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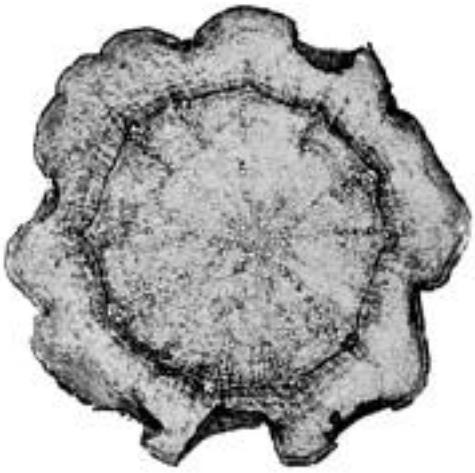

FIG. 1-Cross-section of Canaigre Root.
x $5^1/_2$ diameters.

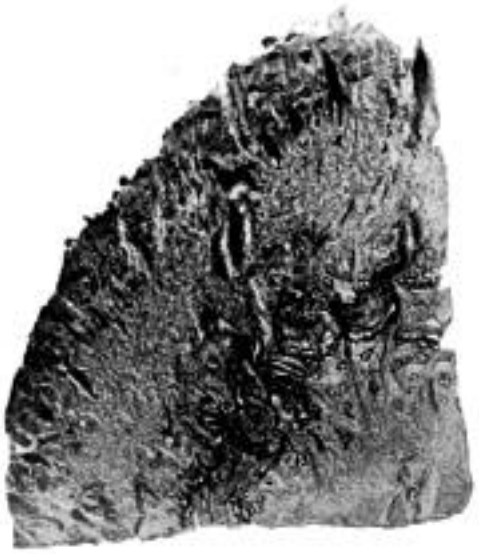

FIG. 2.-Cross-section of Chinese Rhubarb.
x $5^1/_2$ diameters.

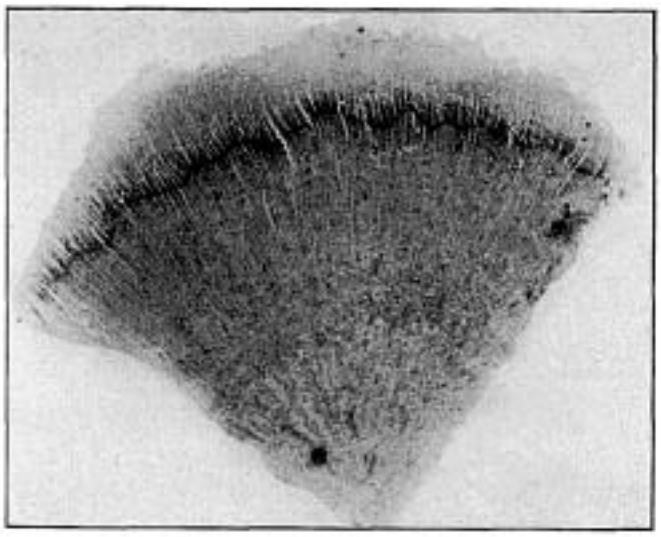

FIG. 3.-Cross-section of Rheum Rhaponticum.
x $5^1/_2$ diameters.

A BRIEF STUDY OF THE RHUBARBS AND A PROBABLE ADULTERANT.

BY L. E. SAYRE,
Member of Research Committee C of Revision Committee of the United States Pharmacopoeia.

Problem twelve proposed by the Committee on Revision of the Pharmacopoeia for 1900 reads: "Rheum-distinguish from Rhaponticum and from Rumex hymenosepalus," the drugs being in the powdered state. The object of this paper is to present the investigations of the author upon the line of work indicated in the query. For the purpose of the study, both microscopical and chemical methods have been employed, and will here be described; and since the greater part of the research has been accomplished by the use of the optical instrument, the methods used and the results obtained by it will first be considered.

In connection with this subject I need only remark that the line of work laid out in former contributions has been adhered to in the present instance. Authentic specimens having been obtained from the Chairman of the Committee, they were carefully prepared, sectioned, and the elements studied in their normal relations to each other. With a thorough knowledge of the structure thus obtained, the drugs in the powdered condition were then observed, and the prominent characteristics noted. Drawings and photographs were made, and appear with this article. It is best, I think, to state here that although the specimens used are doubtless thoroughly representative, care must be used in drawing too general conclusions from the results obtained on account of the limited number of specimens. For the same reason the paper can be considered merely a preliminary one, subject to such corrections as more detailed study of the subject may indicate. The purpose for which the investigation has been conducted is to discover, if possible, some test whereby the substitution of inferior grades of rhubarb for the better one, or admixture with a foreign drug, may be detected.

A study of the true Rheum shows that it is characterized by several features peculiarly its own. Yet despite this there is no exact information, so far as I know, concerning the true botanical origin of the drug. It is commonly ascribed to *R. officinale* and *R. palmatum*, and there is little doubt that one or both of these contribute the major portion of the commercial rhubarb. If but one be the source, then which it is, I think, cannot be said to a certainty.

Rheum officinale is, perhaps, the one usually considered as furnishing the true rhubarb. It is a native of Southeastern Thibet and possibly of China also. In appearance it considerably resembles the ordinary garden rhubarb, with which it has been cultivated in Europe, but differs from it in several particulars. *R. palmatum* is indigenous to Northwestern China. It first became known to Europeans in 1750, and received a description from Linnaeus in 1762. Like *R. officinale* it has been cultivated in foreign countries, the first having been grown in England in 1765.

Rheum rhaponticum, European rhubarb, is the source of the cheap variety of rhubarb. It is a native of Southern Siberia, and is closely related to *R. undulatum*, the common garden variety, Like that, too, it is easily cultivated, and the commercial source of the drug is the gardens of Europe.

These various kinds of rhubarb, although comparatively recent additions to the materia medica of the Occident, have long been known and used by the Chinese. Specific mention of the drug is found in their writings as far back as 2700 B.C. They still collect and prepare it as they did in the early days, and Chinese rhubarb is the

synonym for the best quality of the commercial article.

Rumex hymenosepalus is a member of the same natural order as Rheum, but is a native of the western hemisphere. It has recently come into prominence because of the use to which its tannic acid has been applied. Since this article has to do chiefly with the rhubarbs, no further treatment will be accorded the canaigre. Those interested in the subject, however, will find a good account of the plant in Professor Trimble's work on the tannins.

The samples of Chinese rhubarb used in the present examination, presented the usual fusiform outline and mottled surface. On close examination this latter effect is observed to be due to alterations of a dirty white and a brownish-yellow tissue, and in these colors is particularly observable in fresh fractures or cuts. If such a surface be moistened, though, the white is observed to turn a light, bright yellow, and the former yellow to a striking dull orange color, thus darkening the whole effect. Somewhat the same thing happens by exposure to the air. An observation of a freshly-cut and moistened surface shows that the tissues in numerous places are aggregated into contorted groups, to which effect the mottled or marbled appearance is due. Thin sections show that the lighter groundwork tissue is composed of thin-walled parenchyma cells, while the dark and contorted areas are principally fibro-vascular tissue. The latter, in certain forms of the drug, is regularly arranged into spots having a radiate structure and forming the so-called stellate spots or “Masern” of the Germans. Recent writers state that these are particularly characteristic of the Russian variety, which is no longer on the market. The accompanying drawing (Fig. 1), adapted from Berg, illustrates the effect.

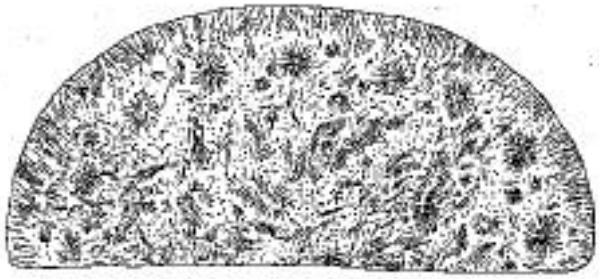

FIG. 4.-Cross-section of Rheum, after Berg.

This peculiar structure is due to the method of growth, whereby the numerous rudimentary leaves on the surface of the rhizome leave the form of their fibro-vascular growth as a permanent record on the parent stem. In the specimens examined this structure did not make its appearance, and I think it will be found that, in its typical form, it rarely does. What really was found was a massed irregularity of the fibro-vascular tissue in certain areas, as shown in the half-tone reproduction of a photomicrograph (*Frontispiece*, Fig. 2). This doubtless corresponds to the stellate structures of the Russian, but it is not carried out to the same extent.

The *Rhaponticum* (*Frontispiece*, Fig. 3) in the particular just mentioned, presents an entirely different aspect, as is easily distinguished from either variety of the Chinese rhubarb. There is a distinct and plainly-marked radiate structure, unbroken by such an arrangement of the vascular tissue as is so apparent in the true rhubarb. As will also be observed, the paring of the rhizome did not extend down to the cambium line,

which appears as a dark line in the figure. The parenchyma here is also thin-walled.

Under higher magnification, the cell contents of the tissues become manifest. In both the *Rheum officinale* and the *rhaponticum* the elements observed are starch grains and calcium oxalate crystals. Of these more extended mention will be made when the powdered form of the substances is considered. *Rumex Hymenosepalus* in the gross and in section offers no points of comparison to the species of *Rheum*. The roughly-wrinkled root is of a dark, krameria-red color, and possesses no trace of the characteristic rhubarb odor. The taste is sharply astringent, and in no wise mucilaginous and disagreeable like *Rheum*. The gritty feeling when ground between the teeth is also absent. In section (*Frontispiece,* Fig. 1) it presents the typical form of a simple root. The thin-walled parenchyma occupying the whole extent of the section is marked off into two areas by the concentric cambium line, in such a manner that the inner central one occupies about two-thirds the diameter of the section. Radiating from the center to the cambium line are about twelve groups of tracheary vessels.

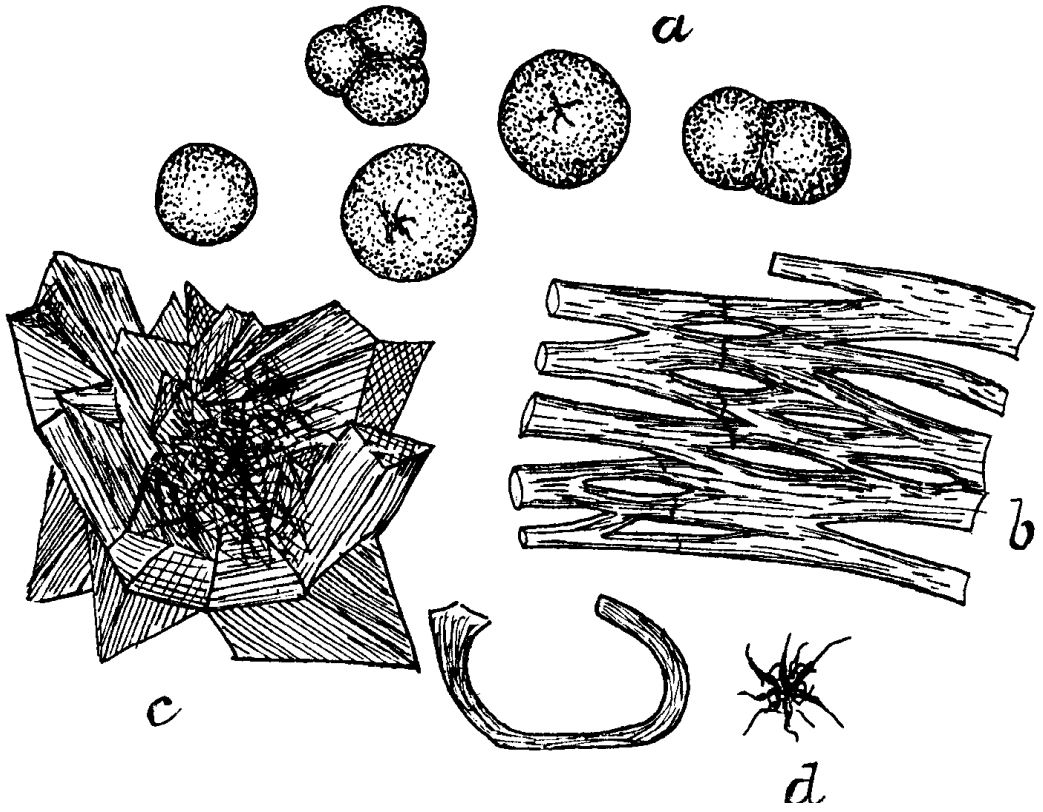

FIG. 5-Chinese Rhubarb. x 450 diameters. *a*, starch; *b*, fragments of pitted vessel; *c*, calcium oxalate; *d*, chrysophanic acid.

In the form of powders the *Rheums* and the canaigre are not easily differentiated, yet a careful examination will not fail to show the presence of the latter, even when mixed with other drugs. The distinction of *R. officinale* and *R. rhaponticum*, however, is a different matter, and the author was not able to select any salient microscopical feature that would serve to distinguish them apart, either individually or in mixtures. But a chemical test was found, which will be described later on.

In a No. 60 powder of either rhubarb the most striking elements observed are the starch grains and calcium oxalate crystals, to which a more careful study adds the fragments of pitted vessels, and crystals of chrysophanic acid. The cell walls of the parenchyma hardly appear at all, and when present are mere fragments. These common elements offer little means for basing a distinction between the two *Rheums*, since in size and form they differ so little. The only distinction observed was the greater number of starch grains in the *rhaponticum*; but this could hardly be used as point of distinction, since it is such a variable character. Numerous measurements of starch grains and the calcium oxalate crystals were made and gave the following averages: Starch, Chinese, .02646 mm. (*Fig. 5*); rhaponticum, .0216 mm. (*Fig. 6*); Calcium oxalate crystals, Chinese, .0716 mm.; *rhaponticum*, .0683 mm. Both elements are thus seen to be larger in the Chinese form, but the difference is not such a one as could be used as a test.

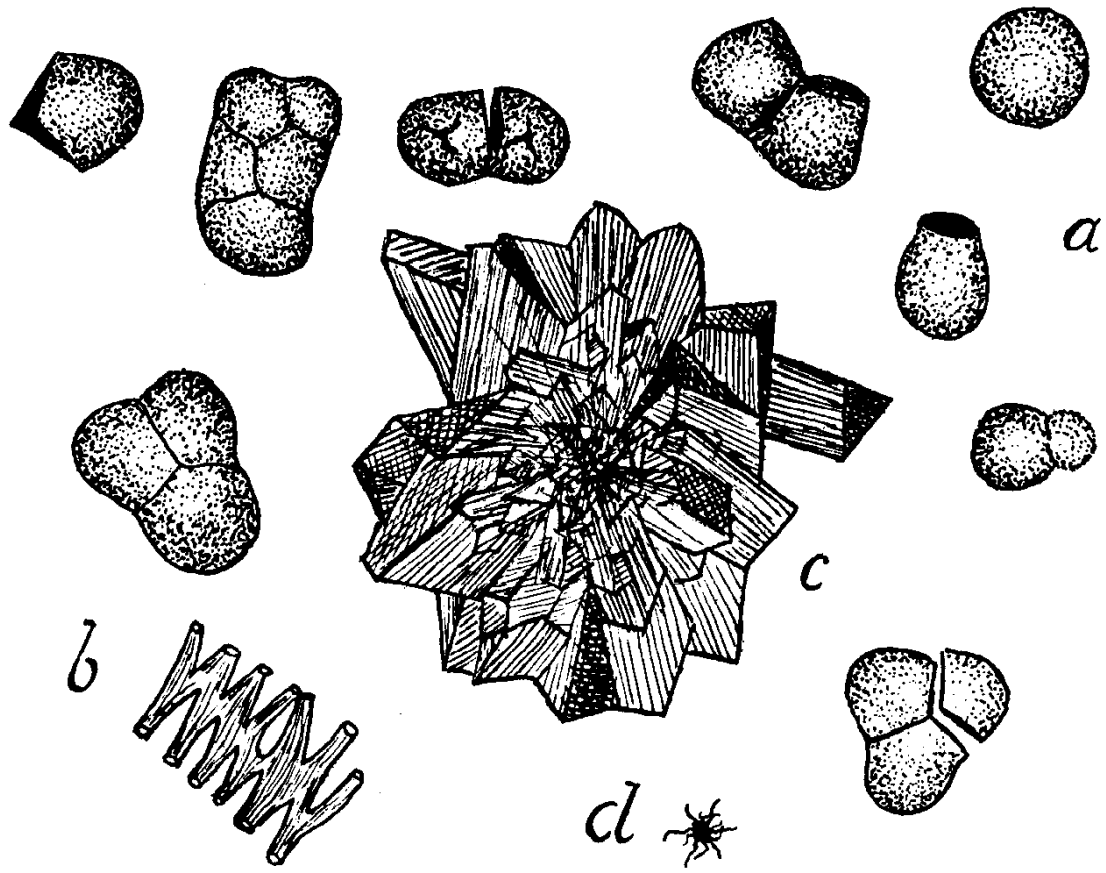

FIG. 6.—Rheum Rhaponticum. x 450 diameters. *a*, starch; b, fragments of pitted vessel; *c*, calcium oxalate; *d*, chrysophanic acid.

The powder of *Rumex hymenosepalus* is marked particularly by the size and form of the starch grains (*Fig. 7*). These are long and slender in form, and exhibit a long, branching hylum, which extends throughout the major portion of the long diameter. The presence of these in a sample of rhubarb powder would at once show that it was adulterated with canaigre, since they differ entirely in form and size from the Rheum starch. A No. 60 powder of this substance also exhibits a much larger proportion of the parenchyma *débris*, the cells of which are much larger than those of the *Rheums*.

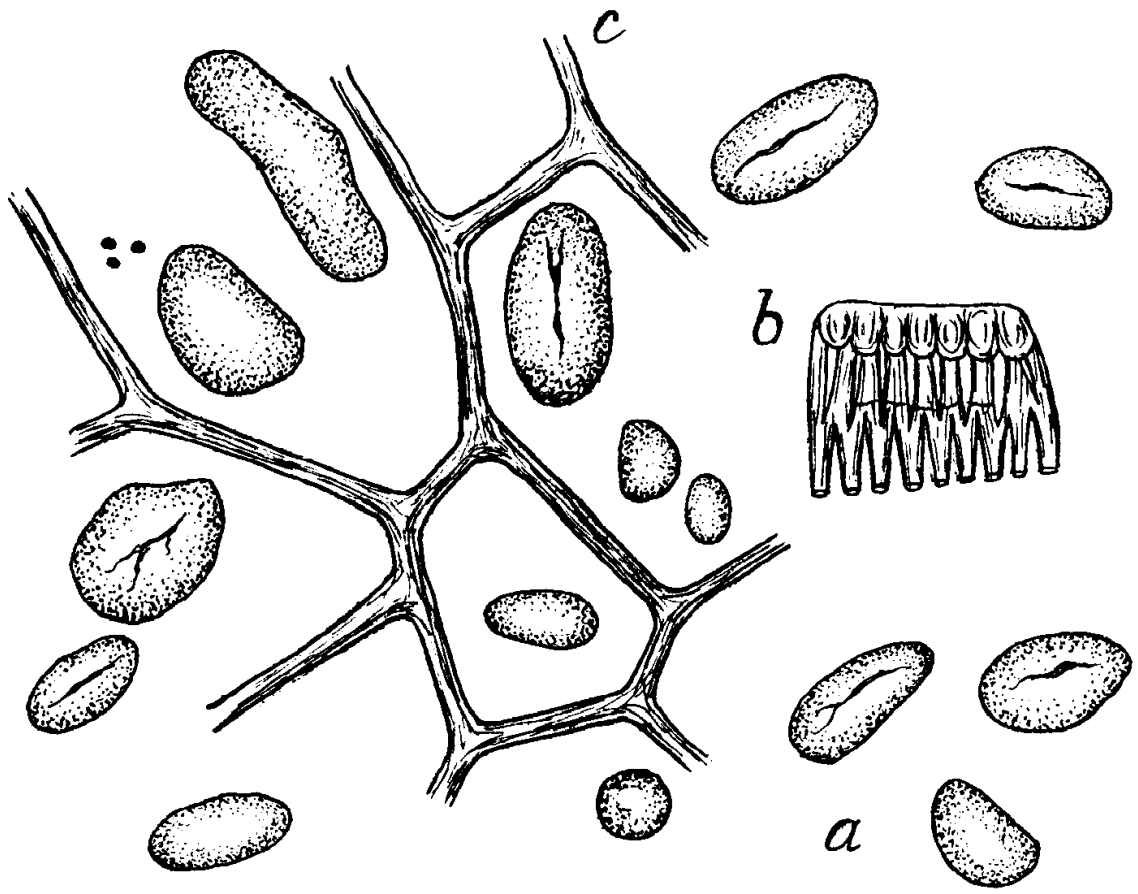

FIG. 7.-Rumex Hymenosepalus. x 450 diameters. *a*, starch; *b*, fragments of pitted vessel; *c*, parenchyma cells.

The distinction between the two forms of rhubarb that could not be made out by the use of the microscope appeared very distinctly under the influence of chemical reagents. Normally, the two powders differ materially in their appearance. For instance, the Chinese gives a fine, soft powder of a distinctly pure yellow color, and with the odor that is so characteristically that of rhubarb; while the *rhaponticum* affords a granular, pinkish-yellow powder, the odor of which is not so strongly rhubarb-like, but is more woody in character. Under the action of alkalis these differences in color become more manifest. Ammonium hydrate proved the most suitable reagent for this purpose. Under its influence Chinese rhubarb turns a dark brick-red color, while the *rhaponticum* exhibits a distinctly salmonred shade. Canaigre with the same reagent gives a brownish color. To apply the test, place upon a glass surface a small amount of powder, and moisten it with a drop or two of ordinary ammonia water. At once the color reaction becomes apparent. A mixture of the two rhubarbs cannot thus be detected, as the pink of the *rhaponticum* is masked by the stronger yellow of the Chinese variety. The stronger alkalis did not afford satisfactory results, since they formed a gelatinous mass with the powders that did not show the colors well.

Briefly, then, the author's results indicate the following facts, viz: That the characteristic elements of the powdered rhubarb are the starch grains, calcium oxalate crystals, and massed acicular crystals of chrysophanic acid, and that these

are so similar in the two forms that no point of distinction is offered, by them. Also, that the reaction to ammonia serves as a means of identifying the pure specimens, but not mixtures. And, finally, that adulteration with canaigre may be detected by the presence of the characteristic long starch grains.

Before making any suggestions as to the manner in which the text of the U.S.P. describing rhubarb may be changed so that powdered rhubarb may be clearly identified, the author desires to make further study of the subject. He would gladly receive the co-operation in this work of any who are interested.

TRUE AND FALSE CACTUS GRANDIFLORUS.[1]

By GORDON SHARP, M.D.

EXPLANATORY.

In the end of 1891 my attention was directed to the night-blooming Cereus, a so-called heart tonic, the correct botanical name of which is *Cereusgrandiflorus*[2], Miller, although it is commonly known as *Cactusgrandiflorus*, Linné. I made several bedside observations with a tincture which has a greenish color. Sometimes I thought I had obtained good results; at other times I had difficulty in deciding whether the preparation had any virtue at all. This, however, is not unusual in treating of disease, especially heart disorders. But between these conflicting opinions I resolved to place the drug on further trial. In time the supply of tincture ran down and another was ordered, but when it came to hand I was astonished to find that, although like the former, it had a pleasant orris-like odor, the color was different, being of a yellowish-brown hue. The pharmacist from whom it was obtained made inquiry, and was told it was quite right, and was the genuine drug, and no further questions were asked. My bedside observations were continued, and sometimes I had a greenish and sometimes a brownish tincture or liquid extract, but oftener the latter. After several further trials I decided to make my own tincture, and with this purpose in view I got a pharmacist to procure me the dried flowering tops, and this he did from a Manchester house. Mr. J. H. Hoseason at this time joined me in investigating the chemistry of the drug, and either jointly or alone we had an agent to obtain supplies from Manchester, Leeds, London, and Edinburgh houses. In one way or other we employed many pounds weight of the drug, and each parcel was certified to be the true Cactus. For reasons which will be obvious later on, I have made particular mention of these facts. We had previously searched the literature of the subject from every possible source, but could find no mention of any analysis of the drug. We resolved to start at the beginning, and I think I may be pardoned when I say we expended endless labor in our task. Our results have been partially recorded in the *Practitioner* of September, 1894, and in the *Pharmaceutical Journal* of November 24, 1894. But the chemistry is the chemistry of *Opuntia decumana*, Haworth, not of *Cereus* (*Cactus*) *grandiflorus*, Miller. We owe the unearthing of this blunder to the learned Curator of the Pharmaceutical Society's Museum in London, Mr. E. M. Holmes. Mr. Holmes investigated this subject last summer, and communicated with me, and I sent him a specimen of the drug we had worked with, and at once the fallacy was discovered. He has written an article on the

[1] *Pharmaceutical Journal*, December 18, 1897.

[2] Currently *Selenicereus grandiflorus* - MM

subject of *Cereus* and *Opuntia* in the Pharmaceutical Journal of August 21, 1897. The pharmacology of my article in the number of the Practitioner already quoted is really the the pharmacology of *Opuntia*, not of *Cereus*.

The question of therapeutical action does not concern a company of pharmacists, but it is almost necessary for me to refer shortly to this aspect of the subject. The therapeutic observations were made from specimens of both Cereus and Opuntia, and also from pills prepared from the formula of Mr. T. W. Sultan. Each pill contains $^1/_{100}$ grain of extract of genuine Cereus. Mr. Sultan does not say $^1/_{100}$ in his pamphlet whether this preparation is an alkaloid, or a resin, or a glucoside; he merely calls it the active principle. After all, then, my practical results are not much affected, if affected at all, by my pharmacological and botanical blunders. I am not alone in my experience, for I have had sent me from various sources samples of tincture, labelled *Cactus grandiflorus*, but which were preparations of *Opuntia*, and yet medical men had assured the senders that they possessed the virtues ascribed to the genuine drug. Since the publication of my article in the Practitioner I have had opportunities of carefully testing genuine *Cereus* alongside strophanthus and our old friend foxglove, and I have come to the conclusion that *Cactus*, whether genuine or spurious, is worthless, and should be discarded by both pharmacist and physician. Why should *Opuntia* have been so widely sold for *Cereus* ?

From the fact that we obtained spurious specimens from so many sources, we must conclude that *Opuntia* has been widely distributed. On first consideration we are strongly tempted to blame the drug merchants for imposing a spurious drug on the buyer. I do not share this view. I believe the mistake arises largely owing to the carelessness of botanists in often calling *Cereus* by the name *Cactus*. I do not know whether *Opuntia vulgaris*, Miller, is another name for *Opuntia decumana*, Haworth, but I do know that *Opuntia vulgaris* is also known as *Cactus opuntia*, Linné. Here, then, may be an explanation of the whole difficulty. The generic name *Cactus* having once got afloat, merchants, pharmacists and medical men have concluded there could be but one *Cactus*.

CHEMISTRY OF CEREUS AND OPUNTIA.

Cereus.—In Mr. Holmes' article in the JOURNAL, he tells us that Bonnett and Bay-Tessier discovered an alkaloid which they named cactine. Mr. E. H. Farr examined the drug in quantity, and found, among other substances, “glucosidal resinous bodies,” and “also an alkaloid which is present in very small quantities only.” The alkaloid must be present in very small proportions, for I failed to get any reaction with Thresh's reagent with three fluid drachms of a one in one extract. I do not like the name “glucosidal resinous bodies,” which Mr. Farr employs, and I hardly appreciate the meaning of the term, but I am, perhaps, as worthy of blame myself, for I find that I suggested that resins might play the part of glucosides. Of one thing I am certain, and it is that some resins do reduce weak Fehling's solution when allowed to stand for an hour or less at the temperature of a water-bath. *Cereus* stems contain a large proportion of chlorophyll, and to this the extracts and tinctures of the genuine drug owe their beautiful green color.

Opuntia.—Still referring to Mr. Holmes' essay, Mr. Farr says: “On working on a

quantity I did get an indistinct reaction for alkaloids and also a very slight reduction with Fehling's solution." Further, referring to the resins, Mr. Farr adds: "The most characteristic one is but very slightly soluble in aqueous solutions, and gives, with ammonia, a deep-yellow color. This one, with at least two of the other resins, reduces Fehling's solution on boiling, and to a fair extent." The experience of Mr. Farr with regard to the resins of *Opuntia* agrees in many points with that of Mr. Hoseason and myself, but we found no alkaloid, and we worked on large quantities and made a large number of trials. However, a significant point is that Mr. Farr only got an "indistinct reaction for alkaloids." The flowering tops and stems of *Opuntia* contain a pigment which I imagine is xanthophyll, and hence the alcoholic tinctures and extracts of the drug have always a yellowish or light-brownish color.

How came Cereus to be employed as a heart tonic? In view of the somewhat dogmatic opinion I have expressed of the worthlessness of *Cereus* and *Opuntia*, one must ask how the drugs came to have tonic properties? Before answering this query, we have to pause and ask ourselves how we have acquired our knowledge of many of our most valuable drugs. We civilized races, who have an intimate acquaintance with the sciences upon which is built the rational treatment of disease, have to acknowledge that to savage tribes or unlettered peoples belongs the credit of bringing under our notice the action of valuable drugs. Only to name one-sacred bark. The Spanish settlers of the Pacific Coast employed this agent long before it was known to us, and those Spanish settlers, we can hardly doubt, got their information from the original occupiers of the soil. In like manner, *Cereus grandiflorus* has been long employed by the West India Islanders in dropsy. Opuntia is also employed, in the form of a decoction, as a demulcent drink.

Both drugs contain a certain amount of resins and pectin (or a similar agent), and these substances have a stimulant action on the kidneys, and would, of course, be useful in dropsies. Now, many dropsies, if not most, have their origin in heart affections. The transition from the treatment of dropsy to the treatment of heart affections is an easy one. But then these peoples employ decoctions in which a large proportion of pectin is present. We employ alcoholic tinctures or extracts in which practically no pectin is present. Besides, these resins and pectins have no action on the heart itself. It must not be inferred from this that I advocate decoctions of *Cereus* and *Opuntia*. Although useful in dropsies, they are no more efficacious than the demulcent drinks known to us, such as barley water, gruels, and others, which we are in the habit of employing as aids in the treatment of dropsies. They are aids, nothing more.[3] We use what lies to our hand, and the West India Islanders do the same.

I have so many people to thank for help in my work on these drugs that I hardly know where to begin; but I must not forget to mention Mr. J. H. Hoseason, late Lecturer on Pharmacy in the Owens College; Mr. E. M. Holmes; Messrs. Parke, Davis & Co.; Burroughs, Wellcome & Co.; Evans, Gadd & Co.; Wyatt (Lancaster), and others.

[3] EDITOR'S NOTE —This is, of course, infuriating to me. All of this work done on *DRIED* Cereus and Opuntia; If only the good Dr. Sharp had enquired (in 1898) of Lloyd, Maisch or Remington, knowledgeable American pharmacists, he would have found that both plants (especially Night-blooming Cereus) are only active when made of green or *FRESH* botanicals, and this obstinant reliance by commercial pharmaceutical manufacturers over the following three decades on the powdered *dry* plant is what led to Cereus being tossed out by 1932 as being ineffectual. Me, I have maintained two large plants that I have been harvesting for over a decade, supplying myself with some of this remarkably effective medicine, made from the *fresh* plant. —MM