# OCCURRENCE AND FORMS OF CALCIUM OXALATE CRYSTALS IN OFFICIAL CRUDE DRUGS.\*

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### INTRODUCTION.

About 75 of the crude drugs listed in the U. S. Pharmacopœia, 9th revision and the National Formulary, 4th edition, are stated to contain crystals of calcium oxalate. These are described in a general way as individual crystals, either prisms or pyramids, as needles or raphides, as sphenoidal micro-crystals, as rosette groups, etc. While there was no reason to doubt the correctness of the identification of the substance as calcium oxalate in the majority of cases, Dr. Carl L. Alsberg, while Chief of the Burcau of Chemistry, suggested to the authors the desirability of making a study of these crystals by the immersion method under the petrographic microscope. This method has been introduced into work of this sort only recently (after the publication of the last editions of the Pharmacopœia and National Formulary), but it has already proved of great value in the identification of crystalline chemical substances.

The idea in this study was to ascertain whether the crystals actually possessed the optical properties of ordinary calcium oxalate (which is the monohydrate,  $CaC_2O_4$ .  $H_2O$ ) in every case; to endeavor to identify any which should prove to have different properties; and to work out the crystallographic orientation of each type of calcium oxalate crystal represented. The technical crystallographicoptical data have been reviewed elsewhere.<sup>1</sup>

### CALCIUM OXALATE MONOHYDRATE.

A specimen of each crude drug was reduced to powder, and a minute quantity was placed on a microscope slide. This was moistened with a tiny drop of an oilv liquid having the refractive index 1.650, attention being given to the distribution of the material in the liquid, and the cover glass was then applied. The liquid used consisted of monobromnaphthalene to which a very little monochlornaphthalene had been added. The slide was then examined under a microscope provided with a revolving stage, nicol prisms, cross-hairs in the eyepiece parallel to the vibration-planes of these nicols, and a substage diaphragm. Crystals were located in the mass by search with the nicols crossed, so that the bulk of the field was dark. Fragments of vegetable matter and starch grains, if present, produced their characteristic polarization effects, but any crystals of calcium oxalate could be readily picked out by their polarization colors, which consist of faint greenish or pinkish tints. When a good distinct crystal of this material was found, it was centered in the field, and turned to extinction position, that is, until it became dark; the upper nicol prism (analyzer) was withdrawn and the substage diaphragm was partly closed. In some cases the crystal would then be invisible, showing that its refractive index, in the crystallographic direction which happened to lie parallel to the vibration-plane of the polarizing nicol prism, was identical with the refractive index of the immersion liquid. As this liquid was chosen to correspond to index gamma  $(\gamma)$  of calcium oxalate monohydrate (the highest of the three refractive indices), this result showed that the crystal was lying with the direction

<sup>\*</sup> Scientific Section, A. Ph. A., Cleveland meeting, 1922.

<sup>&</sup>lt;sup>1</sup> Edgar T. Wherry, J. Wash. Acad. Sci., 12, 196-200, 1922.

yielding index  $\gamma$  parallel to the surface of the slide, and likewise parallel to the cross-hair in the eyepiece which had been found by trial to correspond to the vibration plane of the polarizing nicol. By then observing the shape of the crystal, it was possible to make out something as to its crystallographic orientation.

In case the crystal was still visible when the analyzing nicol was withdrawn and the diaphragm narrowed, the stage was rotated  $90^{\circ}$  and the crystal again



#### Fig. 1.

The crystals in rows 1 and 2 are represented in extinction positions with reference to the nicol prisms, the vibration planes of which are indicated by the dash lines. The positions of the directions in which the refractive indices  $\alpha$ ,  $\beta$  and  $\gamma$  are shown are indicated by the appropriate characters above and to the right in each case. The crystal forms represented are shown by letters, the names of these being: *a*, ortho or front pinacoid (100); *b*, clino or side pinacoid (010); *c*, base (001); *e*, negative unit orthodome (101); and *x*, unit clino or side dome (011). There is no evidence that form *a* actually occurs on any of the crystals, but they are sometimes bounded in part by edges between other faces occupying the same position as *a*.

The crystals in row 3 are twins, that is, are made up of parts of two crystals, one revolved 180° around an axis perpendicular to a given plane, with respect to the other. These are represented in the position half way between the extinction positions on either side. The directions of indices  $\beta$  and  $\gamma$  are shown by the dash lines. The forms are the same as in the other diagrams, the twinning plane being  $e(10\overline{1})$ .

observed. In some cases it would disappear in this position, again giving the location of  $\gamma$ ; but in other cases it would remain clearly visible in all positions, and, on raising the tube of the microscope slightly, a band of light would be seen to spread out from the crystal into the liquid. This showed that the crystal chosen happened to lie in such a position that the direction of index  $\gamma$  was not parallel to the slide, but the directions of the other, lower, indices were so situated instead. A number of other crystals in the same slide would then be examined in like manner.

Having thus established the presence or absence of crystals showing the index  $\gamma$  of calcium oxalate, and having obtained some data as to the shape of the crystal with reference to the direction in which index  $\gamma$  was shown, the process was repeated with immersion liquids made up to match the other two refractive indices of calcium oxalate, alpha ( $\alpha$ ) = 1.490 and beta  $(\beta) = 1.555$ . The first liquid consisted of a liquid petrolatum made from California petroleum and sold for medicinal purposes; the second liquid was a mixture of about 6 parts of this petrolatum with 4 parts of monochlornaphthalene. Nitrobenzene could also have been used for matching index  $\beta$ , as its refractive index, 1.553, is near enough for practical purposes. When crystals disappeared in either of these liquids, it

was possible to make observations as to the shape of the crystal and the orientation of the directions in which these refractive indices were shown.

The series of photomicrographs in Figure 2 show the general features observed. These photomicrographs were made on slides prepared and used for the observations outlined, and with nicol prisms crossed. Figure 1 shows a series of diagrams arranged to correspond with the photomicrographs, and with letters showing the crystallographic orientation and refractive index directions added. Angles slightly different from those here indicated will be shown if the crystals are tilted in other directions than those selected for illustration, so that no significance should be attached to lack of exact agreement in angles between unknown crystals and these shown here. It must also be remembered that the breaking up of crystals with rhombic outline may yield triangular fragments.





Fig. 2.

1b, Prunus (×175) 2b, Eucalyptus (×360) 3b, Quassia (×175) 1d, Veratrum (×190) 2d, Cinnamomum (×175) 3d, Scilla (×60)

With the aid of these figures, supplemented by actual measurement, using the method outlined, of refractive index  $\gamma$ , and if possible one or both of the others,

the identification of very minute grains as calcium oxalate monohydrate may be readily accomplished.<sup>1</sup>

# OTHER OXALATES.

Tetragonal Calcium Oxalate.—A form of calcium oxalate crystallizing in the tetragonal system has been recorded as occurring in several plants, especially in the vari-colored spiderwort, *Tradescantia* (*Rhoeo*) discolor, in the skin of the common onion (Allium cepa), and in several species of cacti, including the official cactus. The authors found it also in hyoscyamus. Its crystallographic-optical properties are as follows:

The crystals are tetragonal prisms, terminated by pyramids, the usual outline being hexagonal; they may also be broken into irregular fragments. They are optically uniaxial and positive. Fresh crystals in tiny drops of sap from the spiderwort, dried on microscope slides and at once matched against immersion liquids of various refractive indices, showed omega ( $\omega$ ) = 1.490 and epsilon ( $\epsilon$ ) = 1.540. On exposure to the air, however, the crystals increase in refractive indices, without obvious loss of transparency or other change, the values obtained on air-dried material from various sources being consistently  $\omega = 1.520$  and  $\epsilon = 1.545$ . On immersion in a liquid with refractive index 1.52 (some sassafras oil has about this value, but a mixture of oils may be used) and revolving the stage, any given crystal of this substance will disappear when some position is reached; this occurs when the prism edge lies perpendicular to the plane of vibration of the polarizing nicol prism, but is striking even though the crystal is so broken that crystallographic directions are not recognizable in it. The other refractive index may be matched so that the crystal will disappear when turned to a certain position, by immersion in benzaldehyde or a mixture with refractive index 1.545.

As to composition, it has been possible to confirm the work of Schmid<sup>2</sup> that the fresh material is probably a trihydrate of calcium oxalate; but the water content varies with conditions in an interesting way. Dr. J. N. Rose of the Smithsonian Institution kindly contributed a specimen of a tree cactus, recently described by Dr. Britton and himself as *Neoabbotia paniculata*,<sup>3</sup> in the wood of which, especially near the bark, were embedded numerous whitish pellets about 1 mm. in diameter. These proved to consist of aggregates of crystalline grains possessing the optical properties of tetragonal calcium oxalate. Accordingly, several grams of these grains were picked out as free from vegetable tissue as practicable, although a little material still adhered to them, and were analyzed in duplicate by J. H. Ellis of the Bureau of Chemistry. The results are compared with the theoretical compositions of the several hydrates in Table 1.

Таві	e 1.—Con	positions	of Calcium (	Oxalate Hy	drates.	
	Found.	3 H <sub>2</sub> O.	21/2 H2O.	2 H <sub>2</sub> O.	1 H <sub>2</sub> O.	Anhydr.
CaO	33.53	30.79	32.39	34.17	38.38	43.78
C	13.22	13.18	13.86	14.62	16.43	18.74
0	[29.30]	26.36	27.73	29.25	32.86	37.48
$H_2O\ldots\ldots\ldots\ldots$	23.95	29.67	26.02	21.96	12.33	
					·	
	100.00	100.00	100.00	100.00	100.00	100.00

<sup>1</sup> For a bibliography of previous work on the recognition of calcium oxalate, its occurrence in plants in general, etc., see N. Patschovsky, *Beih. Bot. Centralbl.*, 37, 261–380, 1920.

<sup>2</sup> E. E. Schmid, Ann. Chem., 97, 225-241, 1856.

<sup>3</sup> N. L. Britton and J. N. Rose, Smithsonian Misc. Coll., 72 (No. 9), 6 pp. (1921).

On heating the air-dried material, which was optically homogeneous, to  $105-110^{\circ}$  C. for a few hours, it lost about 4% of water, and microscopic examination of the powder showed well-defined crystals of the monohydrate beginning to appear, in the midst of unchanged tetragonal grains. After heating to  $150^{\circ}$  C., however, the loss of water amounted to 20.5% and practically all the tetragonal material had disappeared, with the development of distinct crystals of the monohydrate. By the time  $190^{\circ}$  C. was reached; the monohydrate itself was losing water, and crumbling to granular non-crystalline powder. The total water and the carbon were determined by combustion, the carbon content probably being somewhat low. In any case the presence of an indeterminate quantity of organic impurities could not fail to lead to a slight deviation from the theoretical values.

The data seem to indicate, then, that the tetragonal form is a trihydrate, but that at least half a molecule and probably one molecule of the water is held in so loose a manner that it escapes in dry air without loss of transparency of the crystal, but with a slight increase in refractive indices. The second molecule of water begins to go off at slightly above  $100^{\circ}$  C., while the third is stable up to about  $180^{\circ}$  C.

The relatively weak double refraction, such that when observed between crossed nicols the crystals show only first order white or gray colors, together with the fact that every crystal (air-dried) exhibits in some direction the one refractive index 1.52, makes it possible to readily distinguish this form of calcium oxalate from the usual form.

Magnesium Oxalate Monohydrate.—Magnesium oxalate has been identified by microchemical methods in the pericarp of black pepper (*Piper nigrum*) by Plahl.<sup>1</sup> The authors have measured the optical constants of the minute crystals found in this tissue, as follows: Biaxial with large axial angle; negative; refractive indices  $\alpha = 1.375$ ,  $\beta = 1.525$ ,  $\gamma = 1.570$ ,  $\gamma - \alpha = 0.195$ . The double refraction is thus extreme, and between crossed nicols the grains show fifth order colors, even when small. Magnesium oxalate prepared synthetically gave identically the same values, confirming the identification of the crystals in the pepper.

This substance can be readily distinguished from calcium oxalate monohydrate which it resembles, by measurement of the lowest refractive index  $\alpha$ . This index is matched by methyl-ethyl ketone, and when this is used as the immersion liquid many of the crystals of magnesium oxalate will match it and disappear in certain positions, as the stage is revolved, while all the indices of calcium oxalate are higher, so that they will remain visible, and on raising the microscope tube light will seem to enter them. It has been impossible to identify this substance in any others of the drugs studied, but in examining plant materials in general the possibility of its presence should not be overlooked.

Potassium Hydrogen Oxalate.—This compound is present in the foliage of some species of  $Rumex^2$  and other plants, but has not been observed in official drugs. It also resembles the calcium oxalate monohydrate, but has the refractive indices  $\alpha = 1.415$ ,  $\beta = 1.545$ ,  $\gamma = 1.565$ , and so can be distinguished by matching its lowest index by the immersion liquid isoamyl isovalerate.

<sup>&</sup>lt;sup>1</sup> W. Plahl, Arch. Chem. Mikrosc., 5, 320-329, 1912.

<sup>&</sup>lt;sup>2</sup> Cf. G. P. Walton, Bot. Gaz., 74, 158-173, 1922.

In a few of the drugs, especially agaricus, belladonna, and myristica, crystals of properties unlike any thus far described were observed. The nature of these substances is as yet undetermined.

OBSERVATIONS ON INDIVIDUAL DRUGS.

The data for the individual drugs studied are given in the following form:

Name: Official name; botanical name; number of specimen studied.1

Description: Quotations from U. S. Pharmacopœia, IX (U. S. P.) or National Formulary, 4th edition, 1916 (N. F.).

Observations: Supplementary remarks on the descriptive quotations and notes on crystallographic features. The crystals are understood to have shown the optical properties characteristic of calcium oxalate monohydrate, except where otherwise stated. The figure numbers refer to Figure 2.

ABSINTHIUM (Artemisia Absinthium; M. 37311).

Description: "Calcium oxalate crystals in rosette aggregates about 0.01 mm. in diameter." (N. F.)

Observations: The rosettes are rather sparse; their fragments represent broken crystalslike Fig. 2a.

AGARICUS (Polyporus officinalis; M. 37999).

Description: "Many cubical crystals of calcium oxalate from 0.01 to 0.02 mm. in diameter." (N. F.)

Observations: Shows large rosette aggregates, as well as single crystals of calcium oxalate, not cubical but like Fig. 2a.

The large crystals of cubical aspect also present show double refraction and hence do not belong to the cubic system. They are optically distinct from calcium oxalate, but their identity is unknown. Tunmann<sup>2</sup> suggests that they may be magnesium or potassium compounds of resinic or agaric acids. The published description would accordingly seem to require revision.

ALETRIS (Aletris farinosa; M. 37310).

Description: "Raphides \*\*\* from 0.025 to 0.045 mm. length." (N. F.)

Observations: The raphides or needle-like crystals are not numerous; they are mostly like Fig. 1d, occasionally 2d.

ALTHAEA (Allhaea officinalis; M. 28034).

Description: "Calcium oxalate crystals few, in rosette aggregates from 0.02 mm. to 0.03 mm. in diameter." (U. S. P. IX.)

Observations: The rosettes become, in the powdered drug, broken up into angular flakes; there are also occasional complete crystals or twins. Forms, Figs. 2c and 3c.

ALTHAEA FOLIA (Althaea officinalis; M. 37313).

Description: "Calcium oxalate in rosette aggregates up to 0.025 mm. in diameter." (N. F.) Observations: The rosettes are more or less broken up into angular fragments, of the form

2c.

ANISUM (Pimpinella anisum; M. 36738).

Description: "Cells \*\*\* containing a small rosette aggregate of calcium oxalate." (U. S. P. IX.)

Observations: The rosettes are very small and fragments are difficult to locate; those studied represented broken crystals like Fig. 2a.

APII FRUCTUS (A pium graveolens; M. 37283).

Description: "Cells containing fixed oil and alcurone grains, the latter each containing a small rosette aggregate of calcium oxalate." (N. F.)

Observations: The rosettes are small and not numerous; some of the fragments resemble Fig. 2a. Small rhombs are also occasional, Fig. 2b.

<sup>1</sup> The numbers used are serial numbers of the collection of the Microchemical Laboratory Bureau of Chemistry.

<sup>2</sup> O. Tunmann, Schweiz. Wochsch. Chem. Pharmazie. 47, 157-164, 1909; Pflanzenmikrochemie, p. 153 (1913). ARALIA (Aralia racemosa; M. 37309).

Description: "Rosette aggregates of calcium oxalate from 0.03 to 0.07 mm. in diameter." (N. F.)

Observations: The rosettes are not numerous; fragments are represented by Fig. 2a.

ASCLEPIAS (Asclepias tuberosa; M. 37314).

Description: "Calcium oxalate crystals in rosette aggregates up to 0.04 mm. in diameter." (N. F.)

Observations: The rosettes are numerous; broken fragments are like Fig. 2a.

ASPIDOSPERMA (Aspidosperma Quebracho blanco; M. 36886).

Description: "Crystals being in prisms frequently terminated by pyramids and from 0.008 to 0.03 mm. in length." (U. S. P. IX.)

Observations: The crystals are numerous, mostly like Figs. 2a, 3a and 3b. They frequently lie on face x and then do not extinguish well, one optic axis being approximately perpendicular to this face, showing only index  $\beta$ .

AURANTII DULCIS CORTEX (Sweet Orange Peel; M. 37106).

Description: "Oceasional membrane crystals of calcium oxalate in monoclinic prisms, from 0.02 to 0.035 mm. in diameter." (U. S. P. IX.)

Observations: The crystals are numerous, largely like Figs. 3a, 3b and 3c, with some 2a.

Note: Bitter Orange Peel (Aurantii amari cortex) showed forms similar to the above.

BELLADONNÆ FOLIA (Atropa Belladonna; M. 36764).

Description: "Calcium oxalate in sphenoidal micro-crystals." (U. S. P. IX.)

Observations: Very small sphenoidal crystals are numerous, but are not calcium oxalate monohydrate, for this substance is holohedral and not sphenoidal in crystallization. Moreover, their highest refractive index,  $\gamma = 1.63$ , is distinctly less than the corresponding value for calcium oxalate, while their lowest index,  $\alpha = 1.50$ , is slightly greater. Their nature is unknown, and the description might well indicate this fact.

BELLADONNÆ RADIX (Atropa Belladonna; M. 36765).

Description: "Sphenoidal micro-crystals numerous, from 0.003 to 0.010 mm. in length." (U. S. P. IX.)

Observations: The crystals are identical with those in the leaves of the same plant, just described, and are not calcium oxalate.

BRAYERA (Ilagenia abyssinica; M. 37996).

Description: "Rosette aggregates of calcium oxalate up to about 0.075 mm. in diameter." (N. F.)

Observations: The rosettes are not abundant; fragments are represented by Fig. 2a.

BUCHU (Barosma betulina, M. 36804, and Barosma serratifolia, M. 36808).

Description: Not described as containing calcium oxalate in U.S. P. IX.

Observations: Rosettes are present but not abundant, in both species. Fragments from these showed the optical properties of calcium oxalate monohydrate, being represented by Figs. 2a or 2b.

CACAO PRAEPARATA (Theobroma Cacao; M. 38026).

Description: Not described as containing calcium oxalate in the National Formulary.

Observations: Crystals can be located, though only with difficulty, in the powdered nibs, occurring for the most part in rosettes of minute micro-crystals. Optical data could not be obtained with certainty on these crystals. Occasionally, in the perisperm tissues are seen forms resembling Figs. 2a and 3c, and the substance is probably calcium oxalate.

CACTUS (Selencereus (formerly Cactus) grandiflorus; M. 38270).<sup>1</sup>

Description: "Spongy parenchyma containing large crystals and raphides of calcium oxalate." (N. F.)

Observations: The raphides or needle-like crystals (Fig. 1d) are frequent, and crystals like Fig. 3c occasional; both were found to be calcium oxalate monohydrate. In addition, a considerable quantity of tetragonal calcium oxalate is present in the form of irregular fragments, showing  $\omega = 1.520$  and  $\epsilon = 1.545$ ; this might well be mentioned in the description.

CALENDULA (Calendula officinalis; M. 37284).

Description: "Rosette aggregates of calcium oxalate from 0.002 to 0.004 mm. in diameter." (N. F.)

<sup>1</sup> Kindly furnished by Dr. J. N. Rose of the Smithsonian Institution.

Observations: Besides the rosettes, fragments of which are like Fig. 2a, prisms represented by Fig. 3a are occasional.

CALUMBA (Jateorhiza palmata; M. 36755).

Description: "\*\*\*containing one or more prisms of calcium oxalate from 0.01 to 0.03 mm. in length, or numerous sphenoidal micro-crystals." (U. S. P. IX.)

Observations: Crystals like Fig. 2c are present but scarce; no sphenoidal micro-crystals were observable in the specimen examined.

CANELLA (Canella Winterana (alba); M. 38252).

Description: "Calcium oxalate in rosette aggregates up to 0.05 mm. in diameter." (N. F.) Observations: Rosettes are numerous.

CANNABIS (Cannabis sativa; M. 36754).

Description: "Rosette aggregates of calcium oxalate from 0.005 to 0.025 mm. in diameter." (U. S. P. IX.)

Observations: Besides the aggregates there are a large number of minute irregular flakes, evidently broken from the rosettes, represented by Figs. 2a and 2b.

CARUM (Carum Carvi; M. 36761).

Description: "Aleurone grains \*\*\* not infrequently containing a small rosette aggregate or prism of calcium oxalate." (U. S. P. IX.)

Observations: The drug occasionally shows very minute crystals resembling Figs. 2a and 2b. CARDAMOMUM SEMEN (Elletaria Cardamomum; M. 36749).

Description: "In mounts made with hydrated chloral T. S. single prisms or crystals in rosette aggregates may separate in the cells of the endosperm and perisperm." (U. S. P. IX.)

Observations: Crystals like Fig. 1b are numerous, while occasionally 2b is represented.

CARYOPHYLLUS (Eugenia aromatica; M. 36758).

Description: "Calcium oxalate in rosette aggregates from 0.01 to 0.015 mm, in diameter," (U. S. P. IX.)

Observations: The rosettes are numerous, the fragments broken from them being represented by Fig. 2b; crystals like Fig. 1b are also occasionally present.

CASCARA SAGRADA (Rhamnus Purshiana; M. 36891).

Description: "\*\*\* the crystals \*\*\* being in the form of monoclinic prisms from 0.008 to 0.015 mm. in length." (U. S. P. IX.)

Observations: The crystals are numerous, the principal forms corresponding to Figs. 1b, 1c, 2b and 3c.

CASCARILLA (Croton Eluteria; M. 37285).

Description: "Calcium oxalate in monoclinic crystals." (N. F.)

Observations: Rosettes and prisms are occasional in the powdered drug. Fragments from the rosettes show forms corresponding to Fig. 2a, while the prisms are usually twinned, like 3a.

CASSIA FISTULA (Cathartocarpus Fistula; M. 38031).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: Crystals with the properties of calcium oxalate monohydrate occur, although they are not numerous, in the pod; the forms are represented by Figs. 1a, 1b, 1c, 2a and 3a. They are less numerous in the pulp and seed, but forms like 2a could be occasionally located.

CASTANEA (Castanea dentata; M. 37286).

Description: "Numerous calcium oxalate crystals in rosette aggregates or in monoclinic prisms, from 0.01 to 0.04 mm. in diameter." (N. F.)

Observations: The rosettes are numerous, fragments being represented by Fig. 2a.

снімарнп. (Chimaphila umbellata; М. 37287).

Description: "Calcium oxalate in rosette aggregates mostly about 0.035 mm. in diameter occasionally up to 0.065 mm. in diameter." (N. F.)

Observations: The rosette aggregates are not numerous; fragments are like Fig. 2a.

CHIONANTHUS (Chionanthus Virginica; M. 38043).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: Crystals are present, though not numerous; the forms occurring are shown by Figs. 1a, 1d, and 3b, the properties being those of calcium oxalate monohydrate.

CINCHONA (Cinchona Calisaya; M. 36903).

Description: "Sphenoidal micro-crystals of calcium oxalate numerous." (U. S. P. IX.)

Observations: The sphenoidal or triangular crystal grains are too small to establish their identity, but occasional crystals like Figs. 1b and 2b, evidently calcium oxalate monohydrate, were observed.

CINCHONA RUBRA (Cinchona succirubra; M. 36762).

Description: "Sphenoidal micro-crystals of calcium oxalate, resembling those in cinchona." (U. S. P. IX.)

Observations: As in the preceding drug.

CINNAMOMUM SAIGONICUM (Saigon Cinnamon; M. 36766).

Description: "Cells \*\*\* either filled with starch or containing very small raphides of calcium oxalate." (U. S. P. IX.)

Observations: The raphides or needles are not abundant, although often occurring in bundles; they represent Figs. 1d and 2d.

CINNAMOMUM ZEYLANICUM (Cinnamomum zeylanicum; M. 36904).

Description: "Calcium oxalate in raphides, from 0.005 to 0.008 mm. in length." (U. S. P. IX.)

Observations: The small needles occur rather abundantly; the majority of them correspond to Fig. 1d, some to 2d.

CONDURANGO (Marsdenia Condurango; M. 37288).

Description: "Rosette aggregates of calcium oxalate from 0.015 to 0.04 mm. in diameter." (N. F.)

Observations: Beside the rosettes there are prisms, represented by Figs. 1a and 1b.

CONIUM (Conium maculatum; M. 37289).

Description: "Rosette aggregates of calcium oxalate, the latter from 0.002 to 0.006 mm. in diameter." (N. F.)

Observations: The rosettes are very small and few in number; fragments show the form represented by Fig. 1a.

CONVALLARIAE FLORES (Convallaria majalis; M. 37656).

Description: "Calcium oxalate in raphides up to 0.04 mm. in length." (N. F.)

Observations: The raphides or needles are not numerous; they are mostly like Fig. 1d, occasionally 2d.

CONVALLARIAE RADIX (Convallaria majalis; M. 37290).

Description: "Raphides of calcium oxalate few, from 0.02 to 0.045 mm. in length." (N. F.) Observations: Identical with the preceding drug.

CORIANDRUM (Coriandrum sativum; M. 37767).

Description: "Calcium oxalate crystals numerous, from 0.003 to 0.01 mm. in diameter, mostly in rosette aggregates, either isolated or in aleurone grains." (U. S. P. IX.)

Observations: In the specimen examined there are only crystal fragments, which are very small and not abundant; those that could be studied seemed to be broken from crystals like Fig. 2b.

CORNUS (Cornus florida; M. 38126).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: The drug contains numerous rosette aggregates, and also single prisms, represented by Figs. 2a, 3b and 3c, and possessing the properties of calcium oxalate monohydrate. CORVDALIS (Bicuculla canadensis; M. 37291).

Description: "Very few rosette aggregates of calcium oxalate up to 0.02 mm. in diameter, from the portions of rhizome of Bicuculla canadensis." (N. F.)

Observations: The rosettes are not numerous; they yield fragments of crystals like Fig. 2b. CUBEBA (Piper Cubeba; M. 36768).

Description: "Occasionally a crystal of calcium oxalate." (U. S. P. IX.)

Observations: The drug was found to contain numerous small crystals like Fig. 1b.

CYPRIPEDIUM (Cypripedium hirsulum; M. 38268).

Description: "Calcium oxalate in raphides up to 0.065 mm. in length and occurring isolated or in bundles, occasionally imbedded in a mucilage-like plasma." (N. F.)

Observations: The raphide bundles are not numerous, and are so firmly embedded in mucilage-like plasma as to be separated with difficulty for the purpose of optical study. Needles that could be isolated resembled Fig. 1d.

### DAMIANA (Turnera diffusa; M. 37995).

Description: "Numerous crystals of calcium oxalate in rosette aggregates up to 0.03 mm. in diameter and occasionally in prisms." (N. F.)

Observations: The fragments from the rosette aggregates are represented by Fig. 2b; no prisms noted.

DIOSCOREA (Dioscorea villosa; M. 38269).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: Calcium oxalate monohydrate is present in the form of raphides, though not abundant; they are represented by Fig. 1d.

ERIODICTYON (Eriodiciyon californicum; M. 36802).

Description: Not described as containing calcium oxalate in U. S. P. IX.

Observations: Rosettes of calcium oxalate monohydrate are occasional though not numerous; they usually average from 0.02 to 0.03 mm. in diameter. Fragments from them are like Figs. 2c and 3c.

EUCALYPTUS (Eucalyptus globulus; M. 36747).

Description: "Calcium oxalate crystals \*\*\* in the form of rosette aggregates or monoclinic prisms varying from 0.015 to 0.025 mm. in diameter." (U. S. P. IX.)

Observations: The large number of different forms of crystals correspond to Figs. 1a, 1b, 1c, 2b and 3c.

EUONYMUS (Euonymus atropurpureus; M. 37293).

Description: "Calcium oxalate in rosette aggregates from 0.015 to 0.035 mm. in diameter, the amount in different specimens showing some variation." (N. F.)

Observations: The rosettes are not numerous; fragments are represented by Fig. 2b.

FRANGULA (Rhamnus Frangula; M. 37531).

Description: "Prismatic crystals of calcium oxalate varying from 0.007 mm. to 0.015 mm. in diameter." (U. S. P. IX.)

Observations: Various habits of crystals are numerous, Figs. 1a, 1b, 2a, 3a, and 3c, as well as irregular flakes, being represented.

GALANGAL (Alpinia officinarum; M. 38130).

Description: Not described as containing calcium oxalate in National Formulary.

*Observations:* Rosette aggregates are present in the powdered drug, though not numerous; irregular fragments from these proved to have the properties of calcium oxalate monohydrate.

GALEGA (Galega officinalis; M. 38135).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: The drug contains numerous prisms, the largest proportion of them being represented by Figs. 1b, 2a, 3a and 3b, undoubtedly calcium oxalate monohydrate.

GALLA (Nutgalls; M. 38051).

Description: Not described as containing crystals in U.S. P. IX.

Observations: Crystals of calcium oxalate monohydrate were found to be rather numerous in the sample examined, consisting of forms similar to those found in the bark of Quercus alba (Figs. 1b, 1c, 2a, 3a); rosette aggregates are also rather numerous. Since nutgalls are excressences on the young twigs of Quercus species, it is possible that these crystals had their origin in the oak tissues, and some samples may not contain them.

GELSEMIUM (Gelsemium sempervirens; M. 36763).

Description: "Calcium oxalate in monoclinic prisms from 0.015 to 0.03 mm. in diameter." (U. S. P. IX.)

Observations: The crystals correspond to Figs. 1c, 2c, 3a and 3c; irregular flakes are also frequently present.

GERANIUM (Geranium maculatum; M. 38058).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: The drug contains numerous large rosettes and fragments broken from them, also prisms represented by Figs. 2a, 2c and 3c, all undoubtedly calcium oxalate monohydrate.

GLYCYRRHIZA (Glycyrrhiza glabra (Spanish Licorice); M. 36729).

Description: "Cells \*\*\* containing numerous starch grains, or prisms of calcium oxalate." (U. S. P. IX.)

Observations: Relatively large crystals like Figs. 2a and 3a are abundant. They occasionally lie on face x, do not extinguish well, and show only index  $\beta$ .

GOSSYPII CORTEX (Gossypium herbaceum; M. 37316).

Description: "Rosette aggregates of calcium oxalate from 0.009 to 0.025 mm. in diameter." (N. F.)

Observations: The rosettes are numerous, fragments usually resembling Fig. 2b.

GRANATUM (Punica Granatum; M. 37760).

*Description:* "Calcium oxalate crystals in rosette aggregates, monoclinic prisms or crystal fibers, the individual crystals from 0.01 to 0.018 mm. in diameter." (U. S. P. IX.)

Observations: The rosettes are very numerous; the individual crystals correspond to Figs. 1b and 1c.

HAEMATOXYLON (Haematoxylon campechianum; M. 37994).

Description: "Wood parenchyma with occasional crystals of calcium oxalate." (N. F.)

Observations: The drug shows numerous prisms, represented by Figs. 2a and 3b.

HAMAMELIDIS FOLIA (Hamamelis virginiana; M. 37318).

Description: "Calcium oxalate in monoclinic prisms, from 0.01 to 0.035 mm. in diameter." (N. F.)

Observations: The prisms are numerous, being represented by Figs. 1b, 2a and 3c. HELONIAS (Chamaelirium luteum; M. 37295).

Description: "Numerous raphides varying from 0.025 to 0.035 mm. in length." (N. F.)

Observations: The separated needles or raphides are like 1d, occasionally 2d.

HYDRANGEA (Hydrangea arborescens; M. 37369).

Description: "Raphides numerous, from 0.07 to 0.13 mm. in length." (N. F.)

Observations: The single needles are represented by Fig. 1d and occasionally by 2d. HYOSCYAMUS (Hyoscyamus niger; M. 36732).

*Description:* "Calcium oxalate crystals usually in the form of 4- to 6-sided, isolated prisms, sometimes in twins, from 0.015 to 0.025 mm. in length, also occurring in spherical aggregates, 0.02 mm. in diameter, and occasionally in sphenoidal micro-crystals." (U. S. P. IX.)

Observations: Examination showed the presence of numerous crystals and irregular fragments, but they do not represent calcium oxalate monohydrate. Their index lengthwise is about 1.525, that crosswise 1.545, showing them to be the tetragonal form of calcium oxalate which might well be noted in the description.

IGNATIA (Strychnos Ignatii; M. 38062).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: Crystalline material with the properties of calcium oxalate monohydrate is present though very scarce in this drug; the only form found was that represented by Fig. 2a.

IPECACUANHA (Cephaëlis Ipecacuanha; M. 36745).

Description: "Calcium oxalate in raphides from 0.015 to 0.04 mm. in length, few." (U. S. P. IX.)

Observations: The raphides or needles are not numerous; those found are mostly like Fig. 1d, occasionally 2d.

IRIS (Iris florentina; M. 37298).

Description: "Calcium oxalate in large prisms up to 0.5 mm. in length." (N. F.)

Observations: The fragments from the prisms are usually of the form represented by Fig. 3c. IRIS VERSICOLOR (Iris versicolor; M. 37297).

Description: "Calcium oxalate in prisms, up to 0.35 mm. in length. (N. F.)

Observations: Same as preceding.

JALAPA (Exogonium Purga; M. 36740).

Description: "Calcium oxalate in rosette aggregates from 0.01 to 0.035 mm. in diameter." (U. S. P. IX.)

Observations: Fragments of the rosettes appear to be broken from crystals like Figs. 1b or 2b.

JUGLANS (Juglans cinerea; M. 37299).

Description: "Calcium oxalate from 0.01 to 0.05 mm. in length. (N. F.)

Observations: The drug contains both large rosette aggregates and prisms. Fragments of the former are represented by Fig. 2c, the prisms by Figs. 1b, 2a, 2b, and 3c.

JUNIPERUS (Juniperus communis; M. 37300).

Description: "\*\*\* each enclosing a polygonal crystal of calcium oxalate." (N. F.)

Observations: The prisms are fairly numerous, being represented by Fig. 1a.

LAPPA (Arctium Lappa; M. 38065).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: Occasional irregular fragments in the drug resemble calcium oxalate, al-

though they could not be certainly identified; they sometimes have a form like Fig. 2a.

LIMONIS CORTEX (Cilrus medica; M. 36748).

Description: "Occasionally membrane crystals of calcium oxalate." (U. S. P. IX.)

Observations: The crystals are not numerous, although irregular flakes, also crystals like Figs. 1a, 2a and 3c, can be located without difficulty.

MALVAE FOLIA (Malva sylvestris; M. 37319).

Description: "Rosette crystals of calcium oxalate. (N. F.)

Observations: The rosettes are numerous, fragments being represented by Fig. 2b.

MATICO (Piper angustifolium; M. 38267).

Description: "Calcium oxalate crystals few in parenchyma tissue of the venation, in the form of raphides or monoclinic prisms." (N, F.)

Observations: The crystals are scarce, prisms represented by Figs. 1a, 1b and 2b, also needles 1 ike 1d, being only occasionally found.

MELILOTUS (Melilotus officinalis; M. 38265).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: Small, single prismatic crystals with the properties of calcium oxalate monohydrate are present though not abundant in the drug, many being represented by Figs. 1b, 2a, 3a and 3b.

MYRICA (Myrica cerifera; M. 37320).

Description: "Crystals of calcium oxalate in monoclinic prisms up to 0.02 mm. in diameter, or in rosette aggregates up to 0.035 mm. in diameter." (N. F.)

Observations: Fragments of rosettes resembled Fig. 1*a*; prisms resembled Figs. 2*a*, 2*b*, 3*a* and 3*c*.

MYRISTICA (Myristica fragrans; M. 36810).

Description: Not described as containing calcium oxalate in U.S. P. IX.

Observations: Rod-like and flat triangular crystals occur in the drug. Some of these crystals had a refractive index 1.49 in one direction, but a slightly lower index in the other direction. This indicates that these crystals do not represent calcium oxalate monohydrate, but the nature of the substance is unknown.

PAREIRA (Chondodendron iomeniosum; M. 38085).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: The drug contains numerous prismatic crystals, the different forms being represented by Figs. 1a, 1b, 2b, 3a and 3c, all showing the typical optical properties of calcium oxalate monohydrate.

PASSIFLORA (Passiflora sp.; M. 38266).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: The drug showed the presence of rosette aggregates, the fragments of which proved to be calcium oxalate monohydrate.

PHYTOLACCA (Phytolacca decandra; M. 38096).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: Needles are abundant in the drug, being usually represented by Fig. 1d and occasionally by Fig. 2d; they have the optical properties of calcium oxalate monohydrate.

PILOCARPUS (Pilocarpus Jaborandi, M. 36744, and Pilocarpus microphyllus, M. 36734).

Description: "Cells occasionally containing rosette aggregates of calcium oxalate from 0.01 to 0.025 mm. in diameter." (U. S. P. IX.)

Observations: The rosettes are numerous, as are also irregular fragments, evidently broken from them; Figs. 1b and 2b appear to be represented.

PIMENTA (Pimenta officinalis; M. 37321).

Description: "Rosette aggregates of calcium oxalate from 0.006 to 0.017 mm. in diameter." (N. F.)

Observations: The rosettes are numerous, fragments resembling Fig. 1a.

#### PINUS ALBA (Pinus Strobus; M. 37303).

Description: "Few monoclinic prisms of calcium oxalate about 0.02 mm. in diameter." (N. F.)

Observations: The crystals must be very scarce, as none could be definitely located in the specimen examined.

#### PIPER (Piper nigrum; M. 36805).

Description: Not described as containing calcium oxalate in U. S. P. IX.

Observations: A few minute crystals were present in the drug. While these had the general aspect of calcium oxalate monohydrate, trial with refractive index liquid 1.375 (methyl-ethyl ketone) showed them to have one index as low as this value, indicating them to represent the magnesium compound instead.

PODOPHYLLUM (Podophyllum peltatum; M. 36746).

Description: "Calcium oxalate crystals few, in rosette aggregates from 0.05 to 0.08 mm. in diameter and occasionally in raphides from 0.03 to 0.09 mm. in length." (U. S. P. IX.)

Observations: The rosettes are few and no needles or raphides were found. Fragments from the rosettes are numerous though small, representing broken crystals like Figs. 1b and 2b,

PRUNUS SEROTINA (Prunus serolina; M. 36751).

Description: "Calcium oxalate in crystals consisting of monoclinic prisms, from 0.015 to 0.04 mm. in diameter, also in rosette aggregates from 0.01 to 0.04 mm. in diameter." (U. S. P. IX.)

Observations: The drug is rich in crystals, especially those shown in Figs. 1b, 1c, 2a and 3c.

#### QUASSIA (Picrasma excelsa; M. 37188).

Description: "Calcium oxalate in crystal fibers near the medullary rays, in 4- to 6-sided prisms, from 0.006 to 0.03 mm. in length." (U. S. P. IX.)

Observations: The crystals are very numerous, their forms corresponding to Figs. 2a, 3a and 3b.

QUERCUS (Quercus alba; M. 37322).

Description: Not described as containing calcium oxalate crystals in National Formulary.

Observations: Large prisms and rosettes are numerous in the drug, forms represented by Figs. 1b, 1c, 2a and 3a being shown; all have the optical properties of calcium oxalate monohydrate.

QUILLAJA (Quillaja Saponaria; M. 37305).

Description: "Calcium oxalate in monoclinic pyramids and prisms from 0.035 to 0.2 mm. in length." (N. F.)

Observations: The crystals are very numerous, their forms being represented by Figs. 1a, 3c and probably 2c.

RHAMNUS CATHARTICA (Rhamnus cathartica; M. 38097).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: Crystals with the properties of calcium oxalate monohydrate are present though not abundant in the drug; they are aggregated in rosettes, fragments from which are represented by Fig. 2b.

RHEUM (Rheum officinale; M. 36756).

Description: "\*\*\* It exhibits calcium oxalate in rosette aggregates, mostly from 0.05 to 0.1 mm. in diameter occasionally attaining a diameter of 0.15 mm." (U. S. P. IX.)

Observations: The rosettes are of relatively large size; irregular shaped fragments from them are numerous, Fig. 1c being most often represented.

RUBUS (Rubus villosus; M. 38136).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: Rosette aggregates of calcium oxalate monohydrate are numerous in the drug, fragments from them being represented by Fig. 2a and occasionally 3a.

RUMEX (Rumex crispus; M. 37306).

Description: "Calcium oxalate crystals in rosette aggregates from 0.025 to 0.06 mm. in diameter." (N. F.)

Observations: The rosettes are numerous, irregular fragments resembling Figs. 1a and 2b. Since potassium hydrogen oxalate has been found in the foliage of some species of Rumex (see introduction) it was sought for in the drug. Evidence of its presence, however, was lacking, since

all of the fragments showed one index considerably more than the highest (1.565) of this substance. SANTALUM ALBUM (Santalum album; M. 37307).

Description: "Single crystals of calcium oxalate." (N. F.)

Observations: Crystals are infrequent in the powdered drug, those studied, however, corresponding to calcium oxalate monohydrate.

SANTALUM RUBRUM (Pterocarpus santalinus; M. 36752).

Description: "Also occasional groups of crystal fibers with calcium oxalate in the form of monoclinic prisms from 0.01 to 0.02 mm. in diameter." (U. S. P. IX.)

Observations: Crystals occur fairly frequently in the drug and are relatively large in size. Figs. 2a and 3a seem to be most often represented.

SARSAPARILLA (Smilax medica; M. 36743).

Description: "Calcium oxalate in raphides, from 0.006 to 0.035 mm. in diameter, occurring singly or in groups." (U. S. P. IX.)

Observations: The needles are not numerous, and are difficult to release from the bundles. Figs. 1d and 2d are represented.

SCAMMONIAE RADIX (Convolvulus Scammonia; M. 36739).

Description: "Calcium oxalate crystals numerous, in monoclinic prisms from 0.01 to 0.045 mm. in length." (U. S. P. IX.)

Observations: The crystals are numerous, as are also irregular fragments. Forms like Figs. 2b and 3c seem to be characteristic, with 1b less frequent.

SCILLA (Urginea maritima; M. 36757).

Description: "While examined under the microscope it exhibits numerous single crystals and bundles of long raphides of calcium oxalate." (U. S. P. IX.)

Observations: Needles of two different sizes occur, some being ten times as large as others. Both sizes are numerous and correspond to Figs. 1d and 2d, and both have the properties of calcium oxalate monohydrate.

SENNA (Cassia acutifolia; M. 36742, and Cassia angustifolia, M. 36753).

Description: "Calcium oxalate in rosette aggregates, from 0.009 to 0.01 mm. in diameter, and 4- to 6-sided prisms, about 0.015 mm. in length, usually in crystal fibers." (U. S. P. IX.)

Observations: The crystals correspond to Figs. 1a, 1b, 2a and 3a.

STILLINGIA (Stillingia sylvatica; M. 36737).

Description: "Occasionally crystals of calcium oxalate in rosette aggregates about 0.035 mm. in diameter." (U. S. P. IX.)

Observations: The rosettes are only occasional; irregular fragments are also few, broken from crystals like Fig. 2b.

STRAMONIUM (Datura Stramonium; M. 36741).

Description: "Calcium oxalate either in rosette aggregates, from 0.01 to 0.02 mm. in diameter, or in rod-like crystals, or in the form of sphenoidal micro-crystals." (U. S. P. IX.)

Observations: The rosettes are numerous; irregular fragments from them represent broken crystals like Figs. 1b and 2b.

TRIFOLIUM (Trifolium pratense; M. 38114).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: The drug contains numerous very small prisms, many of the forms present being represented by Figs. 1a, 2a, 3a and 3b, and all showing the optical properties of calcium oxalate monohydrate.

ULMUS (Ulmus fulva; M. 36759).

Description: "Calcium oxalate in monoclinic prisms, mostly in crystal fibers, the individual crystals from 0.01 to 0.025 mm. in diameter." (U. S. P. IX.)

Observations: The crystals are numerous, Figs. 1c, 2a, 2b and 3a being most often represented.

UVA URSI (Arctostaphylos Uva-ursi; M. 36730).

Description: "\*\*\* crystal fibers with monoclinic prisms, from 0.006 to 0.015 mm. in diameter." (U. S. P. IX.)

Observations: Crystals like Figs. 1b, 2b and 3a are abundant, and represent calcium oxalate monohydrate.

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VANILLA (Vanilla planifolia; M. 37325).

Description: "Bundles of raphides of calcium oxalate." (N. F.)

Observations: The powdered fruit showed numerous raphide bundles and broken fragments of crystals. However, it proved impossible to bring the crystal fragments into close enough contact with liquids for the determination of refractive indices, so that their identification as calcium oxalate could not be confirmed.

VERATRUM VIRIDE (Veratrum viride; M. 28234).

Description: "Calcium oxalate in raphides, from 0.015 to 0.15 mm. in length." (U. S. P. IX.)

Observations: The needles are numerous, mostly like Fig. 1d, and occasionally 2d.

VIBURNUM OPULUS (Viburnum Opulus; M. 37308).

Description: "Calcium oxalate in rosette aggregates, 0.015 to 0.04 mm. in diameter." (N. F.)

Observations: The drug is rich in rosettes and irregular fragments, the latter resembling Figs. 1a and 2b.

VIBURNUM PRUNIFOLIUM (Viburnum prunifolium; M. 36735).

Description: "Crystals of calcium oxalate from 0.015 to 0.035 mm. in diameter, occurring mostly in rosette aggregates, occasionally in crystal fibers; monoclinic prisms of calcium oxalate few." (U. S. P. IX.)

Observations: The rosettes are numerous, as are also irregular fragments broken from forms represented by Figs. 1a, 2a and 3a.

XANTHOXYLI FRUCTUS (Xanthoxylum americanum; M. 38116).

Description: Not described as containing calcium oxalate in National Formulary.

Observations: The capsule material was found to contain rosette aggregates of calcium oxalate monohydrate, readily located but not abundant. Fragments from these rosettes are represented by Figs. 1*a* and 3*c*. The seeds did not show the presence of crystals.

XANTHOXYLUM (Xanthoxylum americanum; M. 36750).

Description: "Calcium oxalate chiefly in monoclinic prisms from 0.01 to 0.025 mm. in diameter, occurring in crystal fibers and in parenchyma cells of the primary cortex." (U. S. P. IX.)

Observations: The crystals, and irregular fragments, are numerous, usually like Fig. 1b, also 1a and 3a.

 TABLE 1.—Calcium Oxalate Monohydrate Present in More or Less Well Defined Prismatic

 Crystals, the Types Occurring Most Characteristically or Frequently Being Indicated by Numbers

 Corresponding to Those on Figure 2.

Agaricus <sup>1</sup>	2a	Cubeba	1 <i>b</i>
Althaea <sup>1</sup>	2c, 3c	Eucalyptus <sup>2</sup>	1a-c, 2b, 3c,
Apii fructus <sup>1</sup>	2b	Frangula <sup>2</sup>	1a, 1b, 2a, 3a, 3c
Aspidosperma <sup>2</sup>	2a, 3a, 3b	Galega <sup>2, 3</sup>	1b, 2a, 3a, 3b
Aurantii amari cortex <sup>2</sup>	2a, 3a, 3b, 3c	Galla <sup>1,3</sup>	1b, 1c, 2a, 3a
Aurantii dulcis cortex <sup>2</sup>	2a, 3a, 3b, 3c	Gelsemium	1c, 2c, 3a, 3c
Cactus <sup>1</sup>	3c	Geranium <sup>1, 2, 3</sup>	2a, 2c, 3c
Calendula <sup>1</sup>	3a	Glycyrrhiza <sup>2</sup>	2a, 3a
Calumba	2c	Granatum <sup>1</sup>	1b, 1c
Carum	2a, 2b	Haematoxylon <sup>2</sup>	2a, 3b
Cardamomum semen	1b, 2b	Hamamelidis folia <sup>2</sup>	1b, 2a, 3c
Caryophyllus <sup>1</sup>	1b	Ignatia <sup>8</sup>	2a
Caseara sagrada <sup>2</sup>	1b, 1c, 2b, 3c	Iris	3c
Casearilla <sup>1</sup>	3a	Iris versicolor	30
Cassia fistula <sup>3</sup>	1a-c, 2a, 3a	Juglans <sup>1,2</sup>	1b, 2a, 2b, 3c
Chionanthus <sup>1,3</sup>	1a, 3b	Juniperus	1 <i>a</i>
Cinchona <sup>1</sup>	1b, <b>2</b> b	Limonis cortex	1a, 2a, 3ı
Cinchona rubra <sup>1</sup>	1b, 2b	Matico <sup>1</sup>	1a, 1b, 2b
Condurango <sup>1</sup>	1a, 1b	Melilotus <sup>3</sup>	1b, 2a, 3a, 3b
Соглиз <sup>1,8</sup>	2a, 3b, 3c	Myrica <sup>1,2</sup>	2a, 2b, 3a, 3c

Pareira <sup>2, 3</sup>	1a, 1b, 2b, 3a, 3c	Scammoniae radix <sup>2</sup>	1b, 2b, 3c
Prunus serotina <sup>2</sup>	1b, 1c, 2a, 3c	Senna <sup>1</sup>	1a, 1b, 2a, 3a
Quassia <sup>2</sup>	2a, 3a, 3b	Trifolium <sup>3</sup>	1a, 2a, 3a, 3b
Quercus <sup>1, 2, 3</sup>	1b, 1c, 2a, 3a	Ulmus <sup>2</sup>	1c, 2a, 2b, 3a
Quillaja <sup>2</sup>	1a, 2c, 3c	Uva ursi <sup>2</sup>	1b, 2b, 3a
Santalum rubrum	2a, 3a	Xanthoxylum <sup>2</sup>	1a, 1b, 3a

<sup>1</sup> Included also in one of the other lists.

<sup>2</sup> Especially rich in crystals of large size and perfection.

<sup>3</sup> Not recorded as containing calcium oxalate in U. S. P. IX or N. F.

TABLE 2.—Calcium Oxalate Monohydrate Present in Rosettes of Crystals, or Fragments Broken from Them, the Types of Crystals Which These Most Frequently Appear to Represent Being Indicated by Numbers.

Absinthium	2a	Galangal <sup>3</sup>	irreg.
Agaricus <sup>1</sup>	irreg.	Galla <sup>1,3</sup>	irreg.
Althaea <sup>1</sup>	2c, 3c	Geranium <sup>1, 2, 3</sup>	irreg.
Althaea folia	2c	Gossypii cortex <sup>2</sup>	2b
Anisum	2 <b>a</b>	Granatum <sup>1,2</sup>	irreg.
Apii fructus <sup>1</sup>	2a	Jalapa	1b, 2b
Aralia	2a	Juglans <sup>1,2</sup>	2c
Asclepias <sup>2</sup>	2 <b>a</b>	Malvae folia <sup>2</sup>	2b
Brayera	2a	Myrica <sup>1,2</sup>	1a
Buchu <sup>3</sup>	2a, 2b	Passiflora <sup>8</sup>	irreg.
Calendula <sup>1</sup>	2a	Pilocarpus <sup>2</sup>	1b, 2b
Canella	irreg.	Pimenta <sup>2</sup>	1 <i>a</i>
Cannabis	2a, 2b	Podophyllum	1b, 2b
Caryophyllus <sup>1,2</sup>	2b	Quercus <sup>1,2,3</sup>	1b, 1c, 2a
Cascarilla <sup>1</sup>	2a	Rhamnus cathartica <sup>1</sup>	2 <b>b</b>
Castanea	2a	Rheum <sup>2</sup>	1¢
Chimaphila	2a	Rubus <sup>2,3</sup>	2a, 3a
Condurango <sup>1,2</sup>	irreg.	Rumex <sup>2</sup>	1a, 2b
Conium	1 <i>a</i>	Senna <sup>1,2</sup>	irreg.
Cornus <sup>1,3</sup>	irreg.	Stillingia	2b
Corydalis	2b	Stramonium <sup>2</sup>	1b, 2b
Damiana <sup>2</sup>	2b	Viburnum opulus <sup>2</sup>	1a, 2b
Eriodictyon <sup>3</sup>	2c, 3c	Viburnum prunifolium <sup>2</sup>	1a, 2a, 3a
Euonymus	2b	Xanthoxyli fructus <sup>3</sup>	1a, 3c

<sup>1</sup> Included also in one of the other lists.

<sup>2</sup> Especially rich in large or typical rosettes.

<sup>1</sup> Not recorded as containing calcium oxalate in U. S. P. IX or N. F.

 TABLE 3.—Calcium Oxalate Monohydrate Present in Acicular Crystals or Raphides, the Types

 Represented Being Numbered as in Tables 1 and 2.\*

Aletris	1d, 2d	Helonias <sup>2</sup>	1d, 2d
Cactus <sup>1,2</sup>	1 <i>d</i>	Hydrangea <sup>2</sup>	1d, 2d
Chionanthus <sup>1,3</sup>	1d	Ipecacuanha	1d, 2d
Cinnamomum saigonicum	1d, 2d	Matico <sup>1</sup>	1 <i>d</i>
Cinnamomum zeylanicum <sup>2</sup>	1d, 2d	Phytolacca <sup>2, 3</sup>	1 <i>d</i> , 2 <i>d</i>
Convallariae flores	1d, 2d	Sarsaparilla	1d, 2d
Convallariae radix	1d, 2d	Scilla <sup>2</sup>	1d, 2d
Cypripedium	1d	Veratrum viride <sup>2</sup>	1d, 2d
Dioscorea <sup>8</sup>	1d		

\* It is noteworthy that most of the monocotyledonous plants used as drugs are in this list.

TABLE 4.—Calcium Oxalate Monohydrate Present in Irregular Flakes the Derivation of Which Is Indeterminate, or in Poorly Developed Crystals (When Any Crystal Outlines Are Recognizable, They Are Numbered). Cinchona<sup>1</sup>..... triang. Coriandrum..... 2b Cinchona rubra<sup>1</sup>..... triang. Santalum album..... 1b TABLE 5.—Tetragonal Calcium Oxalate Present. Cactus<sup>1</sup> Hyoscyamus TABLE 6.—Crystals Present Probably Calcium Oxalate but not Certainly Identified. Cacao praeparata<sup>3</sup>..... 2a, 3c (?) Vanilla..... 1d (?) Lappa<sup>3</sup>..... 2*a* (?) TABLE 7.—Crystals Present Magnesium Oxalate Monohydrate. Piper TABLE 8.—Crystals Present from Unknown Substances. Belladonnæ radix Agaricus<sup>1</sup> Belladonnæ folia Myristica TABLE 9.-Calcium Oxalate Reported, but not Found. Gentiana lutea<sup>4</sup> Pinus alba TABLE 10.-Not Available for Study. Cocillana <sup>1</sup> Also included in one of the other lists. <sup>2</sup> Especially rich in typical crystals. <sup>3</sup> Not recorded as containing calcium oxalate in U. S. P. IX or N. F. <sup>4</sup> H. Zornig, Schweiz, Apoth.-Zeit., 60, 725, Dec. 1922. TABLE 11.-No Crystals of Calcium Oxalate or of Any Substance Resembling It Present. Aconitum Mentha Viridis Delphinium Adonis Digitalis Menyanthes Mezereum Allium sativum Drosera Nux Vomica Amygdala dulcis Dulcamara Echinacea Papaveris Fructus Angelicæ Fructus Angelicæ Radix Ergota Paracoto Реро Apocynum Eupatorium Euphorbia Pilulifera Petroseleni Radix Arnica Petroselinum Asarum Farfara

Ficus Physostigma Aspidium Foeniculum Pimpinella Baptisia Berberis Fraxinus Populi Gemmæ Boldo Fucus Prunum Brvonia Grindelia Pulsatilla Pyrethrum Capsicum Guaiaci Lignum Cataria Helianthemum Rhus Glabra Caulophyllum Humulus Rosa Gallica Rubi Fructus Centaurium Hydrastis Rubi Idæi Fructus Chirata Inula Chondrus Kava Sabal Cimicifuga Kola Sambucus Cocculus indicus Krameria Sanguinaria Coffea Tosta Leptandra Sassafras Sassafras Medulla Colchici Cormus Linum Colchici Semen Lohelia Scoparius Colocynthis Macis Scutellaria Coptis Matricaria Senecio Crocus Mentha Piperita Senega

TABLE 11 (Continued).—No Crystals of Calcium Oxalate or of Any Substance Resembling It Present.

Sinapis Alba Sinapis Nigra Solanum Spigelia Staphisagria Strophanthus Sumbul Taraxacum Thuja Thymus Trillium Triticum Valeriana

Verbasci Flores Verbasci Folia Verbena Zea Zedoaria Zingiber

## SACCHARIN FEEDING OF RATS.\*.1 B. FANTUS AND L. HEKTOEN.

The importance of saccharin as a sweetening agent for medicine and in diabetes mellitus justified, it seemed to us, the undertaking of a prolonged feeding experiment.

## EXPERIMENT I.

To determine the effect of prolonged ingestion of relatively enormous quantities of saccharin, parallel observations were made on 25 young rats (5 males, 20 females), in each of three good-sized cages. Group I A received 10% saccharin in its food, Group I B received 1% saccharin in food, Group I C served as control.

After preliminary trials, the following food formula was adopted: Cornmeal, 200 Gm.; White Flour, 100 Gm.; Meat, 50 Gm.; Water, 200 cc. This was given the control animals, while for the other groups the required amount of soluble saccharin (sodium benzoylsulphonicimide—Heyden Chemical Works) was added. The mixture was then molded into cakes. The only other food the animals received was a small amount of lettuce or carrots, once a week. More food was given than could be eaten, though the exact amount of food consumed was determined only at the beginning of the experiment, until the animals had attained full growth and the food consumption became fairly constant.

The collective weight of the animals in each cage was determined daily at first, and at weekly intervals later on in the experiment. From Chart 1, which gives the average weight of the animals of each group, it will be seen that the animals fed on food containing 10% saccharin did not do as well as the controls. The weight curve of the animals receiving 1% saccharin was practically equal to that of the controls up to the 24th week, when the saccharin-fed animals commenced to lag slightly behind. This difference in weight might be due to difference in food consumption, which probably explains the lower weight curve of the animals that received 10% saccharin, who did not consume as much food as the animals of the other two groups. The animals that received 1% saccharin consumed practically the same amount of food as the controls.

During the course of the experiment, animals died from time to time, practically always from acute or chronic bronchopneumonia. A few animals died from cerebral abscesses. By the end of the 36th week, 16 animals had survived in Group I A, 13 animals had survived in Group I B, and 19 animals in Group I C.

All the rats were now killed by chloroform; and it was found that all of the rats of the saccharin groups and most of the rats of the control group had more or

<sup>\*</sup> From the John McCormick Institute for Infectious Diseases.

<sup>&</sup>lt;sup>1</sup> Scientific Section, A. Ph. A., Cleveland meeting, 1922.