

EDITORIAL

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PHARMACEUTICAL PUBLICITY.

THE methods of publicity of associations, and of branches of the AMERICAN PHARMACEUTICAL ASSOCIATION have frequent consideration in the JOURNAL. Recently, occasions have suggested new ideas and officials have put them into practice; contact and mutual interest of physicians, the public and pharmacists result in helpful publicity.

The Pennsylvania Pharmaceutical Association arranged a display at the Scranton meeting of the State Medical Association for acquainting physicians with the products of the U. S. Pharmacopœia and National Formulary. Likewise, the Virginia Pharmaceutical Association had a display at the Roanoke meeting of the Medical Society of Virginia of U. S. P. and N. F. products. The interest developed at the convention of the American Medical Association, under the direction of the AMERICAN PHARMACEUTICAL ASSOCIATION, and the evident desire of physicians to acquire a knowledge relative to materia medica of their own selection will have an effect and influence on prescription practice throughout the country. (See comment of Adley B. Nichols in August JOURNAL, page 742.) These exhibits at State meetings bring the message nearer home and the coöperative efforts at these conventions make district and local coöperation along these lines possible. The first step is closer relationship with physicians; those who have taken part in national and state displays will gladly communicate suggestions to others—it is one of the many opportunities stimulated by the formation of the Conference of Pharmaceutical Association Secretaries. (See also U. S. P. and N. F. Propaganda by O. U. Sisson, September JOURNAL, page 965.) Illustrations of the exhibits will be found elsewhere in this issue, together with further information regarding them. Your attention is also invited to "Plans for Institute Work in Iowa" by Secretary J. W. Slocum.

Pharmacy Week programs were pronounced successes nearly everywhere and so long as the professional thought directs, these annual occasions will be welcomed by the public and physicians. The directing thought should be that outlined in the "History of Pharmacy Week" by Robert J. Ruth, printed in July JOURNAL, page 696. Pittsburgh had a five days' celebration to which the public generally, including physicians and students, were invited and the response was most gratifying; further reference is made under "Local Branches."

The schools and colleges of pharmacy, equipped for making window displays, held to the educational motif, showing departments devoted to pharmacy, drug-yielding plants of the section in which the display was made, etc. Another window treated only one official item—phenol—in acquainting the public with the products derived therefrom, the therapeutic properties, application in public health activities, the dangers of handling it by those not qualified and who look upon it only as something to sell at a profit. The windows also instilled a better understanding of the practice of pharmacy, of the educational requirements, the service and protection given the public by qualified pharmacists. The educational maps have

heretofore been explained; as an informative effort and map printing the work was a success; likewise, as background of the display in the window, but in the reductions necessary for a photograph and still greater reductions in illustrations for magazines, the pictures do not show to advantage. Further deductions will be made in the legends under half-tones.

Window displays and pharmaceutical exhibits have a value, if there is an idea back of them to be conveyed to the public. Some of those featuring displays in drug stores are possessed with the thought that the people know drugs and medicines are sold and dispensed within and that items for display should be of merchandise from which greater profit-producing results can be expected. The purpose of this comment is not to discuss that phase, *but to point out the value of displays*—which acquaint the public with the importance of pharmaceutical education and service, the dangers in purchases of medicines from the unqualified, because below or above standard, indifferently put up or stored; sources of drugs, apparatus used in manufacturing, essentials of care and cleanliness—*that you are intensely interested in the conservation of public health.*

OPENING OF THE WASHINGTON BICENTENNIAL CELEBRATION.

OPENING the Washington Bicentennial Celebration at Baltimore, 1500 public school children planted 152 cherry blossom trees at Fort McHenry, a tree for each public school in Baltimore. The program was carried out under the chairmanship of James E. Hancock, a pharmacist, member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1907, son of a pharmacist—the late John F. Hancock, president of the AMERICAN PHARMACEUTICAL ASSOCIATION, 1873–1874, member of the ASSOCIATION for sixty years, from 1863 until his demise in 1923.

As president of the Society of the War of 1812 in Maryland, Mr. Hancock presided over the ceremonies. The trees are the gift of Wilbur D. May and the presentation was made by Dr. David E. Weglein, superintendent of Public Schools. Colonel Alvin K. Baskette, third corps area U. S. A., who has been in charge of restoring the fort, accepted the trees. In his remarks Colonel Baskette stated that the fort should not be considered a playground but should be visited in reverence, as a shrine to keep patriotism alive.

The ceremonies were under the auspices of the National Society, Daughters of the Revolution. Among other speakers, besides those mentioned in the foregoing, were: John H. Ferguson, representing Mayor Jackson; former Mayor, James H. Preston, chairman of the Bicentennial Committee for Baltimore; Jerome Stern, representing Mr. May; Mrs. Eugene J. Grant, national regent, Daughters of the Revolution. The invocation was delivered by Rev. George H. Buck, chaplain of Maryland Society Sons of the American Revolution. The children, accompanied by the Municipal Band, which furnished the musical program, sang "The Star Spangled Banner" and saluted the flag, which could be seen above the ramparts. The celebration was impressive and the program well arranged and carried out accordingly. The fact that Baltimore was the first city to erect a Washington monument made its selection as first, fit in the schedule of the celebrations which will continue through a twelve-month period. It is also the birthplace of a national flag and of the National anthem.

PROCEEDINGS OF THE CELEBRATION OF THE 300TH ANNIVERSARY
OF THE FIRST RECOGNIZED USE OF CINCHONA.*

THE table of contents of this publication includes an introduction by Anton Hogstad, Jr., an address of welcome by Dr. George T. Moore, Director of the Garden, and the following technical contributions: "Three Centuries of Cinchona," by Leo Suppan; "The Chemistry of Cinchona Historically Considered," by Edward Kremers; "The Medicinal Use of Cinchona," by George Dock; "Dr. John Sappington, Pioneer in the Use of Quinine in the Mississippi Valley," by Robert J. Terry; "Cinchona Culture in Java, Its History and Development," by M. Kerbosch; "Minor Alkaloids of Cinchona Bark," by Frederick Rosengarten; "The Cinchona Alkaloids in Medical Science," and especially, "The Quinine-Malaria Reaction as a Touchstone of Chemo-Therapy," by Torald Sollmann; "The Rôle of Quinine in the Cure of Malaria," by Kenneth F. Maxcy.

This is a botanical work of a very unusual character and of a high order. To bring together in one volume a summary of the taxonomic labors of so many eminent botanists as have written on Cinchona, including extensive field observations as well as herbarium studies, to follow with a detailed history of the behavior of the plants under cultivation in foreign countries, to discuss the pharmacognosy of their products, their chemical constituents and the variation of these in the several species and under varying treatment, their relations to human disease and their economic history, was an undertaking as wisely conceived as it has been successfully executed. The only serious omission is that of a study of the cultivation of the trees in the midst of their native forests, an omission that contributes not a little to the failure to have solved some of the problems that have been raised in the discussions recorded. The result of this series of contributions is to supply a volume of monumental importance, and one that will serve as a storehouse of information for all time.

Although every article included in this book is a masterpiece, the contribution of Suppan is entitled to special commendation. It is probably the best historical account of the development of our knowledge of Cinchona that exists in print. Most writers on this subject have been content to abstract and comment on such works as Markham's "*Peruvian Bark*," but this paper of Suppan's shows evidence of extensive and intense study of the technical literature of his subject, and an easy familiarity with it. He is not so fortunate, however, in his later pages, wherein he deals with the species and commercial products. It appears that his descriptions are mostly taken from his authors and that his decisions do not evidence personal familiarity with the things themselves. It is still more unfortunate that, in reaching his conclusions, he has neglected to take advantage of the evidence supplied by the South American plantations. In fact, this, which is in some respects the most informative portion of the whole Cinchona history, is not even mentioned. We note the following items of special interest in his admirable work.

The persistence of the evil results of Weddell's unfortunate, although temporary, misinterpretation of the relations of *C. Josephiana* is very notable in Suppan's discussion. So far as economics are concerned, these results were early eliminated

* Held at the Missouri Botanical Garden, St. Louis, October 31–November 1, 1930. Published by the Missouri Botanical Garden. Pages 258. Price \$5.00.

by the abandonment of the cultivation of that species, but scientific records as to taxonomy, pharmacognosy and chemistry are still littered with errors based on the examination of materials that originated in that obtrusive plant or of hybrids that developed from it in the Eastern plantations. It is unfortunate that Suppan, in the presentation of a historical work that is destined to exert great influence for a long time to come, did not improve his opportunity for the correction of this basic mistake, and thus terminate its farther extension. No more significant statement could be made than that which appears on page 89: "up to 1860, Dr. de Vry had obtained only 0.4% alkaloids from *Cinchona Calisaya* an analysis which was confirmed by Mr. Howard. Both declared it an inferior species. This was unfortunate, for the species was a hardy one, and as it required less care than the others, it has been extensively propagated." "Up to 1860," was the very period when *C. Josephiana* was being cultivated under the name "*C. Calisaya*," and no other species present there at that time could have given this low yield. It is also the species that is "hardy," and easily cultivated, which is not at all true, relatively considered, of *C. Calisaya*. On page 118, Suppan gives a fairly good description of this bark, but makes the astonishing statement that it was "medicinally not inferior to the genuine." Coming to *C. ovata*, var. *rufinervis* Wedd., which is in fact the most tomentose form of that species, Suppan refers to its bark as *Cascarilla Carabaya*, and quotes Weddell's statement that it was extensively used to adulterate the true *Calisaya*. This has always been true, even after cultivation had removed all reasonable excuse for the substitution. A typical *C. ovata* bark could scarcely be mistaken for that of *C. Calisaya* in mature condition, because the former is nearly smooth externally, while the latter is reticulately fissured and is much thicker. *Calisaya* bark, when young, is not fissured, and may wrinkle longitudinally in drying, in which condition one can easily be mistaken for the other. The extent to which the spurious bark was substituted by the collectors may be judged from the following occurrence. On arrival at Sorata, all bark packages were opened and each quill was examined separately by an expert. Originally, the spurious bark was destroyed as encountered, but the brilliant idea occurred to the largest buyer, of storing the rejected bark, insuring it at full value as though genuine, and having it burned to secure the insurance. It is recorded that a quarter of a million dollars was thus fraudulently obtained.

On page 119, Suppan says of it, "That *Carabaya Bark* was perhaps derived from *C. ovata* var. *B. rufinervis*, which in Peru is called *Cascarilla Carabaya*, or from the variety *a vulgaris*, as Weddell suggested, or from any variety of *C. ovata* at all, is uncertain. Pereira says that it was first imported into London in 1846, and that it came from Carabaya." This uncertainty of Weddell was explained and dissipated by information subsequently gained in Bolivian plantations, where I have seen innumerable trees showing every degree of variation, from those which were almost pure *Calisaya* to others that were almost pure *ovata*. It could not be otherwise than that a number of varieties, some referred to one and some to the other species, should have been proposed by those who did not know of the parental origin of the forms.

Suppan's excellent description of these barks gives evidence of perplexing variability in their characters.

As to Weddell's *morada* and *verde* varieties, mentioned on page 115, the explanation is entirely different from that of hybridity. Both forms are abundant and

conspicuous in the plantations, but there never has been any explanation offered for their occurrence. They have a common origin, it is said, even from the same seed pod, and the seed of either will produce both forms. Some workmen thought that they could distinguish the two by the appearance of their bark, but I was not able to satisfy myself positively that this was so. Neither did there appear to be any difference in their alkaloidal content, although there have been conflicting statements in regard to this. It was not so with the *zamba* (black) variety which had a characteristic appearance and was of superior quality. It had a strong resemblance to Ledger bark, and always suggested to me the possibility, if not probability, of a hybrid origin between that and *Calisaya*. It appears to be what Weddell has called *C. Calisaya*, var. *microcarpa*.

Suppan's reference on page 65 to the value of the length of the stamens in classification records a view that had to be abandoned (as was similarly true in the case of *Erythroxylon*) when it became known that *Cinchona* is very subject to dimorphism and even trimorphism, a structure that is responsible for the ready hybridization of the species.

Various references are made to published statements that *Cinchonas* were found in the vicinity of Honda, Columbia and also in the vicinity of Bogota. While not able to offer a positive statement on this subject, it seems to me very unlikely that the genus occurs in either of these places. The related genus *Remijia* is abundant there, and it seems probable that its two species were mistaken for *Cinchonas*. Suppan, by the way, overlooks the presence of quinine in *Remijia* bark, when he says that quinine does not occur in any of the related genera.

Kerbosch's "History of Cultivation in Java" brings into review the principal facts of this history, in so concise and so practical a way as to leave the reader with a clear picture of the course of events in that connection. Although there are enlightening references to *Cinchona* cultivation in British India, these references are not so numerous or full as they might have been made, in the interest of a better understanding of the author's own subject. Even in the matter of his own history he sometimes leaves the picture slightly deficient in detail, and in one instance, actually misleading. Some of his conjectures regarding botanical relationship do not appear justified by observations made in the native homes of the species. His views, briefly stated, are as follows: That from a genetic standpoint, *Cinchona Ledgeriana* is the original of what may be called the *Calisaya* group; that *C. Calisaya* itself is a hybrid of *Ledgeriana* with another species, probably *C. Josephiana*; that *C. Calisaya* has a number of forms or varieties which vary perceptibly in "botanical" characters and from 2% to 6.9% in alkaloidal content.

These deductions, it must be remembered, were based on observation of the plants as they grew in the Oriental plantations. None of the eminent botanists who studied the plants in their native home offered these particular suggestions, which appear quite inconsistent with facts of my knowledge. *Cinchona Calisaya* is in fact the most definitely characteristic of all the species that I have known in the field, with the possible exception of *C. Josephiana*. If it could be a descendent of *C. Ledgeriana* at all, it would be so by variation and not through hybridity. If a hybrid plant, it would undoubtedly grow associated with one or both of the parents, while if a variety, it would be more likely to have a distinct range of its own, and this is in fact the case. *Calisaya* grows in the northern part of Bolivia and adjacent

Peru, while *Ledgeriana* has a distinctly southern range, notwithstanding that the two overlap. That *C. Josephiana* should be one of the parents of *Calisaya* is specially improbable, both on the ground of physical characteristics, and because of the very distinct altitudinal distribution of the two. It is difficult to see how there could be any general mixing of *Josephiana*, a straggling shrub of high, dry, sunny hillsides, with a large tree like *Calisaya*, growing in the deep forests of the lower ranges. So far as appearances indicate, the *Ledger* tree might much more easily be a hybrid of *Josephiana* and *Calisaya* than for the case to stand as suggested by Kerbosch. However, this view also is opposed by the facts as to range of the two species and by their relative alkaloidal content.

Coming to the so-called varieties of *Calisaya* in the Java plantations, which proved so perplexing in regard to their variable alkaloidal content, I note that precisely the same condition was observed in the Bolivian plantation, but in the latter case the matter was fully explained. This explanation was not merely suggested, but it was abundantly proved; that the lower yielding forms were not "varieties" of *Calisaya*, but clearly hybrids of that species, mostly with *C. ovata*, the latter being regarded as the "weed" of Bolivian *Cinchonadom*, a hybridization which it was found impossible to prevent in the Bolivian plantations, no matter how carefully the process of seed production might be guarded. These views regarding botanical relationship, which Kerbosch has accepted, belong to the early literature of the subject, and were based on very fragmentary evidence. The evidence afforded by the Bolivian plantations, which has supplied the key to correct interpretation, appears to have been greatly neglected by those engaged in the study under review. In no case has Bolivian cultivated bark, proceeding from trees definitely identified as pure *Cinchona Calisaya*, and those barks similarly identified by pharmacognostic methods, shown any such variation in alkaloidal content as that above quoted. Barks so identified have been fairly uniform in their yield of approximately four or five per cent of alkaloid. The entire literature of alkaloidal content of bark supposed to be from *C. Calisaya* and showing such wide variation of content, has been based on false assumptions of botanical identity. In all cases of Bolivian cultivated barks, where the identity could be established, the low-yielding barks have been proved to be of hybrid origin.

Kerbosch omits all mention of the greatest of all mistakes made in connection with *Cinchona* cultivation, namely, that of stocking the Oriental plantations with *C. Josephiana*, in the belief that it was a variety of *C. Calisaya*. This mistake was originally made by Weddell, in 1849, but ten years later, when he realized the enormous losses that had been sustained, especially in British India, as a result of acting on this belief, he corrected his mistake and unqualifiedly declared this plant to be a distinct species.

In his enumeration of the botanists in Bolivia who contributed to the development of *Cinchona* culture in Java, Kerbosch has omitted to emphasize, or even to mention, the position that was taken by Charles Ledger toward the mistaken operations of his associate and chief. It would be a great injustice to this man to perpetuate the neglect of Markham, in his history of *Cinchona*, to record the fact that the latter persisted in the view that the worthless *Josephiana* was a variety of *Calisaya*, and, on that basis, almost confined his collection of plants and seeds to that species, in spite of Ledger's protests. It is true that Ledger was a merchant

and laid no claim to a professional status in botanical work. Nevertheless, he was an ardent lover and a keen observer of plants and his knowledge of the various *Cinchona*s of the Bolivian forests, among which he had long resided, was superior to that of any of the visiting botanists. His commercial operations, moreover, had included trading in *Cinchona* bark, and he had accumulated much evidence as to the superiority of certain kinds and the worthlessness of others. As Kerbosch says, Markham himself was not a botanist and should have given heed to the advice of one with the information that Ledger possessed. The history of Markham's operations contains unmistakable evidence that in his descent of the eastern Andean slope he encountered *Cinchona Josephiana* long before reaching the highest level at which *Calisaya* grew and that, relying on Weddell's opinion, he collected seeds and plants of this species in large quantity. We learn farther that after having visited the region where other species grew, he stopped again on his return and increased his collection of *C. Josephiana*.

With no definite evidence as to the fact, it is easy to see the great probability that hybridization of either *Calisaya* or *Ledgeriana* with *Josephiana* would be almost certain to occur in the British and East India plantations, where the latter species had been planted to the number of hundreds of thousands.

From a personal point of view, I cannot do less than point out that in 1887, I presented to the American Association for the Advancement of Science a careful account of the cultivation of *Cinchona* in Bolivia, which was also published in the *Pharmaceutical Record* of October 1st of that year. The paper was illustrated by abundant herbarium specimens of all the species and forms that I could find there, and by long quills of trunk-bark and wood sections, all of which material is still available for study. As a result of later studies, conducted at the Kew Herbarium, I found it necessary to correct some of my former conclusions, the most important of them being the substitution of the name *Cinchona Josephiana* in nearly all places where that of *C. amygdalifolia* occurs. It now seems desirable to reprint that article with such changes as have been indicated by subsequent study.

It is theoretically true that absolute knowledge of hybrid origin can be secured only by experimental pollination, but in cases like the present, in which thousands of plants are produced under conditions known to favor the crossing of two particular species, and the progeny shows every indication of such origin, the conclusion amounts to practical certainty.

That the Ledger species is subject to the same probabilities of hybridization is indicated by Kerbosch's statement, "In any case, it is certain that the plants obtained from the imported seeds of *C. Ledgeriana* were far from being homogeneous," and he proceeds to show that two distinct variations were found among these plants. This evidence agrees exactly with the experience of the Bolivian planters. One of them showed me a tree of typical *Ledgeriana* which he had planted in an angle of his house, where it was protected so far as possible from the access of foreign pollen, and which he preserved for the production of seed. But he declared that all his precautions could not entirely prevent cross-pollination, and that the seedlings derived from this tree would have to be carefully purged of hybrids before being transferred to the plantation. That hybridization has occurred between *Calisaya* and *Ledgeriana* is also very probable, and Kerbosch gives testimony in support of that supposition, but this, it must be remembered, is a very different

thing from saying that *Calisaya* is not a true species, being a hybrid between *Ledgeriana* and *Josephiana*.

Kerbosch has paid a high tribute to the service performed by Markham, but he might have gone much farther in his eulogy of that remarkable man, without incurring danger of being charged with exaggeration. His journey into the Cinchona forests involved all the sufferings and dangers that are familiar to those who have read accounts of the life and labors of the Cinchona collector, but difficult as was this journey, it was made under comparatively favorable conditions as to beasts of burden, guides and assistants, regularly traveled roads and trails, comfortable shelter at night and a supply of food amidst friendly people. Little did Markham realize, as he made that journey, that on his return he was to be deprived of all these comforts and of most of the barest necessities of life, pursued by enemies, with other enemies lying in wait, encumbered with the precious but troublesome bundles of living plants, and compelled to find a new way through the jungles and over the snowy peaks, in order to avoid watched trails and known passes. The present writer, who has made the transit of the Andes eight times, at different points, has found his journeys difficult and exhausting enough under the best of conditions, and he would be appalled beyond expression at the prospect of being compelled to make the journey over unknown routes, without food and shelter, and with scanty clothing to protect against the frightful cold of those Alpine summits.

The contributions of Sollman and Maxcy are of absorbing interest, but quite disappointing in their revelation of the fact that we do not yet know just how quinine acts in causing the patient to recover from malaria. They do eliminate the idea of a "specific" nature of the cure, as the term is ordinarily used, and show that the quinine, instead of acting altogether directly on the germ, promotes the ability of the body to fight its own battle. This again demonstrates the importance of general systemic treatment and justifies faith in the helpfulness of many remedies on which we depended before quinine and cinchona were known.—H. H. RUSBY.



Phenol window display, University of Minnesota College of Pharmacy.