

that a tarry layer began to separate. Thus about one-third of the tar consists of hydrothymoquinone which can be separated by fractionation and, if necessary, by precipitation with heptane.

This result suggested the possibility of obtaining derivatives of hydrothymoquinone directly from the tar, a thing that had not been previously accomplished.

2.5 Gm. tar were treated with 4.0 Gm. phenyl isocyanate in 20 Cc. solvent* and boiled for 35 minutes at this time. The contents became granular and apparently crystalline after standing for ten days. The flask was reheated. This product was taken up in alcohol, after separation from petroleum, and an oil obtained which deposited some crystals on standing. The alcoholic solution was evaporated and dirt removed as well as possible. The product melted at 237 to 238° and gave the same result after an attempted recrystallization from alcohol. It was by no means colorless yet. An analysis by Dumas' method gave this result:

0.1313 Gm. gave 15.2 Cc. N₂ at 23° and 709 mm., or 12.55 p. c., whereas hydrothymoquinone diphenylurethane contains but 6.93 p. c. The amount of material was too small for further study.

The separation of hydrothymoquinone in quantity from the mother liquid of thymol obtained from *Monarda punctata* on a large scale supports the view that the tar consists in no small part of phenoquinones or quinhydrone, or both. Its isolation in the manner described above suggests the further study of these tar residues for the ketones with which the phenols from the quinhydrone or phenoquinones are assumed to be combined.

BIBLIOGRAPHY.

1. Erlenmeyer, Buchners, *Neues Repert. d. Pharm.*, 23, 1, 1873.
2. Sigel, *Ann.*, 170, 345, 1873.
3. Semmler, *Ber.*, 41, 509, 1908.
4. Miller, *Bull. Univ. Wis.*, No. 693, 49, 1914.
5. Dilipine, *C. R.*, 150, 106, 1910.
6. Pickles, *J. C. S.*, 93, 867, 1908.
7. Zeisel, *Monatsh.*, 6, 989, 1885.
8. Gregor, *Ibid.*, 19, 116, 1892.

THE CAPSICUM MONOGRAPH IN U. S. P. X.

BY E. N. GATHERCOAL AND R. E. TERRY.

The revision of the monograph of Capsicum hinges largely on the desirability of excluding all commercial forms of Cayenne pepper except true African chillies.

That African chillies are the most pungent is generally conceded. J. M. Francis states that the degree of pungency is approximately as follows: Mombassa chillies 50,000 to 100,000, Zanzibar chillies 40,000 to 50,000, Japanese chillies 20,000 to 30,000. Pungency is apparently the only pharmacologic property desired of capsicum as a medicine, hence it is desirable that medicinal capsicum be of the highest pungency and fairly uniform in this property.

* Petroleum boiling at 180-200°.

The imports in pounds of Capsicum, Red Pepper, Cayenne Pepper (these names being used synonymously in commerce) for 1918-19 were as follows:¹

Commercial trade name.	Imported from.	1918.	1919.
PAPRIKA.....	Spain.....	1,469,008	1,826,288
	Italy.....	51,630
MEXICAN CHILLIES.....	Mexico.....	73,329	20,463
	Nicaragua.....	311
	Cuba.....	862
EAST INDIA CHILLIES.....	Dutch East Indies.....	43,000	708
	British Indies.....	11,200
JAPANESE CHILLIES.....	Japan.....	697,848	399,007
SIERRE LEONE CAPSICUM.....	British West Africa.....	4,480
MOMBASSA (Zanzibar) CAPSICUM.	British East Africa.....	366,370	111,999
	Mostly African Capsicums... }	British South Africa.....	420,465
England.....		4,489	212,280
	Chile.....	78,484	38,152
	Aden.....	22,400
	Hong Kong.....	2,500	400
	Canada.....	76,748	11,936
	Netherlands.....	198
		3,232,241	2,721,814

In 1920 heavy imports² of paprika from Spain, chillies from Japan, and capsicums from Italy, British East Indies, Dutch East Indies and England are noted in the trade journals. Also a shipment of paprika through Holland. In January and February of 1921, imports of paprika from Trieste are noted, and of chillies from British East India.

From the official records it would appear that world commerce should be able to supply genuine African chillies to meet the needs of the United States, for medical purposes.

To insure the exclusion of all but African chillies from the monograph of Capsicum there appear to be five points in the present monograph to be considered, namely:

- I. The common names.
- II. The botanical name in the definition.
- III. The number of seeds in the fruit and possibly other points of physical appearance.
- IV. The microscopical distinctions between the various capsicums in powdered form.
- V. The tests.

I. Regarding the synonym "Cayenne Pepper," Dr. H. Engelhardt's criticism that this term is used in the spice trade as the name for the less pungent capsicums, and therefore should be dropped from the U. S. P., is well taken.

II. The botanical name "Capsicum frutescens" is generally applied to any woody or shrubby capsicum plants, and the East Indian and Japanese capsicums are produced on shrubby plants, as well as the true African capsicums. The

¹ "Foreign Commerce & Navigation of the United States," 1919.

² *Drug and Chemical Markets.*

criticism of Dr. H. H. Rusby that the more specific name "minimum" or "fastigiatum" should be used is approved by us, "fastigiatum" preferred.

III. The criticism of Dr. Engelhardt that the maximum number of seeds, 17, should be increased to 20, has been noted. An examination of several commercial capsicums resulted as follows:

Zanzibar (1910).	Sierre Leone (1920).	Japan (1920).	Bombay (1921).
8	12	23	24
14	21	29	24
15	14	13	9
17	15	29	24
19	16	22	15
11	15	24	19
10	13	20	15
10	11	22	10
12	11	20	19
12	13	29	19
12	9	22	48
..	17	49	28
..	47
..	29
..	29
..	29
..	18

IV. That it would be very desirable to present certain distinctive histological features by which African chillies in powdered form could be distinguished from other capsicums is self-evident. We believe this can be done in connection with the outer epidermis of the pericarp.

V. Dr. Engelhardt's criticism to the effect that samples of African chillies now in the market will not comply with the present 2 percent purity rubric has been borne out by our own experience, notably with one lot, apparently Sierre Leone Capsicum, which contains 5% of stems, calyxes and other organic foreign matter. However, we question whether the tolerance should be increased or, if at all, but very slightly. Clean African capsicum has been obtainable in the past, and should be again.

The ash limit of 7 percent and 1 percent of acid-insoluble ash has not been questioned. It might be advisable to reduce the total ash limit to 6.5 percent and thus make it correspond with the U. S. Dept. of Agriculture ruling. E. L. Patch found total ash of 12 samples 5.2 to 10 percent; above 7 percent, 6 samples; below 7 percent 5 samples.

Some recent work is submitted herewith.

Kind.	Source.	Condition.	Total ash.	Acid insol.
PAPRIKAS				
1. Hungarian.	Grown in Indiana	Powdered	5.7	
			5.65-5.675	
2. Hungarian.	Imported Rosen paprika	Powdered	4.94	
			4.82-4.88	
CHILLIES				
4. Japanese...	Powdered	5.5	
			5.31-5.405	
7. Japanese...	Nyassa	Whole	5.47	
			5.55-5.51	

8.	Madras....	Whole	5.29 5.23-5.26	
9.	Madras....	"Cherries"	Whole	4.57 4.55-4.56	
CAPSICUMS.					
10.	East Indian	Lehn & Fink	Whole	4.5 4.3-4.4	
3.	East Indian	Squibb	Powdered	4.89 4.87-4.88	
5.	Japanese...	Kobe	Whole	4.87 4.81-4.84	
14.	Japanese...	Fuller-Morrison	Whole	4.75 4.55-4.65	
15.	Japanese...	Lehn & Fink	Whole	5.416 5.468-5.442	0.57%
16.	Japanese...	Fuller-Morrison	Whole	5.02 4.53-4.775	
17.	Japanese...	Fuller-Morrison	Powdered	7.64 7.65-7.654	1.12%
11.	African....	Sierre Leone	Whole	4.54 4.43-4.485	
12.	African....	Zanzibar	Whole	4.8 4.65-4.725	
13.	African....	Mombassa	Powdered	7.998 8.426-8.212	1.59%

A moisture limit of 7 percent might well be established. E. L. Newcomb found 4.50 percent, 4.10 percent, 5.80 percent. We have found 7.1 percent, 6.9 percent, 5.4 percent.¹

The non-volatile ether extract minimum of 15 percent has been criticized by Dr. A. R. L. Dohme and by W. H. Blome, with the suggestion that it be lowered to 12 percent. If this requirement is designed to exclude capsicums adulterated with foreign material, lacking in ether-soluble constituents, it is all right, but if it is designed to exclude commercial capsicums of inferior pungency, it fails, for Japanese and Indian capsicums of inferior pungency yield, as a rule, higher ether extractives than does African capsicum. As 15 percent is also the standard adopted by the Bureau of Chemistry, U. S. Department of Agriculture, we should dislike to see this standard lowered without a more extended investigation. Our results upon eight samples of known origin are as follows:

2.	Paprika	Rosen paprika	28.53%
7.	Chillies	Japanese, large	20.45%
3.	Capsicum	East Indian, Squibb	20.90%
10.	Capsicum	East Indian	20.35%
17.	Capsicum	Japanese, F. M. & Co	18.50%
12.	Capsicum	African, A. W. & Co., 1912	16.45%
13.	Capsicum	African, L. & F., 1910	17.00%
11.	Capsicum	African, L. & F., 1920	20.40%

W. H. Blome reports 19.5 percent of ether-soluble, non-volatile extractive from one sample of capsicum recently examined; George E. Ewe reports 14.44

¹ Dried at 102° C. for 24 hours.

percent lowest and 15.08 percent highest of four samples of capsicum examined in 1919; Tolman and Mitchell (U. S. Department of Agriculture, *Bulletin* 163) found as follows:

African capsicum... (26 samples)	minimum	14.73%	maximum	19.36%
Japanese capsicum.. (17 samples)	minimum	17.10%	maximum	23.21%
Hungarian paprika.. (7 samples)	minimum	12.21%	maximum	16.43%

Frank M. Boyles (*Jour. Ind. & Eng. Chem.*, vol. 9, p. 301) presents the following data:

Capsicum.	No. of samples.	Total ash.		Aver.
		Max.	Min.	
So. Carolina.....	17	7.75	4.82	5.98
Bombay.....	35	9.35	5.56	6.95
Japanese.....	19	6.84	4.90	6.05
Mombassa.....	7	9.40	4.36	6.08
Korean.....	4	7.70	6.20	
Niger.....	3	6.17	4.27	

Acid Insoluble Ash, in nearly every instance, ran less than 1%, the maximum being 1.77.

Capsicum.	No. of samples.	Non-volatile ether extracts.		Aver.
		Max.	Min.	
So. Carolina.....	17	15.70	10.75	13.92
Bombay.....	35	20.40	12.34	16.47
Japanese.....	5	17.03	12.80	15.56
Mombassa.....	7	25.49	15.75	20.16
Korean.....	2	22.25	19.77	
Niger.....	3	21.96	15.60	

The Scoville organoleptic test has been suggested for incorporation into the Capsicum Monograph. The wording, based on J. M. Francis' statement, might be as follows:

Mix well 1.0 Gm. of powdered Capsicum in 50 Cc. of alcohol, in a stoppered flask, and macerate for 24 hours; dilute 0.1 Cc. of the clear, supernatant liquid with 140 Cc. of distilled water containing 10 percent of sugar; 5 Cc. of this dilution swallowed at once will produce a distinct sensation of pungency and taste of capsicum in the mouth and throat.

An endeavor has been made also to provide a pungent substance of known composition as a standard against which the capsicum could be compared. We have found that pure capsaicin in a dilution of one part in 10,000,000 imparts a pungency equal to the pungency of African capsicum one part in 75,000. As capsaicin is not readily available, piperine might be used as a standard. One part of piperine to 100,000 about equals African capsicum one part in 75,000. Such a test could be worded as follows:

Mix well 1.0 Gm. of powdered Capsicum in 50.0 Cc. of alcohol in a stoppered flask and macerate for 24 hours; dilute 1.0 Cc. of the clear supernatant liquid with 249.0 Cc. of distilled water; one Cc. of this dilution added to 4 Cc. of water containing 12 percent of sugar and swallowed at once will produce a degree of pungency in the mouth and throat not less than the pungency produced by swallowing 5 Cc. of a dilution of one Cc. of a 1 in 100,000 alcoholic solution of capsaicin to 99 Cc. of distilled water containing 10 percent of sugar.

The great objections to these tests are two, *viz.*, the great differences in taste sensibility among individuals, and the fact that taste sensibility is rapidly blunted in most individuals by repeated demands upon it.

The following data are submitted in connection with the taste tests of capsicum

Sample.	Material.	Dilution.	Pungency.
1.	Paprika.....	1-25,000	distinct
	Paprika.....	1-50,000	very slight
8.	Capsicum, East Indies..	1-50,000	plainly perceptible
3.	Capsicum, East Indies ¹ ..	1-75,000	very decided
15.	Capsicum, Japanese.....	1-50,000	plainly perceptible
16.	Capsicum, Japanese.....	1-50,000	plainly perceptible
11.	Capsicum, West African.	1-50,000	hot
	Capsicum, West African.	1-75,000	decided
12.	Capsicum, Zanzibar.....	1-75,000	decided
13.	Capsicum, Mombassa...	1-75,000	decided
	Piperine, Merck.....	1-50,000	hot
	Piperine, Merck.....	1-100,000	decided
	Capsaicin ²	1-1,000,000	very pungent, burning
	Capsaicin ²	1-10,000,000	decided

THE ASSAY OF ACONITE.

BY A. R. L. DOHME.*

The work covered by this paper represents what has been done during the past three years by the Scientific Section of the American Drug Manufacturers' Association who have felt that its results should be made known to the medical and pharmaceutical professions generally.

The primary problem was to attempt to decide whether the chemical assay of aconite and its preparations had any real value, and the resultant problem was to determine if the physiological assay was accurate and trustworthy. The present official assay process U. S. P. IX Revision is a chemical one with an alternative physiological assay, but the chemical assay is the standard. In the U. S. P. VIII there was only a chemical assay as the official process. In both cases the end-product was represented by ether-soluble alkaloids. We have shown that ether-soluble alkaloids are not all aconitine but represent a more or less variable proportion of aconitine and its products of hydrolysis benzoyl-aconine and aconine. This variability alone makes the assay process of little value as an absolute standard of therapeutic efficiency and, as well, makes its relative or comparative value more or less of an uncertain quantity.

In order to determine definitely if the three alkaloids which constitute the ether-soluble alkaloids—aconitine, benzoyl-aconine and aconine—could be separated from one another by chemical means a supply of pure aconitine was procured and hydrolyzed into benzoyl-aconine and some of the latter hydrolyzed further into aconine. After thus converting a number of grammes in this way and obtaining

¹ Squibb's powdered, purchased 1918, labelled: "the dried ripe fruit of *capsicum fastigiatum*; the genuine East Indian variety, * * *"; histologically this presents the characteristic epidermis of African capsicum.

² Sample furnished by Dr. Arno Viehoever of the Bureau of Chemistry, U. S. Department of Agriculture, University of Illinois School of Pharmacy.

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