	·									
Storage										
Tem-					-Weeks of	Storage		·····		
perature	0	1	2	3	4	5	6	7	12	15
5°	129	129	101	118		109	91	114	104	99
25°	1 23	• • •	86	80	81	69	66	59	• • •	••

REFERENCES

Johnson, Balbina A., Anker, Herbert, and Meleney Frank L., Science, 102, 376(1945).
 Hoff, Donald A., Bennett, Ralph E., and Stanley, Alfred R., *ibid.*, 106, 551(1947).

(3) Bond, Glenn C., and Nook, Mary Ann, *ibid.*, 107, 228 (1948).
(4) Food and Drug Administration Bulletin, Tentative Specification for Bacitracin, December 17, 1947.

A Comparative Pharmacognostical Study of Plantago Purshii R. & S. and Plantago aristata Michx. Seeds with the Present N. F. VIII Plantago Seeds*

By ARNOLD C. NEVA[†] and E. B. FISCHER[†]

A pharmacognostic study of the seeds of two domestic species of Plantago is reported. The individual morphological and histological characteristics of the two species have been described. The mucilage-forming capacity of the seeds of *Plantago Purshii* and of *P*. aristata has been determined and the results are recorded.

PART I. DESCRIPTIVE PHARMACOGNOSY

THE FOLLOWING investigation was undertaken to establish a potential domestic source of supply of psyllium seed. The seeds examined pharmacognostically in this study, and compared to those now officially recognized in the present National Formulary VIII, were derived from Plantago Purshii R. & S. and Plantago aristata Michx. In addition to a morphological and histological analysis of the seeds, a comparative evaluation of the mucilage forming capacity of each was made.

A comprehensive review of the literature failed to reveal any previous pharmacognostical studies upon the seeds of the above two species of Plantago named. In contrast, the seeds recognized as official sources in the National Formulary VIII, as well as others used commercially, have been adequately studied and described by Montague (1), Youngken (2), and Skyrme (3, 4).

The seeds of Plantago Purshii R. & S. and Plantago aristata Michx. used in this study were obtained from plants authenticated by members of the Botany Department, University of Minnesota.1

EXPERIMENTAL

Microtechnique Methods Employed .- Considerable difficulty was experienced in making suitable histological sections of the seeds. The difficulty. arose from the fact that the ordinary methods of microtechnique if employed would render impossible the pharmacognostic study of the outer mucilage layer of the seeds desired in this presentation. For this reason double embedding procedures recommended by Johansen (5) and Sass (6) were applied with special adaptations to the problem.

Representative mature fruits containing the seeds were selected and placed in a formalin-aceto-alcohol solution in which the water concentration was reduced to less than 20%. The conventional celloidin method was then employed after bringing the fruits through 95% alcohol, absolute alcohol, and an ether-methyl alcohol mixture. After hardening the celloidin with chloroform, blocks were cut enclosing suitable oriented fruits. These blocks of celloidin

^{*} Abstracted from a thesis submitted to the Graduate Faculty of the University of Minnesota by Arnold C. Neva in partial fulfillment of the requirements for the degree of Doc-tor of Philosophy. Special acknowledgment is given to the American Foundation for Pharmaceutical Education under whose Fellowship grant this work was completed. † Present address: College of Pharmacy, University of Washington, Seattle, Wash. ‡ Professor of Pharmacognosy, College of Pharmacy, University of Minnesota, Minneapolis.

¹ The seeds of the official Plantago species also used in this study were generously supplied by Heber W. Youngken, Sr.

enclosing the fruits were then subjected to the conventional paraffin method and the resulting paraffin blocks were sectioned on a rotary microtome. Ordinarily, the paraffin ribbons of sectioned material are placed in tepid water to allow a spreading of the individual sections. This particular step in the usual paraffin methods was prohibitive since the outer mucilage layer of the seeds would form a swollen undifferentiated mucilaginous film upon contact with water. Instead, the individual sections were placed upon the slides previously treated with Mayer's albumin fixative (7). Then a few drops of xylol were added and the slide was gently heated to allow partial dissolving of the paraffin and spreading of the individual sections. After this the slides were placed in an oven for two hours at a temperature of 52°. At the end of this time they were removed and allowed to dry thoroughly for several days.

In staining, the slides were first placed in a xylolabsolute alcohol solution until the paraffin was removed and only the section in a celloidin matrix remained fixed to the slide. The slides were next transferred to a methyl alcohol-ether solution long enough to remove the celloidin matrix. One-half to one minute was generally required to accomplish this and care was exercised at this point to avoid the loss of the sections from the slide. Following these preliminary steps, the slides were then passed successively through 95% alcohol, the alcoholic staining solutions of 1% safranin and 1% fast green, absolute alcohol, and finally into xylol. The sections were mounted in Clarite X².

DESCRIPTION OF PLANTAGO PURSHII R. & S. SEEDS

External Morphology.—The seeds of *Plantago Purshii* R. & S. vary in length from 2 to 2.25 mm. and in width from 0.75 to 1.25 mm. They are typically boat-shaped concavo-convex bodies, with one end of the seed rounded and the other end more obtuse than rounded. The seeds are rough to the touch and when viewed under low magnification of from 5 to $10 \times$ present a pebbled appearance.

At the mid-section of the seed or a little toward the obtuse end a groove running transversely over the dorsal surface indicates the circumscissile region of the capsular fruit dehiscence. The seed, when viewed from the ventral side, exhibits a deeply furrowed condition that is more or less complete over the entire ventral surface so that a relatively uniform flattened ridge is present around the entire outer margin of the seed.

The color of the seeds when examined from the dorsal surface is light brown over most of the top portion of the seed but appears a darker brown around the seed margin. When the seed is viewed from the ventral surface, on the other hand, the peripheral ridge around the seed margin is of a uniform light brown color but the furrowed concave surface, except the region around the hilum, is covered with a white scaly outer epidermal layer. This white scaly outer epidermal layer is absent also in the immediate region on either side of the hilum. The whitish appearance of the outer epidermal layer on the ventral surface and not on the dorsal surface is due to the fact that on the former this layer does not adhere closely to the pigment layer underneath and for this reason the transparent quality of the outer epidermal layer becomes apparent. The weight per hundred seeds of *Plantago Purshii* R. & S. ranged from 0.072 Gm. to 0.084 Gm. in the over-all consideration of both selected and random picked seeds.

Histology of the Seeds.—Cross, radial, and tangential serial sections of the seeds of *Plantago Purshii* R. & S. were made. The sections so prepared were observed under low (Part A, Fig. 1) and high power fields, oil immersion fields, and also under polarized light.

Embryo.—The embryo in the seeds of *Plantago Purshii* R. & S. is a straight cylindrical structure in the center of the seed composed of the radicle and two long cotyledons. The radicle, found toward the more rounded end of the seed, is a spheroid body made up of a central stellar region surrounded by compact, polygonal, thin-walled, parenchyma cells. The two cotyledons are triangular bodies with somewhat rounded angles composed of compact parenchyma cells with three procambial strands.

Endosperm.—The endosperm forms the general shape and size of the seed. The endosperm cells, varying from 20 to 50 μ in their widest diameter, are irregular to elongate in shape and possess smooth nonpitted walls quite uniformly 1 μ in thickness.

Pigment Layer .-- Forming the outside margin around the entire endosperm and completely adherent to it is a single layer of flattened and tangentially elongated, wavy, thin-walled cells containing pigment substances of indefinite size and shape. The cells vary from 4 to 8 μ in width and the two radial walls are concave and convex, respectively. Each adjacent cell in the single layer possesses oppositely concave and convex radial walls so that all the cells lying in a single layer present a "tongueand-groove" effect. In contrast to the dorsal surface, the cells of the pigment layer making up the ventral margin surface in certain areas assume a spheroidal shape with straight radial walls and the characteristic effect described above is abolished. The cells in these regions are also larger in the radial direction measuring usually 14 to 16 μ in width although the tangential direction correspondingly becomes shortened with some cells measuring only 4 to 6 μ in length.

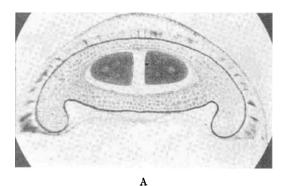
Outer Epidermis.—Surrounding the pigment layer and strongly adherent to it around most of the seed is found the outer epidermal layer.

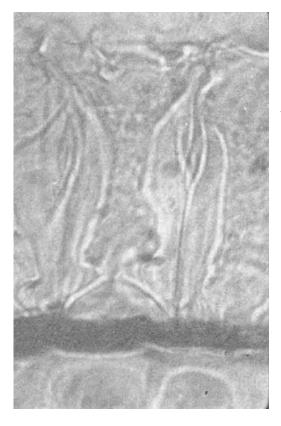
An examination of the outer epidermal layer on the dorsal surface of the mature seed (Part B, Fig. 1) reveals that it is made up of a single layer of colorless cells, rectangular in shape, longer in the radial direction than in the tangential, measuring from 40 to 70 μ in the former and from 20 to 50 μ in the latter direction. When studied in surface view on the dorsal side of the seed these cells are polygonal in outline with from 4 to 8 unequal straight to curved walls and measure from 30 to 80 μ in the longest diagonal.

During the ripening of the seed these outer epidermal cells undergo structural modifications. In the young fruit the outer epidermal cells are all thin walled with a cell lumen containing numerous starch

² Clarite X is a commercial product composed of 70% synthetic resin in toluene supplied by the Neville Co. of Pittsburgh, Pa.

grains as evidenced by iodine T. S. and polarized light studies. In the course of seed ripening, the starch grains within the cell lumen gradually disappear and a mucilaginous deposit is laid down upon the radial walls and to a certain degree upon the inner tangential surface of the outer epidermal cells. In the mature seed the original epidermal cell lumen is greatly decreased in size and assumes





a modified panduriform shape, broadly obovate toward the tangential cell surfaces with concavities on either side along the radial walls.

The mucilaginous deposit laid down is not homogenous in nature but is stratified into distinct lamellate regions that are laid down thickest in the central part of the cell along the radial walls, thus giving the remaining cell lumen its characteristic shape described above. The mucilage lamellae, varying in number from 4 to 8 and measuring from 1 to 2 μ at their widest portion in the innermost lamellae to from 4 to 6 μ in the most peripheral lamellae, are convex in shape and converge toward both the outer and inner tangential cell surfaces. Toward the outer tangential surface the mucilage lamellae, along both radial walls, merge and form only a thin strip of mucilaginous deposit so that the cell lumen reaches nearly between the radial walls and has a cross-section diameter between 35 and 40 μ . In the center of the cell the radial mucilage lamellae attain their thickest deposit and measure in total width from 8 to 20 μ on either side. This reduces the width of the original cell lumen to from 5 to 16 μ . Toward the inner tangential surface of the epidermal cells, on the other hand, the mucilage lamellae do not merge into a single thin strip but retain their individual narrowed lamellate structure and curve sharply toward the cell interior on either side and then back again toward the inner tangential surface after coming together or nearly so. Thus, in most of the cells the lumen is separated completely from the inner tangential surface by a distance of from 6 to 14 μ of mucilage deposit or at most all that remains of the lumen is a narrow cone approximately 1 to 4 μ at its apex.

Toward the ventral surface in the region where the endosperm folds over to form two arms curving toward the center of the seed, the outer epidermal cells are found to be more elongated in the radial direction and vary in measurement from 100 to 120μ in length to from 40 to 55 μ in width.

On the ventral surface of the seed the outer epidermal layer comes up to the hilum on either side but does not cover the hilum itself. The cells in this region are very similar to those described on the dorsal surface of the seed both as to size and structure. Many of the cells are seen to possess distinct simple, round starch grains measuring from 1 to 3 μ in diameter within the cell lumen. In the region where the endosperm curves back toward the center of the seed on either side, the outer epidermal layer becomes detached from the pigment layer surrounding the endosperm and passes directly to the ventral surface of the seed, thus leaving a large intercellular area between the pigment layer and the outer epidermal layer. It is for this reason that the seed presents a whitish appearance when viewed from the ventral surface since the coloration of the pigment layer is not visible directly underneath the detached outer epidermis.

Fig. 1.—Cross and radial sections of *Plantago Purshii* R. & S. *A*, cross section of *P*. *Purshii* R. & S. seed showing cotyledons, endosperm, pigment layer, and outer mucilage cells $\times 70$. *B*, radial view of the outer mucilage cells of *P*. *Purshii* R. & S. $\times 1330$.

DESCRIPTION OF PLANTAGO ARISTATA MICHX. SEEDS

External Morphology.—The seeds of *Plantago* aristata Michx. in general resemble those of *Plantago*

Purshii R. & S. The noticeable difference occurs mostly in the size of the respective seeds. The seeds of the former species are larger, measuring in length from 2.50 to 3.25 mm. and in width from 1 to 1.75 mm. The seeds of this species are also typically boat-shaped or concavo-convex bodies. The dorsal side of the seed is convex in outline and the ventral side is deeply furrowed. In contrast to the seeds of *Plantago Purshii* R. & S., in which a majority are conspicuously rounded on one end and more obtuse than rounded on the other, a majority of the seeds in this species are obtuse on both ends.

The seeds are light brown in color on the dorsal surface and a darker brown around the seed periphery. When examined from the ventral surface, the central portion of the seed is deeply furrowed and a peripheral ridge makes up the seed margin. This peripheral ridge and the region around the hilum are of a uniform light brown color. Between the two regions of the furrowed concave surface, the white scaly outer epidermal layer is visible. The white outer epidermal layer is also visible in the area immediately around the hilum. The range of weight per hundred seeds for both seeds picked at random and for selected seeds was from 0.138 Gm. to 0.179 Gm.

Histology of the Seeds.—The seeds of *Plantago* aristata Michx. were prepared in cross, radial, and tangential sections. In each of the foregoing, the material was cut in serial sections to fully describe the entire seed anatomy and all sections were observed under low and high power fields, oil immersion fields, and also under polarized light.

Embryo.—The radicle and cotyledons of the embryo in the seeds of *Plantago aristata* Michx. are in all respects very similar to those found in the seeds of *Plantago Purshii* R. & S. A cross section of the *Plantago aristata* Michx. (Part A, Fig. 2) shows that the cotyledons are somewhat larger and less triangular in appearance.

Endosperm.—The cells making up the endosperm of the seeds of *Plantago aristata* Michx. very closely approximate those of *Plantago Purshii* R. & S. as to shape and size. The general shape of the endosperm in *Plantago aristata* Michx. seeds differs from that of the seeds of *Plantago Purshii* R. & S. in that the ventral endosperm arms in the former seeds do not fold over toward the center as markedly as in the latter.

Pigment Layer .-- The cells making up the pigment layer when viewed in cross and tangential sections lie in a single layer around the entire endosperm. The cells, containing the coloring matter in the form of numerous spheroidal bodies from 1 to 2 μ in diameter, are somewhat flattened and elongated and vary in radial thickness from 4 to 12 μ and in tangential length from 10 to 50 μ . The radial walls of these cells are straighter than those described previously in the seeds of Plantago Purshii R. & S. and for this reason the "tongue-and-groove" effect previously mentioned is conspicuously absent. Finally, the cells of the pigment layer in certain regions of the ventral surface do not undergo the greater thickening in the radial direction that is found in the seeds of Plantago Purshii R. & S.

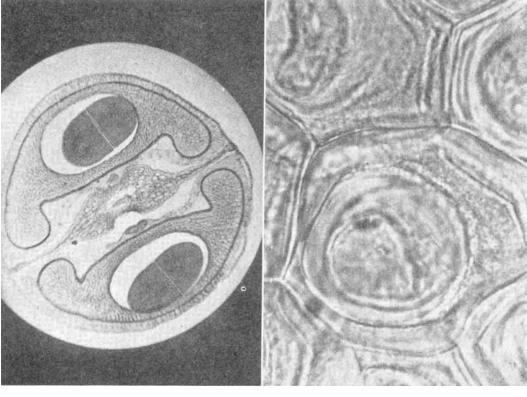
Outer Epidermis.—The cells of the outer epidermal layer are structurally similar to those described under *Plantago Purshii* R. & S. In cross section, the cells of the dorsal surface are rectangular in shape and in contrast to the cells of the outer epidermal layer of the previously described species tend to be longer in the tangential direction than the radial. In actual measurement the cells vary from 40 to 80 μ tangentially to from 40 to 60 μ radially.

When the outer epidermal cells of the dorsal surface are studied in a surface view (Part B, Fig. 2), they are seen to be polygonal in shape with from 4 to 8 straight to curved unequal walls and measure from 30 to 100 μ in their longest diagonal.

The characteristic modifications of cell structure previously mentioned in the discussion of the outer epidermal cells of Plantago Purshii R. & S. are also encountered in the outer epidermal cells of Plantago aristata Michx. In the mature seed the original large cell lumen of the thin-walled outer epidermal cells has been greatly reduced in size and now possesses a modified panduriform shape with broadened inner and outer truncate surfaces and a narrower central connecting lumen region. This modification of the cell lumen has been brought about, as in the epidermal cells of Plantago Purshii R. & S., by the accumulation of a mucilaginous deposit along the radial walls toward the inside of the cell. This mucilage deposit is laid down in a lamellate fashion and in the outer epidermal cells of Plantago aristata Michx. the number of mucilage lamellae vary from 6 to 12 and measure quite uniformly 1 μ in width in the region of thickest deposition. The convex lamellae converge toward both the inner and outer tangential surfaces. In the outer epidermal cells further, there is no pronounced deposition of mucilage along the inner tangential surface so that in most cases the broad inner cell lumen portion lies in close proximity to the inner tangential cell surface. It is not unusual, however, to find cells which possess a deposit of mucilage along the inner tangential cell surface measuring between 10 to 12μ . In the center of the cell the radial mucilage lamellae attain their thickest deposit and measure from 10 to 30 μ in total width on either side. This reduces the width of the original cell lumen to from 10 to 20 μ .

When examined in cross section, the outer mucilage cells toward the ventral surface on either vertical edge of the seed are seen to be elongated radially and measure from 100 to 130 μ in that direction. The cells conform structurally to the same shape as those described on the dorsal surface with the exception that the radial walls become curved and spread out and thus make the cell wider at the outer tangential surface. Obviously, the narrower central lumen becomes elongated under these conditions. The lamellate structure is discernible in the region on either side of the central portion of the cell lumen but the mucilaginous deposit in the peripheral areas along the radial walls presents a homogenous granular appearance when stained with safranine in contrast to the hyaline transparent nature of the lamellate region.

The cells of the outer epidermal layer on the ventral surface, covering the entire surface except the hilum itself, are very similar to those found on the dorsal surface. The outer epidermal layer also becomes detached from the pigment layer surrounding the endosperm in the region of the ventral arms and many of the cells in this detached region of the outer epidermal layer are seen to possess small starch grains approximately 1 μ in diameter within the remaining lumen of the cell.



Α

в

Fig. 2.—Cross sections of *Plantago aristata* Michx. A, cross-section view of *P. aristata* Michx. fruit showing two seeds ×48. B, cross-section view of the outer mucilage cells of *P. aristata* Michx. ×1200.

DESCRIPTION OF THE SEEDS OF P. LANCEO-LATA L., P. OVATA FORSK., P. PSYLLIUM L., AND P. ARENARIA L.

Since the morphological and histological features of the seeds official in the N. F. VIII and also those of P. lanceolata L. have been adequately covered in previous works, the reiteration of this information does not seem necessary at this time.

The outer epidermal layer of these seeds in comparison to the outer epidermal layers of the seeds of *Plantago Purshii* R. & S. and *Plantago aristata* Michx. show differences in structure which are readily discernible (Fig. 3) and it is clearly evident that the seeds of *P. Psyllium L., P. indica L., and P. lanceolata L. possess an outer epidermal layer that* is composed of a rather narrow zone of tangentially elongated mucilage cells completely filled with a mucilaginous deposit. The outer epidermal layer in the seeds of *P. ovata* Forsk. is made up of cells that are radially elongated with a larger outermost portion and a narrowed basal portion which frequently contains a cone of starch grains. The remainder of the cell contains the mucilaginous deposit. Table I shows the comparative weights and sizes of all seeds tested.

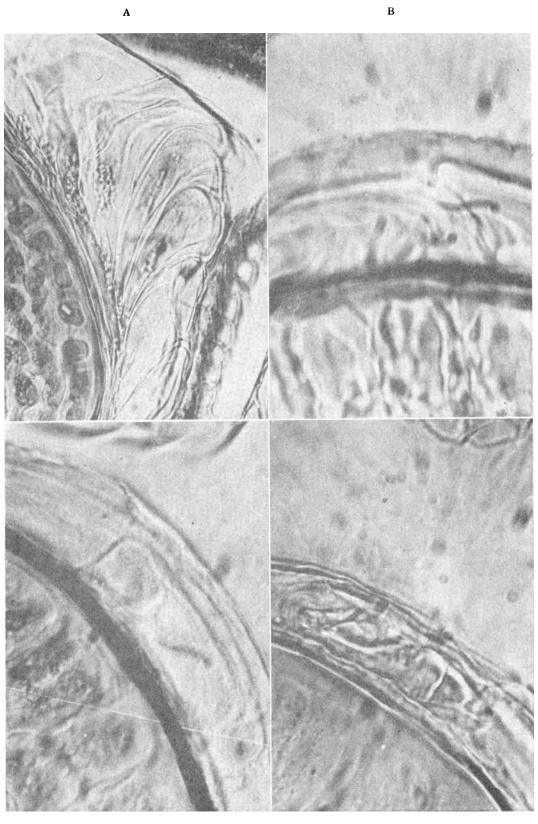
PART II. DETERMINATIVE PHARMACOG-NOSY

The comparative mucilage determinations, on the basis of the current N. F. VIII method of testing, were carried out in order to evaluate the mucilage forming capacity of the seeds of *Plantago Purshii* R. & S. and *Plantago aristata* Michx. in comparison to the current official species of *Plantago*. The values submitted on the basis of the present N. F. test are intended to serve simply as qualitative determinations to point out the comparative mucilageforming capacities of the various species of *Plantago* seed considered in this study.

The total and acid-insoluble ash determinations were likewise carried out for the seeds of *Plantago Purshii* R. & S. and *Plantago aristata* Michx. in order to compare the results with the minimum ash limits specified in the N. F. VIII monograph on Plantago Seed.

Mucilage Determinations .-- Mucilage determina-

Fig. 3.—A, outer mucilage layer of the seed of P. ovata Forsk. in radial view $\times 1180$. B, outer mucilage layer of the seed of P. Psyllium L. in radial view $\times 1180$. C, outer mucilage layer of the seed of P. indica L. (P. arenaria W. & S.) in radial view $\times 1500$. D, outer mucilage layer of the seed of P. lanceolata L. in radial view $\times 1180$.



D

tions were made according to the official N. F. VIII method of testing (8). The results are summarized in Table II.

Ash Determinations .-- Ash determinations, employing powdered seed of a No. 30 fineness, were made according to the official N. F. VIII methods. The values obtained are recorded in Table III.

SUMMARY

A pharmacognostic study has been made of the seeds of two domestic Plantago species. The individual morphological and histological characteristics of the seeds of these two species have been described and the following facts have been observed:

1. The use of the double embedding procedure has been outlined which proved satisfactory in the preparation of microscopic slides of material containing mucilaginous tissues.

The weight and size of the seeds of Plan-2. tago Purshii R. & S. and Plantago aristata Michx. have been determined in comparison to the seeds of those Plantago species official in the N. F. VIII.

The total ash and acid-insoluble ash values 3. for the seeds of Plantago Purshii R. & S. and Plantago aristata Michx. have been determined and found to be within the ash limits specified in the N. F. VIII for those species which are official.

The mucilage forming capacity of the seeds of Plantago Purshii R. & S. and Plantago aristata Michx. has been determined and the following results have been obtained:

The seeds of Plantago Purshii R. & S., forming an average volume of 11.0 cc. on the basis of the official N. F. Test equivalent to a value of 55.0 per cent, possess a mucilage forming capacity slightly greater than do the seeds of *Plantago* ovata Forsk. which had an average volume of 10.9 cc. equivalent to a value of 54.5 per cent.

TABLE I.--COMPARATIVE WEIGHTS AND SIZES OF SEEDS TESTED

Species	Wt. of 100 Seeds, ^a Gm.	Length of Seeds, Mm.	Width of Seeds, b Mm.
P. Purshii	0.072 - 0.084	2.0 - 2.2	0.75 - 1.25
P. aristata	0.138 - 0.179	2.5 - 3.25	1.00 - 1.75
P. lanceolata	0.138-0.181	2.0 - 3.00	1.00 - 1.50
P. ovata	0.186 - 0.195	2.5 - 3.25	1.25 - 1.75
P. Psyllium	0.073-0.090	2.0 - 2.75	1.00 - 1.25
P. indica	0.133-0.161	2.25 - 3.00	1.00 - 1.50

^a 10 determinations made on selected and random picked seeds of each species.
 ^b 50 determinations made on selected and random picked seeds of each species.

Material tested	Wt., Gm.	Detns.	Final Reading (Av. Volume), Cc.	Mucilage Vol., %
P. Purshii	30	30	11.0	55.0
P. aristata	30	30	14.4	72.0
P. ovata	30	30	10,9	54.5
P. lanceolata	30	30	4.9	24.5
P. indica ^a	6	6	14,3	70.0
P. Psyllium ^a Coml. Psyllium (P. indica and P.	6	6	19.2	95.8
Psyllium)	30	30	16.9	83.0
Total	162 Gm.	162		

TABLE II.-COMPARATIVE VALUES OF SEEDS TESTED

" Limited material available.

TABLE IIIASH	DETERMINATIONS
--------------	----------------

Seed	Wt. of seed Used, ^a Gm.	Total ash (Av. Wt., Gm.)	Total Ash (Av. %)	Acid- insoluble Ash (Av. Wt. Gm.)	Acid- insoluble Ash (Av. %)
P. Purshii	4.00	0.153	3.83	0.022	0.560
P. aristata	4.00	0.140	3.50	0.003	0.084
P. ovata	4.00	0.112	2.82	0.008	0.210
P. lanceolata Coml. Psyllium ^b (P. indica	4.00	0.092	2.32	0.002	0.048
and P. Psyllium) ^b	4.00	0.123	3.09	0.002	0.048

^a Three determinations made of each species. ^b The ash determinations were made on a commercial product called French Psyllium which is a mixture of the seeds of the two species given.

The seeds of *Plantago aristata* Michx. possess even a greater mucilage forming capacity on the basis of the official N. F. VIII test with an average volume of 14.4 cc. equivalent to a value of 72.0 per cent. This is greater than the value obtained for the seeds of *Plantago indica* L. which was found to form an average mucilage volume of 14.3 cc. equivalent to 70.0 per cent.

The highest value of all the seeds tested was that of Plantago Psyllium L. with an average mucilage volume of 19.2 cc. equivalent to 95.8 per cent. The lowest value of all the seeds tested was that of Plantago lanceolata L.

The mixture of Plantago indica L. and Plantago Psyllium L., found in commerce under the name French Psyllium, was found to possess an average mucilage forming capacity of 16.9 cc. equivalent to 83.0 per cent.

The mucilage determinations employing the official N. F. VIII method showed that the seeds of both Plantago Purshii R. & S. and Plantago aristata Michx. possess significant mucilage forming capacities on a comparative basis to the other seeds now recognized in the National Formulary.

The values obtained in all the mucilage determinations made were above the minimum values specified in the N. F. monograph on Psyllium Seeds.

REFERENCES

(1) Montague, J. F., "Psyllium Seed, The Latest Laxa-tive," Montague Hospital for Intestinal Ailments, New York, 1932. (2) Youngken, H. W., Sr., THIS JOURNAL, 24, 207-11.

(1935).

(1935).
(3) Skyrme, E. W., Quart. J. Pharm. Pharmacol., 8,
(4) Skyrme, E. W., *ibid.*, 8, 198(1936).
(5) Johansen, A. D., "Plant Microtechnique," McGraw-Hill Co., Inc., New York, 1940, pp. 126-54.
(6) Sass, J. E., "Elements of Botanical Microtechnique,"
McGraw-Hill Co., Inc., New York, 1940, pp. 79-87.
(7) Bausch and Lomb Optical Company, Calalogue D, 111, p. 123, Rochester, N. Y.
(8) National Formulary, ed. 8, Mack Printing Company, Easton, Pa., 1947, p. 400.

Easton, Pa., 1947, p. 400.

The Preparation and Toxicity of Antimonyl 2-Aminothiazole Tartrate*

By DONALD B. MEYERS† and JAMES W. JONES‡

A method for the preparation of a new organic antimony compound is described. Toxicity data on this compound are reported.

THE VALUE of the therapeutic action of antimony in a variety of infectious diseases, mostly tropical in origin, has been recognized since 1907 following the work of Plimmer and Thomson (1) who demonstrated experimentally the trypanocidal action of tartar emetic.

The therapeutic effect of intravenous injections of tartar emetic in cases of infantile kala-azar was discovered in Italy in 1915 by Di Cristina and Caronia (2). The same year the compound was introduced into the treatment of kala-azar in British India (3).

Today it is recognized that intravenous injection of tartar emetic is highly effective against a number of tropical diseases due to animal parasites; especially against kala-azar, bilharziasis, filariasis, Delhi boil, and granuloma inquinale, while good results have been obtained in leishmaniasis, sleeping sickness, and frambesia (4).

Since the recognition of the therapeutic action of antimonyl potassium tartrate, a number of organic compounds have been introduced as less toxic and less irritant (5-7). In such compounds antimony exists in either the trivalent or the pentavalent form. The chief advantage of such compounds is their lower toxicity as compared to inorganic antimony salts or tartar emetic.

Antimony in any type of molecule has definite parasiticidal action (8, 9). It is commonly agreed that the compounds in which antimony occurs in the pentavalent state are less toxic than those in which it is in the trivalent form and, for the most part, are as effective in their antiprotozoan activity, especially in the case of kala-azar (6, 10). However, as a trypanocidal agent and in the treatment of bilharziasis, the compounds with antimony in trivalent form have proved to be the more effective (11-13),

This investigation was undertaken to prepare

^{*} Received Aug. 3, 1948, from the College of Pharmacy, State University of Iowa, Iowa City, Iowa. An abstract of the thesis presented by Donald B. Meyers in partial fulfillment of the requirements for the degree Master of Science in the Graduate College, State University of Iowa of Iowa

Carduate student and fellow of the Carbide and Carbon
 Chemicals Corporation, State University of Iowa.
 Professor, State University of Iowa; College of Pharmacy.