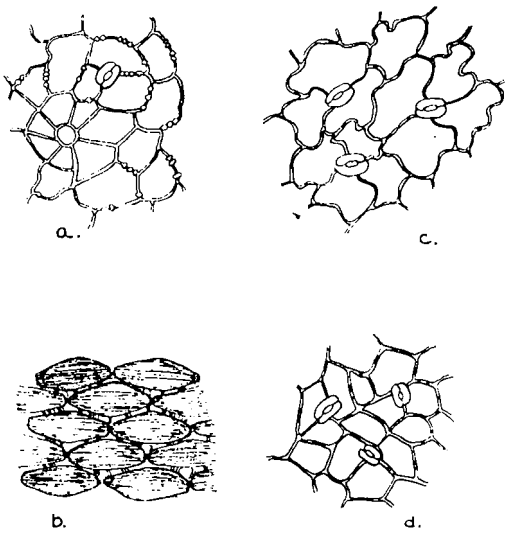

Fig. 4.—*Digitalis ambigua.* Epidermal Tissue: *a.* Upper epidermis showing granulated walls and hair base; *b.* Upper epidermis over large vein showing striations; *c.* Lower epidermis showing wavy walls and numerous stomata; *d.* Lower epidermis showing rectilinear walls and stomata.

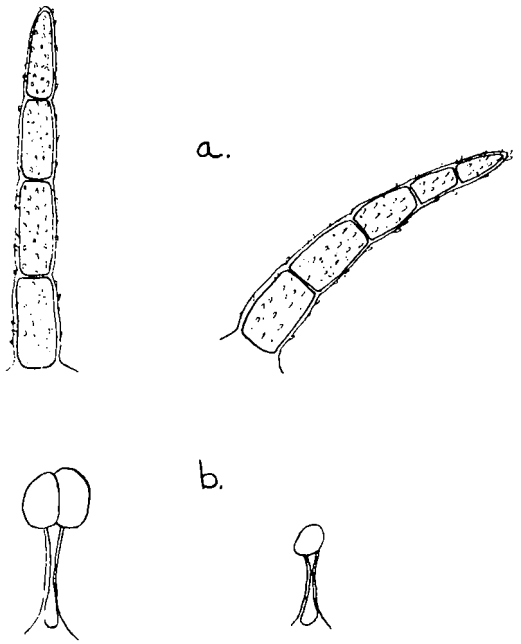

Fig. 5.—*Digitalis ambigua.* Hairs: *a.* Non-glandular, × 110; *b.* Glandular, × 250.

under high magnification and give the hair a warty appearance.

The most diagnostic and distinguishing characteristics of powdered *Digitalis ambigua* are the surface sections and the non-glandular trichomes as described above.

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The Examination of and Standards for Imported Drugs from 1790 to 1908*

By Lyman F. Kebler†

Following the presentation of my paper on establishing the Drug Laboratory, before this section, at the Atlanta meeting, a prominent member of this Association, reminded me of the low quality of some of the imported drugs for many years and the findings of Dr. Rusby, in particular, presented at a meeting of this Association abut the time the Drug Laboratory was organized, and asked why we did not start on the import work

* Presented to the Historical Section A. PH. A., Richmond meeting, 1940.

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earlier? I explained to him as well as I could briefly that the work on drugs, at the ports was started as soon as feasible and funds were available. In order to make the information more readily available, I thought it might be of service to present a brief sketch on the examination of drugs and the standards therefor, at the ports of entry, covering a little more than a century. The examination of imported drugs and chemicals began with the tariff act of 1790 (1). This act provided, among other things, for the inspection and testing of wines and alcohol. Except for revenue purposes, tariff law standards are of little value. Later tariff acts gradually expanded the work, but adulterated, spurious and low grade drugs and chemicals kept coming into the country. Pharmaceutical chemists exposed and continued to expose, some of these shortcomings for years without any apparent improvements. The leading apothecaries and physicians became greatly disturbed. Improvements in drug standards and education came slowly in our country. The United States Pharmacopœia came in 1820 and several colleges of pharmacy were founded previous to the enactment of the 1848 drug and chemical import law.

THE 1848 DRUG AND CHEMICAL IMPORT LAW

This law was enacted largely through the combined efforts of the medical and pharmaceutical professions. The latter exposed some of the villainous adulterations and substitutions, memorialized Congress, and the former, in a memorial to Congress, pointed out the harm done by such medicines to both physicians and their patients. These unfortunate and even serious conditions appealed to members of Congress. Senator John A. Dix, of New York, in April 1848, introduced a bill on the subject. In the House a Committee was appointed to study the problems. Hearings were had. Some awful conditions were disclosed. Representative Thomas O. Edwards, a physician of Ohio and chairman of the above Committee, gave the subject close attention, particularly from the viewpoint of physicians. On June 2, 1848, he reported (2) for the Committee and submitted a bill to the House, which bill was speedily passed (3) and referred to the Senate. The Senate substituted the Dix Bill, which bill was somewhat amended, passed both branches of Congress and became a law June 26, 1848 (4). This law recognized as authorities the United States, the Edinburgh, London, French and German Pharmacopœias and Dispensatories. It must be said that this law was most liberal in the number of authorities recognized. All of these works conained good methods for determining the purity of many chemicals used as medicines but were defective in the matter of crude plant drugs and their derivatives.

The enforcement of this law was placed in the hands of the Secretary of the Treasury. On July 8, he issued instructions, directing that the drugs, chemicals and medicines, imported from the respective countries, whose pharmacopœias and dispensatories were recognized by the law, must comply with the standards contained therein and that all other drugs, chemicals and medicines, originating in other countries must comply with the United States Pharmacopœia and Dispensatories. This law has never been repealed.

The Secretary of the Treasury on October 10, 1848 appointed (5) Congressman Edwards to study and ascertain how well the law was enforced and working. The Doctor made a very favorable and exhaustive report (6).

Dr. M. J. Bailey, special examiner at the port of New York, reported (7) on the practical operation of the law June 9, 1849. This report in a measure supported the findings of Dr. Edwards but was less optimistic. Dr. Bailey pointed out that there are few physicians, even recent graduates of our best medical schools, versed in the practical detection of drug adulteration and that the majority of those who prepare and sell drugs are deficient therein. This is in a measure true even in our own time.

The ugly head of politics, in the matter of appointing drug examiners, soon intruded itself, and became an early disturbance. The best interests in the drug trade combatted this intrusion but lost heart in the end. Political preference and not ability obtained. In this connection the reader is referred to Curt P. Wimmer's "History of the College of Pharmacy of the City of New York," page 203 (1929). He certainly presents an assortment of troublesome elements then worrying the apothecaries.

LACK OF EFFICIENT STANDARDS FOR LAW ENFORCEMENT

A lack of efficient standards for some drugs for law enforcement purposes, soon became evident. This was true for all of the authorities recognized at the time. The pharmaceutical profession became greatly annoyed. Reliable standards must be had for medicines. The Trustees of the New York College of Pharmacy became so disturbed because of the lack of standards for some important drugs and the difficulties resulting therefrom, that they sent invitations to the then existing Schools of Pharmacy, to send delegates to a meeting called for October 15, 1851 (8). At this meeting Dr. Charles B. Guthrie was elected president. The belief prevailed that the lack of adequate standards could not be over-emphasized. Standards were proposed for a number of drugs, but unfortunately no methods for determining the several percentages

proposed, were provided. Why the job was not completed the records do not show. The lack of reliable standards harks back to the II or 1840 revision of the United States Pharmacopœia, a work which the revisors had no idea would become a legal standard.

These difficulties were pressing at the time, when the III or 1850 revision of the United States Pharmacopœia, there were two editions, was under way. Why the Committee of Revision did not, under the circumstances, provide better standards with methods of analysis is not clear. There certainly were some methods available at the time, to provide for some of the deficiencies. Under the cricumstances the port examiners were compelled either to utilize the existing methods, or devise some of their own, or let the proposed standards go by default. Under the conditions uniformity at the various ports was not possible. It is interesting to note that standards for some drugs were published in 1857 (9) by the Treasury Department, but again no methods were given. Virtually the same standards were published by the Treasury Department as late as 1884, but still no methods of analysis.

REPORT OF DRS. GUTHRIE AND BAILEY ON WORKINGS OF 1848 LAW

The Secretary of the Treasury commissioned Dr. Charles B. Guthrie to study the workings of the law. His general report (10) is full of the good things the law accomplished and was accomplishing, but there was still much to be done. He pointed out that the imperfect standards for crude drugs and medicines in works on pharmacy and materia medica made it necessary for each examiner to fix his own standard for such important drugs as opium, scammony and the cinchona barks, which did not make for uniformity. He pointed out that the publicity given the subject was working a revolution in the drug trade. Public opinion demands it. Said he: "A man is no longer considered competent to sell, dispense and deal out medicinal articles affecting the health, life and happiness of his fellow-beings, simply because he can calculate a percentage or make a profit. Physicians, professors of materia medica and teachers of practical pharmacy and chemistry are feeling it."

From a reading of this report one gets the impression that the detailed report, referred to, copy of which I have been unable to locate, might not make things look so favorable. The political discord in the matter of the drug examiners gives color to this idea.

Dr. M. J. Bailey's report made about the same time (11) presents quite a different picture, of conditions obtaining regarding drug importations. He calls attention to the large amounts of drugs rejected by him at the port of New York, since the enactment of the law. He alleged that he had rejected all told 610,000 pounds of adulterated, spurious drugs and drugs unfit for medicinal use. Among the rejections may be cited: 304,135 pounds of spurious Peruvian bark, 31,838 pounds of senna, 6864 pounds of iodine and 3720 pounds of potassium iodide. He observes that the best devised system of standards and tests, would be of little avail, unless the work is entrusted to a personnel having the requisite education, and being honest and competent.

DRUG ADULTERATION AND DEFECTIVE STANDARDS THE IMMEDIATE CAUSES FOR ORGANIZING THE AMERICAN PHARMACEUTICAL ASSOCIATION

Previous to the adjournment of the above assembled delegates, provisions were made for the President to send invitations to authorized bodies, to name delegates to a convention to meet the first Wednesday in October 1852, for the purpose of organizing a National Association, to meet annually. The call for such a convention, to meet in Philadelphia, October 6, 1852, was issued by the President, Dr. Guthrie. The delegates assembled in Convention, in accordance with the call (12). President Guthrie was unable to attend. This Convention resulted in the formation of the AMERICAN PHARMACEUTICAL ASSOCIATION. It may therefore be said that the defective standards and adulterations were the immediate causes for the formation of this ASSOCIATION in 1852.

One would naturally assume that with all of this agitation about defective standards and lack of methods of analysis, the voids would have been bridged to some extent at least, by the IV or 1860 revision of the United States Pharmacopœia, or the V or 1870 revision but neither provided much help. Both revisions prescribed a percentage content of certain alkaloids for opium and some cinchona barks, but no methods for estimating the same. In the case of opium, the morphine was to be determined by an "Official Process," but no "Official Process" was given. Scammony was required to contain 75 per cent of ether soluble material. A minimum and a maximum percentage of alcohol was prescribed for both brandy and whisky.

The British Pharmacopœia of 1864, which became an authority under the 1868 English Food and Drug Law, embodied material advancements in tests and methods of analysis. It required, for example, a percentage content of certain alkaloids for opium and some cinchona barks, with methods of analysis. Similar improvements did not come in the United States Pharmacopœia until the VI or 1880 revision, which revision was recognized as a standard by a number of the State Food and Drug Laws, enacted during the eighteen eighties. Subsequent revisions of this work embodied similar advancements of their time.

The tariff laws and the revenue derived therefrom, it is often alleged, played a more important role than did pure and safe medicines for the sick. It must, however, be conceded by all that in spite of the many handicaps encountered in the enforcement of the law of 1848 that material improvements in imported drugs resulted in the course of years.

EXTENSION OF POWERS OF THE SECRETARY OF AGRICULTURE TO IMPORTATIONS

In 1890 Congress passed a reprisal law (13) covering the importation of adulterated and otherwise, of foods and drugs. Its enforcement was vested in the Secretary of Agriculture, but required a proclamation by the President, to make it effective. The drug portion was apparently never called into action.

The appropriation act for the Department of Agriculture, March 1, 1899, authorized the Secretary to refuse entry of adulterated foods and drugs, which from an examination he had reason to believe would be dangerous to the people of the United States. Subsequent appropriation acts for the Department, contained the same authorization. In time a limited fund was made available for the work but it was restricted to foods. The above gives some idea as to the environment in which the Drug Laboratory found it necessary to adjust its early activities. More will be pointed out later. The above restriction to use the available money for port work for foods were first, because of the limited funds available, second, because drugs were already being inspected under the 1848 drug import law and third neither Dr. Wiley nor I wished to disturb the work of our friends engaged therein. But we kept more or less in touch with it. Indeed Dr. Rusby and I discussed the problems from time to time as we met. In time sufficient money was made available to establish branch laboratories at several ports by the Bureau of Chemistry. Their work was still restricted to foods, but the Drug Laboratory was permitted to have the force collect samples of drugs for examination. The records show that during the fiscal year ending June 30, 1904, a number of drug samples were taken and examined. This line of work was, however, largely crowded out, because of a study of the purity of chemicals, some of which were imported, testing out methods of analysis, the examination of proprietary medicines for Congress in connection with the proposed Food and Drug Legislation and nostrums for the Post Office Department, in the matter of the fradulent use of the mails.

In addition to the limited funds there was a decided shortage of available qualified workers, under the restrictions imposed by the Civil Service Commission. I am a staunch advocate of the principles of Civil Service, but freedom of action is often hindered, probably to the good in the long run. When we wanted to add to our force the Commission prescribed a four year University training or its equivalent which practically barred most of the College of Pharmacy graduates and others at the time, most of whom had much less training for a degree. The Commission was inflexible in this matter. Let me cite just two cases—Drs. H. H. Rusby and Charles H. LaWall. After the employment of Dr. Rusby it was found necessary to cover him into the Classified Service. After outlining the work and the salary to be paid, the Commission ruled that such a position called for a Ph.D. degree or its equivalent. It developed that Dr. Rusby had had only a short two-year course that led to a medical degree. We were at first afraid that the Commission would not pass him, the outstanding man in his field. His outstanding practical experience and contributions just got him a passing mark.

Dr. LaWall was an eminent analyst, an outstanding teacher, thoroughly versed in every branch of the drug trade, but had only a short two-year course in a College of Pharmacy. The Commission prescribed a four year University degree, or its equivalent, in his case. His outstanding practical work and contributions, as in the case of Dr. Rusby, just gave him a passing mark. Others with a longer academic training, but far less qualified, received higher grades and therefore were accorded preference to positions. This did not make for a good feeling.

Under these circumstances I urged longer courses and higher training in our Colleges of Pharmacy. I know that this advice was gratuitous and was not kindly received in some quarters, but I had experienced the mental sufferings of some of my friends and hoped to help obviate like grief to future graduates.

SERVICES OF THE BEST QUALIFIED AND AVAILABLE MEN SOUGHT AND SECURED

It was the aim of Dr. Wiley and myself to secure the services of the best qualified and available men and I believe that we were largely successful. For the port of New York City and other ports along the Atlantic Coast, we secured the services of Drs. Rusby, L. D. Havenhill and Charles H. LaWall; for New Orleans and other Gulf ports, Dr. Edsel A. Ruddiman; for Seattle, Dr. Charles W. Johnson; for San Francisco, Dr. Albert Schneider and for some of the inland ports, Professor J. O. Schlotterbeck.

The New York port was by all odds the most important, Drs. Rusby and Havenhill were put in direct charge of the drug work. Dr. Havenhill entered the service June 5, 1907, and Dr. Rusby, July 13, 1907. The former on a full time basis and the latter on a per diem basis. If the decisions of our port workers were contested, the appeals came to Washington. Certain attorneys, at the beginning, protested many of them, not so much as to their findings but on the principle that we were going beyond the law, which some at the beginning felt would not be enforced. Some of the importers contended that they could bring in anything they desired, by marking the goods as to their true character which was largely correct, but they further maintained that after the goods are once entered, they could do anything with them they desired. We held that defective drugs, though properly marked at the port of entry, could only be used in the manufacture of other preparations, by carrying along the importation markings, except when the preparation is standardized, or used for the manufacture of an active ingredient, say quinine, or the deficiency is otherwise adjusted. We even carried our position into court and were there sustained. It is true that if

an importation crossed the state lines properly marked we were helpless as to what was done within the states. That problem rested with the states.

BEGINNING OF WORK ON DRUG IMPORTS AND SOME FINDINGS

Before we were even organized for the drug work, the San Francisco force came across an importation of smoking opium, detained the shipment and sent several cans to Washington for a decision. I studied the case at considerable length. It looked like a borderline case. There was an import duty of $6.00 a pound, which raised the question as to whether the Treasury Officials might not object to its exclusion. I decided on a course of action. In time I took the case to Dr. Wiley for his decision, related the whole story as I saw it and stated my opinion and the reasons therefor, that it was a close case, but thought that under the import section of the law we could keep it out. He lifted his eyebrows, asked a few questions, then said: "I agree with you, it is a dangerous product and it is our duty to keep it out if we can—prepare instructions to that effect." Our decision set things in motion. Attorneys representing the importer, the shipper, a banker and an insurance company protested vigorously but the Treasury Officials sided with us. We stood firm. All finally agreed to abide by our decision without carrying the case either to the Secretary or the President, as was often done, during the early days. This settled the question of importing smoking opium. We believed the decision was right and in the interest of humanity. Other importations were offered, but the above set a precedent which made future action on like shipments easy. We were told that our action simply meant smuggling the stuff, which of course was not our problem.

Dr. L. D. Havenhill spent a short time in Washington to get a line on the work before going to New York, but Dr. Rusby being more or less conversant with the work at the New York port began his work directly at the port. After a little more than a month and a half given to the work, Dr. Rusby seemed to be rather pleased with the good quality of the drugs imported (14) at the time. This of course was gratifying to him because of his previous experience and the fact that the appraiser had told him that he would find things bad, but his jubilation did not last many months. It happened to be one of those anomalous affairs. At the end of fourteen months of inspection work he had a different story to tell (15).

As a prelude let me say that the "Committee on Drug Adulterations," of this ASSOCIATION, in its 1906 report (16) alleged that "adulteration as such, with intent, is quite rare." Some members did not agree with the claim and Dr. Rusby's findings at the port, at the end of fourteen months showed quite the contrary. Let me just note a few of the intentional adulterations he found and his remarks thereon. If a consignment was rejected at the New York port some importer, would brazenly threaten to reship it to a port where "we know we can get it in" and some actually did it, for a time. We were of course at the outset unable to cover all of the ports of entry as thoroughly as the City of New York. Indeed some of the adulterated or low grade drugs were imported in bond and sent to some of the inland ports like Chicago, Minneapolis, Detroit and St. Louis. Here again we were unable early to provide trained workers, but we caught up with them in time.

A consignment of five tons of powdered olive pits made its appearance. The importer alleged that it was to be used "as a filler for chicken food." We were suspicious, but could not refuse them entry. In time an examination was made of some of the powdered goods of the importer and not unexpectedly found olive pits in five samples of his powdered drugs. A large dealer on being informed that his ground belladonna root contained 50 per cent of ground olive pits, protested loudly but later found the report to be correct and learned that his miller was systematically indulging in such practices. Kamala, powdered gentian and ipecac were found mixed with goodly amounts of ground olive pits. Turmeric was adulterated with wheat starch.

In another instance an importer strenuously objected to the rejection of "belladonna root," that was all poke root and that it did not contain any belladonna root at all. Dandelion root contained 48 per cent of ash, including small stones sifted to about the size of the fragments of the root. Saffron adulterated with calendula, artificially colored and weighted. Cut dandelion root entirely substituted with chicory trimmings. Artificial benzoin. Digitalis leaves mixed with stramonium leaves. Maracaibo bark substituted for cinchona bark. Senna leaves broken, 30 per cent of ash. Belladonna leaves containing from 50 to 80 per cent of stems and fruit. Not much adulteration here that is not intentional. Relative to the results in this report Dr. Rusby says: "The importance of this demonstration can hardly be over-estimated. The plea of non-intent has been in the past the strongest defense offered. It should not have been regarded as a good one, even if justified, for responsibility is fixed, with or without good intent. The evidence this day presented, of a strictly legal character, is conclusive that there is a large amount of adulteration, pursued on a systematic and scientific basis, and with the employment of expert assistance. It is a very easy, safe and agreeable thing for men to publicly claim non-intent for each other, but a very disagreeable and more or less dangerous for one to publicly charge evil intent. Pharmaceutical education has been just as guilty of false pretense and fraudulent output as has drug purveying, and the present situation is going to show the necessity of the states' making suitable provision for the thorough education of inspectors and assayers, from their preliminary education up to their technical training."

These are very positive, far reaching charges;

ones that the Chief of the Drug Laboratory would hardly venture to make, even though they were all within his knowledge and experience. He would have lain himself open to violent attacks from many quarters but he knew that they were all true and the half had not been told.

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Book Reviews

The Nature of the Chemical Bond and the Structure of Molecules and Crystals, by LINUS PAULING. 2nd Edition. xvi + 450 pages. Cornell University Press, Ithaca, N. Y., 1940. Price, $4.50.

This book is a clear explanation of the different ways in which atoms are held together to form molecules. It takes up the structures of many inorganic and organic compounds in detail and, in so doing, it gives the results of electron diffraction measurements and descriptions of a considerable number of x-ray analyses of crystals. This, the second edition, contains 21 pages more than the first largely because of the addition of two sections and the discussion of some newly determined structures. The book is of particular interest because, although it outlines the ideas involved in the quantum mechanical treatment of valence and structural chemistry, it describes the new developments in a thorough and satisfactory manner without resorting to the use of higher mathematics.—A. G. D.

Annual Review of Biochemistry. Volume IX. JAMES MURRAY LUCK and JAMES H. C. SMITH, Editors. 744 pages. Annual Reviews, Inc., Stanford University P. O., Calif., 1940. Price, $5.00.

This, the ninth volume of the series, covers the scientific contributions made during 1939. In addition, reviews on the following topics have been included: plant pigments, biochemistry of the lower fungi, biochemistry of malignant tissue, organic acids of plants, clinical application of biochemistry, soil microbiology and the application of microchemistry to biochemical analysis. Three new topics are presented—the biochemistry of the viruses, application of radioactive indicators in biology and insect biochemistry. The volume contains both author and subject indexes.—A. G. D.

Kingzett's Chemical Encyclopædia. Revised and Edited by RALPH K. STRONG, Ph.D. D. Van Nostrand Company. 6th Edition. 1940. 1088 pages. $14.00.

This, the sixth edition of Kingzett's Chemical Encyclopædia, presents a book considerably enlarged in size and contents over previous editions. Reference is made to many new industrial solvents and the section on chemical engineering has been expanded to include a consideration of materials, energy, apparatus and economics. The section on bacteria has been brought up to date, the section on coal carbonization has been completely rewritten and the sections on proteins and vitamins have been enlarged. A new feature of the book is its tabulation of production and imports by countries of widely used chemical commodities. One of the most valuable features of the book is believed to be its inclusion of many commercial names of chemicals, thus making it a commercial index to chemicals as well as a dictionary. The volume should prove to be useful as a reference work for every day use by pharmaceutical chemists and pharmacists.—A. G. D.

The AMERICAN PHARMACEUTICAL ASSOCIATION has received a copy of the annual report for the year 1939 of the Egyptian Government Central Narcotics Intellegence Bureau for the Alexandria, Port Said, Suez, Cairo and Provincial Branches. The report covers activities with respect to seizures on land and sea in the territory within the above jurisdiction. The narcotics named are Indian hashish, heroin, opium, etc. The records of the offenders are searched for prior offences and these are made of record. Information is also sought as to the history of the individuals—their trade or profession, habits, frequency of imprisonment, dosage amounts of the narcotics consumed—the dosage, if chemists are required to discover the addiction, determining the legal phase. Interesting illegalities of cases enter into the reports. The illegal drugs are hidden in various ways—in the stomachs of camels—illustrations show tins containing opium, hashish, etc.—E. G. E.

Reference Book of Inorganic Chemistry, by LATIMER and HILDEBRAND. The Macmillan Company. 4th Edition. $4.00.

The fourth edition of this reference book follows the third by only two years, which is indicative of