Report on the Progress of Pharmacy

For the Year 1912

(Fourth Installment.)

Allantoin: The Active Constituent of Comfrey—Method of Isolation.—At the request of Dr. C. J. Mackalister, an investigation of the rhizome of the common comfrey (*Symphytum officinale*) was undertaken by A. W. Titherley and N. G. S. Coppin in order to ascertain, if possible, the constituent which was responsible for its remarkable therapeutic properties (see *Comfrey Rhizome* under "Materia Medica"). The results of their exhaustive investigation prove these properties to be due to a crystalline principle, which they have identified with allantoin, a constituent of urine, and obtainable synthetically by the oxidation of uric acid. The allantoin was obtained by Soxhleting a number of portions of the coarsely powdered dried rhizome with alcohol to exhaustion, evaporating the separate extractions to about one-fourth the volume for weight of the drug used and setting the concentrated liquid aside for at least twelve hours, during which time an incrustation was formed, consisting of impure allantoin and sugar. This was removed and treated with a small quantity of water, the same being used successively on all the portions (six) so as to remove the sugar without appreciable loss of the sparingly soluble crude allantoin, which was recrystallized from hot water and eventually obtained absolutely pure. It formed perfectly colorless and transparent crystals which melted at 227° with decomposition and gas evolutions and previous darkening in color, and proved to be identical in every respect—in composition, character and reactions—with allantoin obtained synthetically from uric acid by cautious oxidation, using Behrend's method slightly modified. The authors conclude that the rhizome of *Smyphytum officinale* contains allantoin to the extent of 0.6 to 0.8 per cent, calculated on the air dried material, and that the therapeutic properties of the rhizome are due to this constituent. It also contains large quantities, not estimated, of soluble carbohydrates (gums and sugars), together with catechu resins and tannins, and a small quantity of volatile oil.—Pharm. Journ. and Pharmacist, Jan. 27, 1912, 92-94.

Chrysarobin vs. *Chrysophanic Acid: Question of Pharmacological Identity.*—In a recent number of Rep. de Pharm (1912, No. 6), P. Lemaire calls attention to the variability of commercial chrysophanic acid, which he attributes to the fact that more or less pure chrysrobins are generally supplied under the name of "chrysophanic acid." In consequence the preparations made with the commercial acid are very variable as supplied in different pharmacies. Commenting on this, the Pharm. Ztg. observes that it is a common practice of the wholesale drug trade in Germany to refer under Acidum Chrysophanicum in their price list simply to chrysarobin for definition and description; an obvious error, since the G. P. clearly defines what is to be understood by chrysophanic acid; but unfortunately it mentions under the list of synonyms that chrysarobin is identical with acidum chysophanicum *crudum*. Quoting from Merck's Index III, 1910, it is pointed out that chrysophanic acid, which is a distinct oxidation product of chrysarobin, and therefore not identical, and that while it is probable that when chrysophanic acid is prescribed, chrysarobin is intended, this should not be dispensed under the name of acidum chrysophanicum unless the word "crudum" is also appended to the title. Leger, who describes tests for the distinction of the two substances (in Jour. de Pharm. et Chim., 1912, No. 12), expresses the opinion that the substitution of chrysarobin when chrysophanic acid is prescribed is inconsequent, and suggests that the designation of the latter in prescriptions be omitted. He says a study of the literature convinces that the pharmacological activity of the two substances is not identical, and that therefore here also substitution should be strictly avoided.—Pharm. Ztg. LVII (1912), No. 55, 554.

Digitalis Leaves: Constituents.—In a comprehensive review of the constituents of Digitalis leaves published in E. Merck's Annual Report, 1912, a detailed description of

the digitalis glucosides and of other principles associated with them that have been announced from time to time will be consulted with great interest. Preliminarily the work of Homelle, Quevenne, Walz, Nativelle, Schmiedeberg and Kiliani, which led to the discovery of the innumerable digitalis glucosides—among them some that have proven to be of pronounced therapeutic value—is discussed and this is followed by a review of the digitalis substances themselves, their synonymous designations and their derivatives. The fact that this embraces a list of more than one hundred different names gives evidence of the interest which has been taken and the immense amount of research work that has been done, but at the same time also the difficulties that have been encountered in the endeavor to isolate from digitalis leaves a single substance uniting in itself the complete activity of the drug.—Pharm. Ztg. LVII (1912), No. 48, 481.

Rubber Planting in Malaya: An Interesting Account.—C. B. Kibble writes interestingly about the cultivation of rubber trees (*Hevea Brasiliensis*) and the collection and preparation of rubber from them in Malaya, his account being highly interesting in the light of the recent developments regarding the collection of rubber in South America and of the atrocities practiced in the remote Peruvian districts in the upper Amazon region. Speaking from personal observation, he says that all over State of Perak large tracts of jungle land have been, and are still in process of being cleared, in order to plant rubber; and there are many extensive plantations run by Europeans (both individual and companies), as well as numberless small plots owned and worked by Malays, Chinese, or Tamils. The first cuttings and seeds of *Hevea* were sent from Ceylon to the Straits Settlements, and from the trees so obtained seeds were distributed to other parts of Malaya. The first record found by the author of such specimens being dispatched is in 1877, when cuttings from one-year old trees were sent from Peradynia — this statement being apparently confirmed by the age of the largest trees which were said to be twenty-five or thirty years old. As regards the labor on the large estates, the work is usually done by Tamils, who are recruited in India and shipped over in gangs; but there is nothing like slavery about this, for they are well paid and treated, and have special officials set apart to explain to them the conditions under which they are engaged and to investigate their grievances. Owing to the favorable climatic and soil conditions prevailing, trees are ready for tapping when from three to five years old, the determining factor being the size, not age. The bark is first incised when the trunk has attained a circumference of at least fifteen inches, at a height of three feet from the ground, the usual method of tapping being first a "Y" and then the "quarter herringbone." The cups in which the latex is collected are now usually of pretty highly glazed earthenware —these having superseded glass cups, they in their turn replaced tins, and these probably the original coconut-shells. The tappers go their rounds early in the morning, and the day's yield has been brought well in before mid-day. After the latter has been strained and measured, it is coagulated, usually by the addition of acetic acid. The coagulated latex, after being washed and pressed, is either made into crepe or lace, or left as sheet or biscuit rubber. In the former case, expensive and up to date machinery is used; in the latter nothing more exciting than an ordinary hand mangle is required. Before being packed the coagulated and pressed rubber is thoroughly dried and smoked, the finished product being a warm, dark red-brown color, and just transparent when held up against the light. Smoking is usually done by hanging the rubber up, or laying it on open grating shelves in a hut, and lighting a fire of coconut husks beneath. The present outlook is that in another ten years' time there will be miles of mature rubber trees in Malaya.—Pharm. Jour. and Pharmacist, Jan. 20, 1912, 61-62.

Oleum Ricini Sulphuratum: A New Chemical Compound Compatible with other Medicaments.—M. R. Huerre describes a new synthetic compound and the method of its preparation. It is obtained by the action of sulphur upon ricinum oil at a temperature of 140°, the reaction reaching its maximum between 155° and 165°C. When sulphur and ricinus oil are heated up to 100°, simple solution of the surphur is effected, the latter being precipitable as such by the addition of solvents; but the product obtained at the higher temperature is apparently a distinct chemical compound, which with a content of 4.2 per cent. of sulphur no longer responds to the ordinary reactions of that element. The sulphurated oil is miscible without decomposing solutions of various substances which under

ordinary conditions are readily decomposed by sulphur. It is soluble in all proportions in acetic acid, amylalcohol (even when mixed with ethylalcohol) in either, ethylacetate, amylnitrite, amylacetate, methylsalicylic ether, many volatile oils, chloroform, carbon bisulphide, creosote, guaiacol, benzin (benzene? Rep), xylol, &c. This property, and the fact that it is not incompatible with many of the medicaments used in dermatological practice would seem to make it a valuable adjunct for the treatment of skin diseases. Thus, by means of ethereal solution, combinations with salicylic acid, pyrogallol, resorcinol, menthol, salol, thymol, &c., may be effected; in acetone solutions, oil of cade, camphor, and menthol; in chloroform solution, chrysophanic acid, pyrogallic acid, resorcin, &c.; in short, it may be incorporated with any of the substances named, with collodion, traumeticin, plasters, and liniments in any desired combination. — Pharm. Ztg. LVII (1912), No. 47,478; from Les Nouv. Remedes (Paris) 1912, 193.

Olive Oil: Detection of Peanut Oil.—According to Dr. L. Adler the presence of 5 per cent. or more of peanut oil in olive oil may be detected by saponifying 1 cc. of the suspected oil with 5 cc. of 8 per cent. alcoholic potash solution in a 100 cc. Erlenmeyer flask on a boiling water bath, for four minutes, with frequent shaking; then cooling to 25°, adding accurately 1.5 cc. of a diluted acetic acid (1 vol. glacial acid, 2 vol. water) and 50 cc. of 70 per cent. (vol) alcohol, shaking well, heating, if necessary, to remove any turbity, and then carefully cooling by immersion in cold water and with shaking until the temperature is reduced to exactly 16°C. If, no turbity results, after occasional shaking within 5 minutes, the temperature is further reduced to 15.5° C, and if then, after waiting another 5 minutes, no turbity results, the sample contains less than 5 per cent. or no peanut oil at all.—Pharm. Ztg. LVII 1912, No. 55,555; from Ztschr. f. Unters. d. Nahr. —u. Genussm. 23 (1912), No. 12.

Saponins: Biological Estimation in Drugs. —At the March Session (1912) of the German Pharmaceutical Society, Professor R. Kobert delivered an extremely interesting and instructive address in which he points out that the biological valuation of the active constituents of drugs (supplementary to the chemical valuation), which is now conceded to be practically indispensible in the case of digitalis, may be confidently extended with advantage to other drugs and more particularly to those containing saponins, such as Quillaya, Senega and Sarsaparilla, for example. The physiological action of these vegetable substances is highly interesting. Applied externally the saponins exert epithelium destructive activity, and are strongly irritant, properties which have been utilized as expectorants (Senega), &c. Internally administered the saponin drugs exert diuretic and perspiratory action, and as a consequence of their irritant effect on the stomach and intestines, particularly in large doses, are capable of relieving diarrhoea and emesis. When injected into the blood vessels the saponins are shown to be powerful protoplasmic poisons, destroying the blood corpuscles and apparently dissolving them. This property Prof. Kobert now proposes to utilize for the biological valuation of drugs containing Saponins. If defibrinated blood is diluted with 50-100 times its volume of physiological salt solution and a saponin solution is then added, the opaque blood corpuscles instantly assume a lake-coler and become transparent. This action is however not due to actual solution, but to the fact that the saponins combine with the cholestrin of the blood corpuscles, which then become transparent. The valuation of saponin drugs is carried out as follows.

A decoction of the air-dry drug is made in the proportion of 1:100, and this is added in successive proportions of 1, 2, 3, &c. cubic centimeters to a series of test tubes, each containing 5 cc. of a 2:100 solution of blood in physiological salt solution, followed by sufficient of the salt solution to make up the volume of 10 cc, observing in what dilution haemolytic action sets in. If in addition the activity — value of the saponins contained in the drug is known, the percentage of active substance in the drug is simultaneously determined. In this manner Prof. Kobert has determined a content of 8-19 per cent. of saponins in quillaya bark, and that the activity of the bark remains constant for years. On the other hand, in the case of Senega and Sarsaparilla a diminuation of the active constituents was shown after prolonged keeping. —Pharm. Zt., LVIII (1912), No. 21, 213-214.

Saponin:—Reliability of the Haemolytic Method of its Biological Valuation.—Dr. Cesaro Sormani and also J. Rühle have made comprehensive experiments with the haemolytic method proposed by Prof. Kobert (see

preceding abstract) for the biological valuation of drugs containing saponins. The degree of hoemolysis is ascertained with accuracy in the case of saponin by this method, whereas the reactions of Vamaka as well as the various color reactions for saponin are untrustworthy.—Pharm. Ztg., LVII (1912), No. 55, 555; from Ztschr. f. Unters. d. Nahr. u. Genussm. 23, (1912), No. 11.

Symphytum Officinale (Comfrey): Anatomy and Herbal History.—At the suggestion of Dr. J. C. Macalister, of the Royal Southern Hospital, Liverpool, who has been engaged in experimental inquiries into the therapeutical value of certain substances in the treatment of malign and malignant ulcers, and had learned that infusion or poultices made from the "roots" of comfrey have been used in some parts of the country in this relation, Prof. R. J. Harvey-Gibson, procured a large quantity of comfrey rhizomes, which were submitted to Dr. A. W. Titherley for analysis. This resulted, as described in a separate abstract (see *Allantoin*, under "Organic Chemistry") in the extraction in considerable amount of a crystalline body which was identified as allantoin, a substance by no means of common occurence in plants (it is regarded by plant physiologists as a derivative — probably an oxidation product — of nuclein, and has as yet only rarely been identified in plants.) The clinical aspect of the subject and the results obtained from the use of allantoiin in specific cases are dealt with by Dr. Macalister in a paper published in the Brit. Med. Journ. and are briefly described in a separate abstract. Mr. Harvey-Gibson himself contributes an admirable historical summary of the drug, its reputed virtues and uses from the time of Dioscorides to the time when, in the latter part of the 18th Century its remedial value was discredited by Woodville (Medical Botany, 1794) and others. The author also describes the pharmacognostic character of the drug, from which it appears that the dry material sold as the rhizome of *Symphytum Officinale* contains the massive "rootstock" and roots indiscriminately.—Pharm.. and Pharmacist, Jan. 27, 1912, 91.

Synthetic Caoutchous: Chemical Identity with the Natural Product.—At the recent Jubilee Meeting of the Society of German Chemists one of the most interesting topics of discussion was the advance made in the synthetic production of medicinal and technically useful products. Among the latter the most important doubtless is the successful synthetic production of caoutchouc, the history of which was traced by C. Harries, whose personal researches within the last few years have confirmed the chemical identity of the synthetic and the natural product. While "isopren," which is regarded to be the basis of the synthetic article, has been known for 50 years, the first successful caoutchouc production was by Bouchardat and Tilden 20 years ago, who obtained it by the action of HCl on isopren; but, strange to say, the method described has not since been confirmed as available for its production by other investigators, although priority of discovery has been conceded to the first named investigators. During the past two years the problem of its synthetic production has however been solved by Harries in collaboration with the "Elberfeld Farbenfabriken." The material from which the caoutchouc is produced consists of unsaturated hydrocarbons, which are cheaply and conveniently available, and these hydrocarbons are polymerized by a series of methods devised for the purpose, which are characterized by the author as "ozonizing methods." The chemical identity of the synthetic and natural products is demonstrated by the solubility in various solvents and a series of well-defined properties of the ozonide, which must yield on hydrolysis with H_2O the same cleavage curves and the same products of hydrolysis in the same proportions as does the natural caoutchouc. Some slight deviations from these conditions still remain to be obliterated; but the author is confident that the results so far obtained will lead to the successful production of synthetic caoutchouc, as a large industry in the near future.—Pharm. Ztg., LVII (1912), No. 46, 459.

Zinc Ointment: Exact Determination of Zinc Oxide.—Dr. E. Büttner recommends the following method for the determination of zinc oxide in ointments or pastes with exactitude: From 0.5 gm. (if very stiff) to 2.0 gm. of the ointment is placed into a 150 cc. separtory funnel; 30 cc. of water and 50 cc. of ether are added, and this is followed by the addition of diluted hydrochloric acid with careful shaking until the contents separate into two perfectly clear layers. The aqueous layer is withdrawn, filtered into a beaker, and the filter washed with four portions of 30 cc. of water each with which the ether solution of the fats has been previously washed. From the aqueous filtrate and wash-

ings the zinc is then precipitated as carbonate and from its weight the oxide may be calculated.—Pharm. Ztg., LVII (1912), No. 55, 555; from Südd. Apoth. Ztg., 1912, No. 33.

Editorial Notes and Announcements

JAMES H. BEAL, Editor.....Scio, O.

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RESENTING GRATUITOUS INSULTS TO PHARMACY AND PHARMACISTS.

It has been a favorite doctrine of the Editor for many years that pharmacists invite attacks from the sensational press by failing to protest against them when made.

The same element of human nature that lead the ancient Romans to crowd the gladiatorial amphitheatre leads them to buy the sensational newspaper. They want to see somebody get "spiflicated." The publishers know this, and as a policy they select the man or class who can't or won't hit back. They have found this quality prevailing among pharmacists generally, and so pharmacy comes in for an abundant share of gratuitous and wholly unmerited vilification.

The way to change the policy of the press on this subject is for pharmacists to change their attitude of quiescent acceptance to one of indignant remonstrance against such unjust attacks.

In this connection we quote the following letter by one of our members to the New York Times:

To the Editor of the N. Y. Times:

In last Sunday's N. Y. Times, an editorial appears under caption, "Senna, Broken, U.S.P." Judge Learned Hand being quoted: "The Pharmacopoeia is a book put into the hands of druggists all over the country, men of no great learning—."

Webster defines the terms, druggist, apothecary and pharmacist synonymously, hence the assumption that the pharmacist is the one referred to. It is very regrettable that one of the judiciary should cast an uncalled-for slur upon a calling which is a profession, and morever one which carries with it the greatest responsibilities, life and death, the latter not being subject to review and reversal because of error, for error with the pharmacist, may mean death to the patient, and extinction of the pharmacist's professional career. Callings of this kind are not left to the illiterate. Furthermore in proof of the aforesaid would I point to the U. S. Pharmacopoeia itself, which though not perfect, still is the best book of its kind extant, and its contents are the product of the American druggist. I hope the learned gentleman may become acquainted with some druggists, that is socially, not professionally, for we wish him no ill, and he will find as many bright and learned heads in our profession, as he may find in the legal one.

J. F. BEHRENS.

Possibly the Editor of the Times did not lose any sleep over this single remonstrance, but if any considerable number of the drug-