum ether	7.5 p. c.	6.0 p. c.
Ether	4.5 " "	4.0 " "
Alcohol	2.5 " "	3.0 " "
Water	5.6 " "	6.8 " "
Aqueous alkali (2 p. c. KOH)	16.3 " "	16.6 " "
Aqueous acid (1 p. c. HCl)	5.5 " "	6.0 " "
Marc	58.0 " "	58.0 " "
Total	99.9 " "	100.4 " "

The Bract.—The moisture content, in two determinations, proved to be 4.0 p. c.

Two ash determinations yielded the following results:

	I.	II.
Water-insoluble ash	7.87 p. c.	7.81 p. c.
Water-soluble ash	3.36 " "	3.76 " "
Total ash	11.23 " "	11.57 " "

The water-insoluble ash resolved itself into:

Acid-insoluble ash	3.39 p. c.	3.30 p. c.
Acid-soluble ash	4.48 " "	4.51 " "

The quantitative determination of the ash yielded the following percentages computed with reference to air-dried material:

	I.	II.		I.	II.
Mg	0.10 p. c.	0.10 p. c.	CO_3	0.89 p. c.	0.86 p. c.
Ca	0.74 " "	0.75 " "	SO_4	0.345 " "	0.36 " "
Fe	0.10 " "	0.10 " "	SiO_3	4.15 " "	4.04 " "
Al	0.24 " "	0.24 " "	Undetermined	4.72 " "	4.82 " "
Cl	0.11 " "	0.13 " "			

The preliminary analysis with selective solvents yielded the following results:

Solvent.	I.	II.
Petroleum ether	8.6 p. c.	6.25 p. c.
Ether	2.2 " "	2.50 " "
Alcohol	20.0 " "	18.75 " "
Water	6.0 " "	5.1 " "
Aqueous alkali (2 p. c. KOH)	6.6 " "	6.0 " "
Acid (1 p. c. HCl)	7.9 " "	8.2 " "
Marc	46.2 " "	53.7 " "
Total	97.5 " "	100.50 " "

The Corolla.—The only record of a chemical study of the corolla is that of Hewitt.[1] He found 69 p. c. of water in the recently picked corollas and 6. p c. in the air-dried material. He also made ash determinations and distilled the volatile oil.

Moisture determinations on material collected in 1927 yielded 6.8 p. c. and 6.6 p. c., respectively.

Ash determinations yielded the following results, which, for ready comparison, are tabulated with those of Hewitt.

	Harwood.		Hewitt.		
	I.	II.	I.	II.	III.
Water-insoluble ash	4.09 p. c.	3.99 p. c.	6.00 p. c.	6.11 p. c.	5.52 p. c.
Water-soluble ash	6.20 " "	6.21 " "	4.86 " "	4.80 " "	4.97 " "
Total ash	10.29 " "	10.20 " "	10.86 " "	10.91 " "	10.49 " "

The water-insoluble ash resolved itself into:

	I.	II.
Acid-insoluble ash	1.36 p. c.	1.31 p. c.
Acid-soluble ash	2.73 " "	2.48 " "

Whereas the total ash in the two sets of determinations agreed there is an appreciable difference in the water-soluble and the water-insoluble ash.

The following quantitative determinations of ash constituents are computed with reference to air-dried material:

[1] JOUR. A. PH. A., 17 (1928), 457.

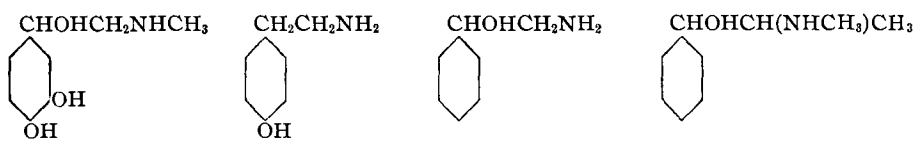
	I.	II.		I.	II.
Mg	0.046 p. c.	0.042 p. c.	CO_3	2.01 p. c.	2.03 p. c.
Ca	0.24 " "	0.24 " "	SO_4	0.27 " "	0.31 " "
Fe	0.073 " "	0.067 " "	SiO_3	1.42 " "	1.37 " "
Al	0.242 " "	0.240 " "	Undetermined	5.71 " "	5.73 " "
Cl	0.24 " "	0.22 " "			

A CHEMICAL EXAMINATION OF PARA-HYDROXYPHENYL METHYLAMINO ETHANOL HYDROCHLORIDE.*,†

BY SAMUEL M. GORDON.

The practitioner of medicine now has available as vasoconstrictor agents a number of substances. The best known of these is epinephrine, first isolated by Abel in 1897; then later by Takamine and others in pure form. The relative ease with which epinephrine undergoes oxidation and the relatively pronounced therapeutic action of very small doses of epinephrine have stimulated interest in the search for compounds having similar pharmacologic properties. The search in part has been for compounds with less pronounced pharmacologic action and greater resistance to the oxidizing influences of the air. Such work has led to the preparation of many interesting compounds. But it is worth noting that of the many compounds prepared under this stimulus, epinephrine still remains the only official drug of this group. The outstanding workers in this field have been the Edinburgh investigators, Barger and Dale. It was these workers who in a large measure clearly elucidated the relation between chemical constitution and pharmacologic properties in the group of compounds related to β-phenylethylamine. As a result of such investigations there has been made available to the clinical worker tyramine (originally isolated from ergot, but now prepared synthetically), ephedrine from the Chinese plant Ma-Huang,[1] and a more recent introduction, phenylamino ethanol, a synthetic product, for which standards have already appeared,[2] and others which are of more or less academic interest at present.

A comparison of the structural relations of these four compounds may serve to bring out the chemical similarities and conversely the differences, due to molecular structure.[3,4]



Epinephrine Tyramine Phenylamino Ethanol Ephedrine

* Contribution from the American Dental Association, Bureau of Chemistry and the A. M. A. Chemical Laboratory. † The work reported herein was completed in June 1929.

[1] The work of Chen and others has revived an interest in this long forgotten Chinese drug. Synthetic forms are now on the market, but up to now only the laevorotatory compound from the plant has been acceptable for inclusion in New and Nonofficial Remedies. Standards have been developed to rule out as far as possible all isomers except laevo ephedrine.

[2] Samuel M. Gordon, JOUR. A. PH. A., 17 (1928), 1195; also Miller and Piness, *J. Am. Med. Assocn.*, 91 (1928), 1033; and "Report of Council on Pharmacy and Chemistry," *Ibid.*, 91 (1928), 1037.

[3] Samuel M. Gordon, *loc. cit.* [4] J. B. Peterson, *Ind. Eng. Chem.*, 20 (1928), 388.