

It is a noteworthy coincidence that Dr. Bertha Van Hoosen of Chicago has been treating cancer with emetin hydrochloride with remarkable success, using this remedy on the assumption that cancer is caused by amebae. Although in error in her assumption, the treatment is nevertheless entirely rational. Emetine is our best amebicide and by destroying the amebal host the sexual cycle of the cancer plasmodium is likewise destroyed and the cancerous growth is as a result completely checked. Nor is emetine the only likely cure for cancer. There are other amebicides worthy of a trial, some that are less toxic than emetine, as acriflavin, amargosin (experiments with this drug are now under way), thiophen, berberin, and even arsphenamin and quinine sulphate. Dr. Abrams of San Francisco claims that cancer can be cured by means of carefully adjusted X-ray emanations or vibrations, the effects produced being closely similar to the effects following the use of large doses of emetin hydrochloride, and he cites numerous cases to substantiate his claim.

To some up briefly, the indications are that cancer is of parasitic origin and that it can be cured without the use of the knife. Experiments are now under way to find a test which will make it possible to ascertain the existence of cancer in its early stages so that the cure may be applied early. Such a test is of the greatest importance, for if the remedy is not administered until the disease is well advanced, fatal toxemias often follow due to the resorption of the great mass of dead cancer tissue. Apparently cancer may be as easily cured and controlled as malaria, as yellow fever, and as syphilis. Perhaps the greatest existing obstacle in the way of an early control of cancer are the surgeons.

UNIVERSITY OF NEBRASKA,  
COLLEGE OF PHARMACY,  
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### ALKALOIDS IN RHIZOMES AND ROOTS OF IPECAC.\*

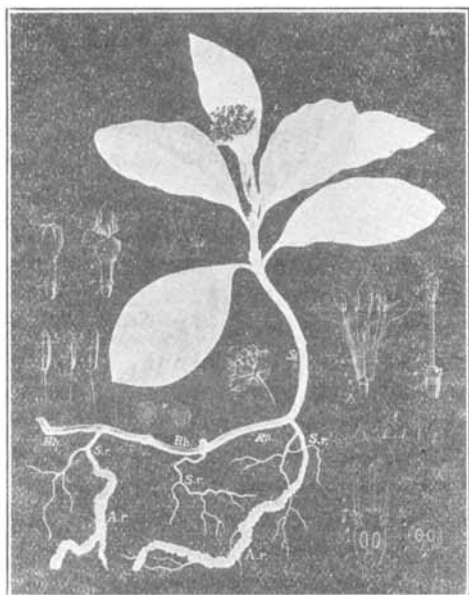
BY ARNO VIEHOEVER AND CLARE OLIN EWING.

Ipecac is a low, straggling, soft-wooded shrub growing in rich forest loam, the base of the stem partly prostrate and more or less covered with vegetable debris. This habit of growth results in a sharp distinction between the lower and upper portions of the stem, the lower portion being quite largely collected with the roots.<sup>1</sup> It is owing to this circumstance, no doubt, that the United States Pharmacopoeia VIII defined ipecac as "the dried root to which may be attached a portion of the stem, not exceeding 7 cm. in length, \* \* \*." Lots complying with this definition might contain as high as 25 percent of stems. The present Pharmacopoeia, however, limits the "stems and other foreign matter" to 5 percent.

A study of the habit of growth of the plant (see illustration) suggests that the lower portion of the axis really represents the rhizome from which the root system branches out. Inasmuch as plants with alkaloids usually contain them in the rhizomes (if these are present) as well as in the roots, one might expect

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<sup>1</sup> H. H. Rusby, *Nat. Stand. Disp.* (1916), p. 866.



Flowering Plant. A.r.—Annulated roots; S.r.—Smooth roots; Rh.—Rhizome; St.—Over-ground stem.

(From Berg, O. C., and Schmidt, C. F. "Atlas der Officiellen Pflanzen," 2nd. Ed. 1891-1902, pl. 15.)

alkaloids: also in the rhizomes of ipecac. As mentioned, the Pharmacopoeia (9th revision) does not permit the presence of more than 5 percent of rhizomes; from the description it is also evident that none of the smooth roots, more or less abundant in the root system of ipecac, are considered desirable as a drug.

From an economical standpoint, as well as from one of interest in the improvement of pharmacopoeial drugs, it seemed interesting to establish the justification for the practical elimination of portions of the ipecac plant representing in a broad sense a normal part of the root system.

As long ago as 1895, Dohme<sup>1</sup> reported analyses of two lots of "commercial ipecac" indicating that the rhizomes ("stems") and smooth roots ("merging portion") contain large amounts of alkaloids, the actual analyses being as follows:

TABLE I.—DISTRIBUTION OF ALKALOID.

Sample.	Alkaloid in root.	Alkaloid in "merging portion."**	Alkaloid in "stems."
A.....	2.0 %	2.13%	1.77%
B.....	2.33%	2.43%	2.15%

\* The usually twisted and slightly annulated portion connecting the smooth "stem" and the distinctly annulated root.

Dr. Dohme, in a private communication, states that one of the samples was Rio and the other Cartagena ipecac. We cannot be certain whether, as assumed, the "stem" consisted entirely of rhizomes and the "merging portion" of smooth roots.

We have examined one sample of "stemmy Rio Ipecac" and one of "stemmy Cartagena Ipecac," both separated into annulated roots, smooth roots, and rhizomes for the amounts of the soluble alkaloids present. The results of the analyses, carried out by Ruth G. Capen, in this laboratory, are given below:

TABLE II.—ALKALOIDAL CONTENT OF IPECAC ROOTS AND RHIZOMES.

Sample.	Annulated roots.	Smooth roots.	Rhizomes.
Rio Ipecac.....	1.94%	2.00%	1.60%
Cartagena Ipecac.....	1.88%	1.05%	1.05%

<sup>1</sup> A. R. L. Dohme, "The Alkaloidal Value of Ipecac Stems," *Amer. J. Pharm.*, 67, 533, 1895.

No other samples of "stemmy ipecac" being available at this time for similar separations and examination, data ascertained in the Bureau as well as given in the literature on the alkaloidal content of "stems" in contrast to roots of ipecac may be of interest:

Table III.—ALKALOIDAL CONTENT OF IPECAC ROOTS AND "STEMS."

Sample.	Variety.	Alkaloid in "stems."	Alkaloid in roots.	Analyst.*	Remarks.
1.....	Rio	1.80	2.01	Paul and Cownley <sup>1</sup>	
2.....	Rio	1.84	3.75	Grant and Zufall	
3.....	Cartagena	2.46	2.36	Grant and Zufall	
4.....	Rio	1.72	....	Luther and Zufall	Whole sample (1.82)
5.....	Rio	1.6	2.13	Zufall and others	
6.....	Cartagena	1.22	2.03	Zufall and others	

\* Analyses, with the exception of the first sample, made in the New York Food and Drug Inspection Laboratory, Bureau of Chemistry.

<sup>1</sup> Paul and Cownley, *Pharm. Journ.*, 69, 256, 1902.

These analyses show the variation of alkaloids in roots as well as in the rhizomes. In four other analyses the amount in the stems was as low as 0.58 or 0.6 percent, respectively, or as high as 2.01 or 2.1 percent, respectively, the one yielding 0.6 percent being Rio, the others not being designated.

It is thus evident that in both Rio and Cartagena ipecac the amount of alkaloids varies greatly in both the roots and rhizomes.

Of special interest in this connection is Table IV, showing the amounts of alkaloids found in samples of ipecac containing various portions of these "stems."

TABLE IV.—PERCENT OF ETHER-SOLUBLE ALKALOIDS IN IPECAC CONTAINING VARYING AMOUNTS OF "STEMS."

Sample.	Variety.	"Stems," %.	Ether soluble alkaloids, %.	Analyst.*
1.....	Cartagena	10	2.16	J. B. Luther
2.....	Cartagena	12	2.05	S. Ginsburg
3.....	Cartagena	13	2.34	E. H. Grant
4.....	Cartagena	13	1.93	S. Ginsburg
5.....	Cartagena	16	1.92	J. B. Luther
6.....	Cartagena	16	2.92	S. Ginsburg
7.....	Cartagena	19	1.78	J. F. Darling
8.....	Cartagena	25	1.97	S. Ginsburg
9.....	Cartagena	25	2.11	S. Ginsburg

\* Chemical determinations made in the New York Food and Drug Inspection Laboratory, Bureau of Chemistry. Amount of "stems" determined by C. J. Zufall.

In spite of the varying amounts of "stems" present, in no case is the alkaloidal content lower than the standard of 1.75 percent required, suggesting that either the "stems" did not decrease the amount, or lowered it only slightly.

As pointed out above, if stems were generally attached to an extent of 7 cm. in length, their amount would approximate 25 percent.

An objection to the admission of rhizomes may be raised on the basis that the alkaloids in the rhizomes are apt to be present in different proportions than in the roots. It may further be pointed out that as a possible consequence discordant clinical results might be obtained following the use of ipecac containing

varying amounts of stems. That such difference in composition actually exists has been pointed out by Paul and Cownley<sup>1</sup> for Rio ipecac.

TABLE V.—NATURE AND DISTRIBUTION OF ALKALOIDAL CONSTITUENTS IN RIO IPECAC.

	Alkaloid in root, %.	Distribution of alkaloid, %.	Alkaloid in stem, %.	Distribution of alkaloid, %.
Emetine.....	1.45	72.14	1.18	65.6
Cephaeline.....	0.52	25.87	0.59	32.8
Third base.....	0.04	1.99	0.03	1.6
Total.....	2.01	100.00	1.80	100.0

This difference in alkaloidal ratio, however, is by no means as marked as that which has been observed in the composition of the two commercial varieties, Rio and Cartagena:

TABLE VI.—AMOUNT AND COMPOSITION OF ALKALOIDS IN RIO AND CARTAGENA IPECAC.

	Alkaloid in Rio, <sup>1</sup> %.	Alkaloid in Rio			Alkaloid in Cartagena.		
		Minas. a.	Matto Grosso. <sup>2</sup> b.	%.	a. <sup>1</sup> %.	b. <sup>2</sup> %.	c. <sup>2</sup> %.
Emetine.....	1.45	1.31	1.00	1.62	0.89	0.61	1.13
Cephaeline.....	0.52	0.60	0.62	0.52	1.25	0.74	0.81
Psychotrine.....	0.04	0.06	0.05	0.06	0.06	0.05	0.06
Ipecamine and Hydroipecamine.....	.....	0.53	0.36	0.53	.....	0.22	0.32
Total.....	2.01	2.50	2.03	2.73	2.20	1.66*	2.32

\* This total, taken from original article, should probably be 1.62.

<sup>1</sup> Paul and Cownley, *Pharm. Journ.*, 4, 2 (1896), 321.

<sup>2</sup> O. Hesse, Liebig's *Annalen der Chemie*, 405, 54, 1914.

In fact, on the basis of the structural, and especially the chemical difference in composition, Rusby<sup>2</sup> suggests that Rio and Cartagena ipecac should be distinctly separated in the definition and description of ipecac. From the data given above it appears that Cartagena ipecac usually has less emetine and more cephaeline than Rio ipecac. However, the analyses should be far more numerous to permit of a definite conclusion. It would especially be highly desirable to have more comparative data on the chemical composition of roots and rhizomes of both Rio and Cartagena ipecac.

#### CONCLUSIONS.

The fact, as shown above, that the rhizomes generally contain the ether-soluble alkaloids of ipecac in substantial, if not comparatively large amounts, in our opinion justifies the suggestion that these rhizomes be not eliminated from the drug, but that they be admitted as part of the official drug, provided that the alkaloidal standard is not lowered thereby.

CONTRIBUTION FROM THE PHARMACOGNOSY LABORATORY,  
BUREAU OF CHEMISTRY,  
DEPARTMENT OF AGRICULTURE.

<sup>1</sup> B. H. Paul and A. J. Cownley, *Pharm. Journ.*, 56, 321, 1896.

<sup>2</sup> H. H. Rusby, "A definition of Ipecac as proposed for the New Pharmacopoeia," *The Druggists' Circular*, 60, 202, 1916.