the severity and gravity of the condition. In conjunction with the various tests under acidosis, recent investigation has yielded other methods which are more or less typical of this condition. These include the determination of the alkali reserve of the blood, sometimes known as "buffer value." The correlation of these facts in all cases of diabetes, in conjunction with the sugar findings in the urine, are necessary for the rightful knowledge of the progress of the case.

Recently the determination of the cholesterol content of the blood has been said to be an aid in the diagnosis of gall-stone formation. Aside from blood chemistry, with its many chemical analyses, the study of other fluids of the body by laboratory tests are highly significant. Especially is this true in gastric analysis. The former examination of a single gastric content has now given way to the fractional method of gastric analysis, by which is meant the determination and findings of stomach content removed at short intervals. The determination for total acidity, free acidity, pepsin, trypsin, lactic acid, occult blood, and bile have great significance in all cases where the stomach is to be studied in relation to the various forms of gastritis, ulcer, and malignant growths.

With this brief synopsis of a few of the laboratory tests and their significance in medicine, there naturally comes the thought of the development of those best fitted to undertake such work. While physicians frequently develop into laboratory workers, especially along serological lines, yet I feel that those who have the fundamental chemical knowledge, acquired from the courses given in our better colleges of pharmacy, would be excellently equipped for this field of physiological chemistry.

While it is true that the physician is the one to interpret the significance of laboratory findings, yet the determinations should be made by one who has a thorough understanding of the basic chemical principles underlying these tests.

A course in physiological chemistry would indeed be an asset to colleges of pharmacy, not only in advancing scientific teaching, but also in preparing men pharmaceutically trained to take up this important, necessary and newer science.

THE CHEMISTRY AND THERAPEUTIC PROPERTIES OF CHAULMOOGRA OIL.*

BY L. E. WARREN.

Within the last few years certain derivatives of chaulmoogra oil have attracted considerable attention in the tropics because of their increasing use in the treatment of leprosy. In India and adjacent countries chaulmoogra oil has been used both orally and externally in the treatment of leprosy since prehistoric times. It has also been used there for rheumatism, syphilis and various skin diseases. However, it is so irritant to the intestinal tract that the oral dosage can seldom be pushed to the curative point in leprosy. It is a current belief among the natives of India that even if the digestive tract of a leper patient can withstand the chaulmoogra oil treatment the disease can not always be cured, *i. e.*, that chaulmoogra oil is not a specific in the treatment of leprosy. Since it seems probable that the derivatives of chaulmoogra oil are destined to have a prominent place in therapy in tropical

* Read before the Chicago Branch, A. Ph. A , May meeting, 1921.

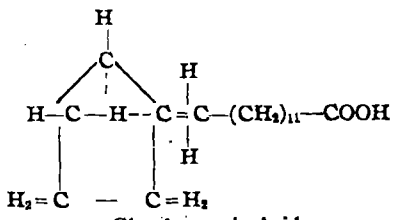
countries, it appears worth while to call the attention of the pharmaceutical profession to this class of remedies, even though the prescription pharmacist in temperate climates may not be likely to have calls for these products. There is a possibility, however, that chaulmoogra derivatives may have curative properties in the treatment of tuberculosis. Should this prove to be the case, pharmacists everywhere will be required to handle this class of substances. In bringing this subject before you it is to be understood that this paper is in the nature of a review or digest and that it records no original investigations.

It was long supposed that the chaulmoogra oil of East Indian commerce was derived from the seeds of *Gynocardia odorata* R. Brown, Family *Flacourtiaceae*, a tree native to the Malay peninsula and North-Eastern India. Bentley and Trimmen[1] describe this plant, as the source of the oil and show a colored illustration of the flower and leaves and a fruiting branch. Chiefly as a result of the researches of Prain and Holmes,[2] it is now known that the true source of chaulmoogra oil is the seeds of *Taraktogenos Kurzii* King. (*Hydnocarpus heterophyllus* Kurz.) This is a handsome tree, a native of Burma. Like *Gynocardia* it belongs to the *Flacourtiaceae* family. The fruit of *Taraktogenos* is of the size of a grape fruit. It contains many irregular-shaped, brown seeds which are rich in oil. Chaulmoogra oil is obtained from the seeds by cold expression. At ordinary temperatures it is a soft solid or semi-liquid, having a peculiar, characteristic odor somewhat like linseed oil.

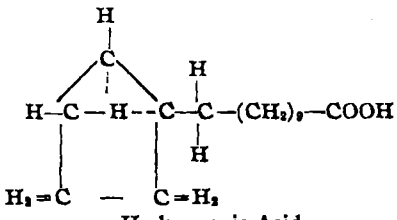
The chemistry of true chaulmoogra oil was very exhaustively worked out by Power and his associates a number of years ago.[3] They found that the oil consists chiefly of the glyceryl esters of two or more new fatty acids, with a small quantity of palmitin and a phytosterol. The new acids isolated differ from any previously known fatty acids in containing a five-membered carbon ring with side chains of diminishing length as the molecular weight decreases. Also, they are unique in being optically active. They contain only one pair of doubly-linked carbon atoms; hence they absorb but two halogen atoms. The acids isolated were named respectively "chaulmoogric acid" and "hydnocarpic acid" by their discoverers. Lewkowitsch[4] has assigned them to a homologous series $C_n H_{2n-4} O_2$ of an entirely new type which he calls the *cyclic* or *chaulmoogric* series. It is probable that the specific bactericidal and medicinal properties of these acids are associated in some way with their molecular constitution. The constitution of two of the members of the series and of a third theoretical one which has not been isolated are given herewith and their properties tabulated. For the sake of comparison the structural formula for oleic acid is given also.

CONSTITUTION OF THE ACIDS OF THE CHAULMOOGRIC SERIES

$C_n H_{2n-4} O_2$

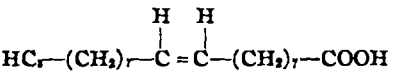


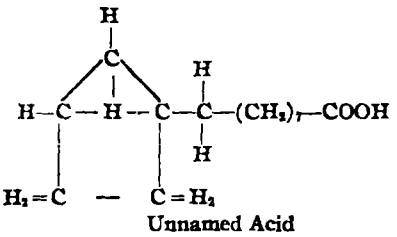
Chaulmoogric Acid



Hydnocarpic Acid

Constitution of Oleic Acid $C_nH_{2n-2}O_2$





Unnamed Acid

TABLE I.—CONSTANTS OF SOME OF THE ACIDS OF THE CHAULMOOGRA SERIES.

Acid.	Molecular Weight.	Iodine Number.	Saponification Number.	M. p.	Specific rotation.
Chaulmoogric	280	90.7 90.1	200.4	68°	+62.1° +56°
Hydnocarpic	252	100.79 100.2	226.6	59°	+68.1°
Unnamed (next lower in series)	224 (calculated)	113.3 (calculated)	250.5 (calculated)	probably liquid at 25° C.	

Power and his collaborators[5] demonstrated that the oils of *Hydnocarpus anthelmintica* Pierre and *Hydnocarpus Wightiana* Blume are physically and chemically similar to the oil from *T. Kurzii*. On the other hand, Power and his associates[6] demonstrated that the oil from *Gynocardia odorata* R. Brown is totally unlike the oils from the chaulmoogra series of plants. It is a liquid at ordinary temperature, is optically inactive and contains none of the cyclic hydrocarbons which are characteristic of the chaulmoogric series. It resembles linseed oil in its chemical properties. From its constitution it is probable that gynocardia oil cannot be of any value in the treatment of leprosy. Goulding and Akers[7] reported that the seeds of *Oncoba echinata* Oliver, an African plant, contain an oil which is very rich in chaulmoogric acid glycerides. De Wolff and Koldewijn[8] have examined the oil from *H. Alpinus* Wight. Its constants indicate that it is very similar to the oils from other hydnocarpus species. Brill has shown that the oils from the seeds of the Ph lippine plants, *H. venenata* Gaertner[9] and *H. alcalae* C. De Condolle,[10] contain chaiulmoogric and hydnocarpic acids (in a form of glycerides) and he suggests that these oils, therefore, are probably therapeutically equivalent, or nearly so, to chaulmoogra oil. Also it was found by Brill that the oil from the seed of *Pangium edule* Reinwardt[10] contains small amounts of the glycerides of the chaulmoogric acid series. It is probable that the oils from several of these plants are sold in the Orient more or less indiscriminately for "chaulmoogra oil." As knowledge of the chemistry of tropical plant products increases it is reasonable to suppose that oils from other plants will be found to contain chaulmoogric acid and its homologues.

The essential properties of the several oils of the chaulmoogric series are given in the accompanying table. The constants given are taken from various sources and in some cases it will be noted that there are considerable variations in the values.

The bibliography of the use of chaulmoogra oil in the treatment of leprosy is so extensive that no attempt will be made here to review the earlier writings and only the more important papers of later dates can be mentioned. At the close of the nineteenth century the belief was gradually becoming fixed in the minds of medical men that chaulmoogra oil was the one drug in the materia medica in which there lay

TABLE II.—COMPARISON OF CHAULMOOGRA OIL AND RELATED OILS WITH GYNOCARDIA OIL.

Physical properties, constants, etc.	*Taraktogenos Kursii*	*Hydnocarpus Wightiana*	*H. Anthelmintica*	*H. Venenata*	*H. Alpinus*	*H. Alcalae*	*Oncoba echinata*	*Gynocardia odorata*	*Pangium edule*
Physical Condition	Soft solid at 25°	Soft solid at 25°	Soft solid at 25°	Soft solid at 25°	Solid	Solid	Hard Opaque solid	Liquid at 20°	Liquid at 20°
Yield of oil from seeds	38%	42%	7.6% 20%	23.3%	50%	25.8%	47%	50%	50%
Melting Point	22–3°	22°	23° 24–25°	22–25° 19–20°	22–6°	32°	34–45°		
Specific gravity at 25° C.	0.951 0.949	0.958	0.953	0.955 0.9471 at 30°	0.898 at 100°	0.950 at 30°	0.898 at 100° at 15.5°	0.925	0.9049 0.937
Specific rotation at 15° C.	+52.0° +50.3°	+57.7°	+25.5° +51.0° +49.50°	+520.3°	+49.5°	+49.6°	+48.8° at 17°	Inactive	+4.28°
Index of refraction	1.476		1.473 1.4725	1.4770	1.4709	1.4770			1.4665
Acid value	23.9	3.8	7.5	15.6 4.4	216.5	3.9	4.5	4.9	0.52
Saponification value	213	207	212 206.2	202.7 200.3	207.5	188.9	192.4	197	190.2 178–183
Iodine value	103.2	101.3	86.4 90.8	97.6 99.1	87.4 84.4	93.1	99.7 96.5	152.8	113.1 89.9
Chaulmoogric acid	Present	Present	Present	Present	Present	Present	Present	Absent	Present small amounts

any prospects for the successful treatment of leprosy. Accordingly searches were begun for better methods of administration of the drug and for the discovery and isolation of the *active principles* of the oil if such there were. Naturally one of the first attempts in these directions was to administer the drug by subcutaneous injection. The first use of the drug in leprosy by the subcutaneous method appears to have been recorded by Tourtoulis-*Bey*[11] of Cairo in 1899, who had employed it for several years with favorable results but who did not consider the remedy a specific. According to Sandwith,[12] Tourtoulis also used the drug intramuscularly with some success. Shortly afterward Hallopeau[13] reported its use by the same method.

During the next decade the administration of chaulmoogra oil was still beset with difficulties. If administered by the mouth, nausea and digestive disturbances follow; if given subcutaneously it is absorbed slowly since it is a heavy oil; by the intramuscular route its administration is painful, due to the pressure on the nerves, and sores are apt to develop due to the slow absorption of the oil. With the object of finding some form of the oil less obnoxious to the patients when given internally, Amaral and Paranbos[14] used the sodium salts of the mixed fatty acids under the name of *sodium gynocardate*. With the same object in view Hollman and Currie* in 1910 used magnesium gynocardate and sodium gynocardate internally. During these years numerous mixtures of chaulmoogra oil with other substances were

*Stated on the authority of Hollmann and Dean, *Jour. Cut. Dis.*, 37, 372, 1919.

prepared in the effort to render it more fluid, improve its absorption, and reduce its irritating properties when given hypodermically. Thus, Jeanselme[15] used a mixture of chaulmoogra oil, camphor and guaicol. A formula devised by Mercado and Heiser[16] came into considerable use. This was composed of chaulmoogra oil 30 Cc., camphorated oil 30 Cc. and resorcinol 4 Gm. A considerable number of other workers whose names will not be mentioned added to the knowledge of the subject.

Increased interest in the treatment of leprosy by chaulmoogra oil was brought about by the reports of Heiser[17] in Manila who administered the oil over long periods of time by subcutaneous injections. He used the camphorated oil and resorcin mixture previously mentioned. His results were encouraging. Of 16 cases reported some were apparently cured, others showed great improvement and in all the disease was arrested. About this time Dr. Leonard Rogers of India was using orally a mixture of the separated fatty acids of chaulmoogra oil which he called collectively "gynocardic acid." On learning of Dr. Heiser's results, Rogers was led to use the sodium salts of these acids subcutaneously[18] and later on intravenously.[19] The intravenous use of the sodium salts produced reactions in the leprous tissues with breaking down of the acid-fast bacilli followed by great improvement of the patient's condition. In 50 percent of the cases which were treated within three years of the onset of the disease,[20] the lesions disappeared. In cases of from three to fifteen years' duration only 25 percent cleared up. Rogers found that the acids with higher melting points (49° to 62°) were more effective than those of lower melting points (37°). He designated the sodium salts of the total fatty acids as *sodium gynocardate* and the corresponding salts of the higher fatty acids as *sodium gynocardate* "A." Rogers' results, although better than those of his predecessors, were still not entirely satisfactory. Since the bacilli which cause leprosy belong to the acid-fast group, Rogers raised the question[19] whether chaulmoogra derivatives might not have a similar destructive action on another acid-fast bacillus, namely that of tuberculosis. Later, Rogers and Mukerjee[21] used the sodium salts of the fatty acids from *Hydnocarpus Wightiana* which they called "*sodium hydnocarpate*" in leprosy. They consider the results very promising. There was a great reduction and frequent total disappearance of the lepra bacilli and the number of cases in which the lesions disappeared in less than a year of treatment is considered noteworthy. Encouraged by the use of "sodium gynocardate" and "sodium hydnocarpate" in the treatment of leprosy, Rogers[21] was led to try the sodium salts of the mixed fatty acids of cod liver oil which he calls collectively "sodium morrhuate." His results in fourteen cases treated for from 4 to 12 months were somewhat encouraging. He says: "A noteworthy feature of the cases was the very frequent improvement in the general health." In a later report[22] six more cases were reported. Of the entire 20, 12 were much improved, one was not improved, 3 were slightly improved and in 5 the lesions had disappeared. In this connection it is interesting to note that Rogers and his collaborators experimented with "sodium morrhuate" in the treatment of human tuberculosis.[23] Rogers was led to undertake these studies because of the effects which he had found "sodium gynocardate" to produce in breaking up the acid-fast bacilli which cause leprosy. Tuberculosis also is caused by an acid-fast bacillus and Rogers reasoned that since "sodium gynocardate" destroys the bacilli of leprosy, it would most likely have a similar

effect on the tubercle bacillus. And since cod liver oil has demonstrated value in the oral treatment of tuberculosis, it seemed reasonable to hope that it would have a curative effect in this disease if given intravenously in the form of its sodium salts. Rogers states that intravenous injections of "sodium morrhuate" in tuberculous patients produce a slight febrile and local congestive reaction similar to that produced by "sodium gynocardate" in leprous patients, which indicates a definite action in the tuberculous tissue. Improvement in tuberculous cases is seen in the reduction and cessation of the fever, lessening of the expectoration and coughs and a constant gain in weight. The bacilli in the sputum gradually decrease in number and may disappear. The researches were not carried far enough to warrant any very positive conclusions, although the results in general appeared to be promising. This work will again be referred to in connection with the germicidal properties of "sodium morrhuate." Other clinicians[24] have believed "sodium morrhuate" to be of some value in the treatment of tuberculosis, but the remedy must be tested further. Muir[25] used sodium gynocardate "A" by the intravenous method in thirty cases of leprosy. His results were very encouraging. Later, Muir[26] published a supplementary report in which the further progress of these thirty lepers was recorded. He used "sodium morrhuate" in the later treatments but not for a sufficient time to obtain any noticeable results except to observe that it was not so destructive to the veins as the gynocardates. Still later, Muir[27] summarized the results obtained by various clinicians in thirteen Indian leper asylums, by the use of "sodium hydnocarpate" and "sodium morrhuate." With the former drug there was improvement in 132 cases, or 72 percent; much improvement in 58 cases, or 32 percent, and in several cases the lesions entirely disappeared. With sodium morrhuate 33, or 28 percent, of the cases were not improved; 48, or 41 percent, were slightly improved; and 31, or 26 percent, were greatly improved. In anesthetic cases the best results were obtained by the use of "sodium hydnocarpate" but this soon caused blocking of the veins. Sodium morrhuate can then be given. In nodular leprosy, according to Muir, the "morrhuate" appears to be as good as the "hydnocarpate." He believes that both drugs are useful in the treatment of leprosy and that one should be used to supplement the other.

In 1918 Carthew[28] reported treatment of eighteen cases of leprosy by intravenous injections with "sodium gynocardate." He concluded that the improvement in general health of leprous patients under this treatment is so universal that all leprous patients regardless of the type or duration of the disease should be given the treatment. He is of the opinion that there is considerable probability that the treatment is specific and curative. In 1920 Carthew[29] reported further work with sodium gynocardate "A" in which his conclusions were distinctly enthusiastic.

During the past 10 years a great deal of work has been done (it still is in progress) at the U. S. Leprosy Investigation Station in the Hawaiian Islands. As a result of a careful survey of the literature, and from experience in the treatment of 42 cases of leprosy, McCoy and Hollmann[30] of this station had concluded in 1916 that chaulmoogra oil "is helpful to many cases of leprosy, perhaps to a majority." They used the Heiser mixture subcutaneously and supplemented the treatment in most cases by the internal use of the oil. Carbon dioxide snow was used locally where indicated. It was found that weekly injections of 5 Cc. of the mixture (2.5 Cc.

of chaulmoogra oil) were about as much as the average patient could bear well. The oil mixture was sterilized at 100° C. before use.

Until 1918 chaulmoogra oil had been given internally, principally either as such or in the form of its fatty acids or their salts. It had been administered subcutaneously and intramuscularly, alone or mixed with various diluents, or as the sodium salts of its fatty acids. It had been given intravenously, for the most part in the form of the sodium salts of its fatty acids. However, in 1918 a new method came into use which seems likely to supersede the others, at least in some countries. This was inaugurated chiefly by the work of Hollmann and Dean.[31] Dr. Hollmann had been engaged for some time in leprosy investigations in the Hawaiian Islands and Dr. Dean, a chemist of reputation, was president of the University of Hawaii.

In working out the constitution of the fatty acids from chaulmoogra oil, Power and his collaborators[32] prepared the ethyl esters, as well as several other esters, of the fatty acids. In 1909[33] a patent was taken out in Germany by a German concern for the process of preparing the ethyl and other esters of the fatty acids of chaulmoogra oil. At about the same time the same firm took out a patent for the products in Great Britain,[34]—all this despite the fact that the products and the methods for their preparation had been described in the chemical literature several years before by Power and his co-workers and their work had been given wide publicity by abstracts in scientific publications. The ethyl esters were sold by the German firm under the proprietary name of "antileprol." So far as can be learned "antileprol" was intended to be taken by the stomach. It attracted but little attention from the medical profession, perhaps a retribution for the injustice of the patent grants. The ethyl esters are liquids which are soluble in water, thus lending themselves to use by subcutaneous, intramuscular, and intravenous injections.

Hollmann and Dean[31] appear to have been the first to carry out intensive treatment of leprosy with the ethyl esters of the fatty acids of chaulmoogra oil. Dr. Dean, as chemist, prepared the esters and Dr. Hollmann administered them. The remedy was given subcutaneously and, subsequently, intramuscularly. Dean originally separated the oil into four fatty acid fractions and then, on account of their insolubility, converted them into their ethyl esters, thus obtaining thinly fluid oils readily absorbable from intramuscular injections. A group of patients was placed on each of these ester fractions, but after several months' trial, all doing equally well, the separation into fractions was abandoned in 1919, after it became evident that the therapeutic agent was inherent in the entire fatty acid series rather than in any separated fraction, and also that its virtue remained unimpared by any of the chemical or physical operations to which it had been subjected, such as its treatment with acid, alkali, alcohol, lead acetate, etc., or even subjection to a temperature of more than 200° C. The hypodermic treatment was supplemented by the oral administration of the free fatty acids of the oil. In some cases the treatment caused reactions in leprous lesions with subsequent improvement. In several cases the patients became bacteriologically negative so that they were paroled from segregation.

So encouraging were the reports of Hollmann and Dean that Walker and Sweeny[35] undertook to discover by bacteriological methods what foundation exists for the

observed efficacy of chaulmoogra derivatives in the treatment of leprosy. They found that chaulmoogric and hydnocarpic acids possess bactericidal properties about 100 times more active than phenol. The bactericidal activity was found to be specific for the acid-fast group of bacteria and inactive against all other bacteria tested. This peculiar, specific, action appears to be a function of the carbon ring structure of the molecule of chaulmoogric acid and its homologues. The fatty acids of cod liver oil, the salts of which constitute the "sodium morrhuate" used by Rogers and others in the treatment of tuberculosis, were found not to possess the specific bactericidal activity of the chaulmoogric series. Consequently there appears to be no rational basis for the use of cod liver oil products in the treatment of leprosy.

The work of Hollmann and Dean at the Hawaiian Station was continued by McDonald[36] with the collaboration of Dean and Wrenshall[37] as chemists. McDonald administered the esters which had been combined with 2 per cent of iodine. He admits that the presence of iodine has no readily defensible reason and he appears to be nearly convinced that the treatment would be as successful without it. At least certain controls who were receiving the esters without iodine appeared to be progressing as well as those receiving the regular treatment. In later reports[38] most of these cases had been paroled as clinically cured. This would indicate that the iodine with which the esters had been combined previously, actually plays no part, or at least only a minor one. McDonald's standard treatment for weekly intramuscular injection consists of the ethyl esters of the entire fatty acids of the whole oil* with 2 percent of iodine chemically combined, the dosage of which begins with 1 Cc. and is increased by 1 Cc. at every second or third injection until from 2 to 6 Cc., according to the age and weight of the patient, are reached. Internally, the patients receive in capsule form the mixed fatty acids carrying 2.5 percent of iodine. The fatty acids are employed rather than their ethyl esters, because they better conform to the normal digestive process which preceeds fat absorption; the treatment, therefore, makes use by mouth of a predigested oil or fat which is semisolid at room temperature, and, in capsule, very easy to take. Its dosage begins with one-sixth Gm. per hundred pounds of the patient's weight, three times a day, an hour or two after meals. This is gradually increased every two weeks until the maximum of 1 Gm. per hundred pounds of weight per dose is reached. Of these two forms of administration, physicians have gradually come to regard the injection as the vastly more important of the two. In fact, McDonald had ten patients on injections alone for several months, and they seemed to do as well as those who took both injections and capsules. In his latest paper[38] he concludes that the oral administration is not necessary. It should be said for the fatty acids, however, that McDonald considers them the most efficient form of the oil ever devised for internal use. He reports that patients go for weeks at a time without a single complaint of digestive disturbance. With an average treatment of 15 months, 78 patients were paroled from the Station between Oct. 1, 1918 and July 6, 1920. In a later report McDonald[39] states that of a total of one hundred,

*In the most recent technique described by McDonald and Dean the ethyl esters are distilled in a high vacuum before being combined with the iodine. This results in a somewhat more mobile fluid which is believed to be more readily absorbed.

forty-two patients have been paroled as no longer a menace to public health, not one of whom has suffered a relapse.

All leprosy workers agree that the treatment with chaulmoogra derivatives is tedious alike for patient and physician. McDonald says:[36] "Leprosy is such a slow, chronic disease, so insidious and sluggish in its attack and, heretofore at least, so stubbornly rebellious to therapy, that it taxes all the powers of patience and courage both of its victim and his medical attendant. Advantage has to be taken of every helpful measure for the maintenance of a steady, persistent and unflagging course of treatment which knows no faltering and no discouragement. As Dyer has aptly said, 'Above all things individualize the patient; watch for improvement. If it does not show in three months, wait six months; wait a year, or longer. Keep on driving at the treatment until the patient dies or gets well.' And the only place for carrying out this eminently wise and sound advice is a leprosy hospital, and best of all one like ours, maintained by the state, backed by a wholesome segregation law which precludes quitting and going home on the whim of the patient, as now obtains in asylums in the Orient."

"There is a wonderful power in association. A group of fellow leprosy hospital patients forget all about the prejudice and horror with which the outside world regarded them. Here, one is as good as another and no one is sensitive about his or her appearance, and they lead a far more happy and contented life than they possibly could outside. They watch each other, compare notes, see the old-timers getting paroled out; they see some improving more rapidly even if their own case is rather slow, so they go patiently on, whereas an isolated patient would get discouraged, give the treatment a black eye, and abandon it. An attack of leprosy fever, which often confines them to bed for several days, our patients endure with the greatest fortitude, because they have learned from observing fellow patients that when they get over that flare-up they will be better than before. A private patient would say that his physician was poisoning him and would quit."

The latest work by McDonald and Dean[38] has been carried out with the esters prepared from the higher boiling fractions of the acids of chaulmoogra oil. These fractions have very high iodine and refractive index values which indicates that they belong to fatty acids which are relatively more unsaturated than the chaulmoogric series of acids. An acid fraction having an iodine number of about 125 (instead of approximately 90 as for chaulmoogric acid or about 100 as for hydnocarpic acid) was esterified and this product administered in the usual way. The preliminary report indicates that the esters of these more highly unsaturated fractions are particularly efficient in leprosy therapy. One patient has been paroled after only six and one-half months' treatment. Dr. Wrenshall is working on the problem of the isolation and separation of these more highly unsaturated compounds. Since the hydnocarpic acid derivatives are believed to be somewhat more valuable in therapy than the corresponding chaulmoogric compounds, it is possible that acids of the chaulmoogric series of lower molecular weights would be still more efficient. Consequently one of the problems now open to the chemist is the synthetic production of acids of this series with shorter side chains and correspondingly lower molecular weights.

It may be seen from this very incomplete revie w of the literature that at present there are two relatively distinct systems of treatment for leprosy with chaulmoogra oil. One of these is now chiefly championed by McDonald and Dean who use principally the mixed ethyl esters of the fatty acids of chaulmoogra oil by deep intramuscular injections. The free fatty acids from the oil are used internally as supplementary to the intramuscular injections. The other system is represented by Rogers and his followers in India who chiefly use the sodium salts of the fatty acids of chaulmoogra oil, for the most part intravenously. Perhaps the advocates of these systems might be called schools,—the "American school" and the "Indian school." The Indian school experimented with the ester treatment but discarded it after a very brief trial. At this time it is scarcely possible to form an estimate of the relative merits of the two schools. From an impartial examination of the results reported, it would appear that the results obtained by the American school represent the largest percentage of clinically cured cases. The less stringent segregation laws of the Orient and the differences in the races and racial customs of the patients in the two geographical sections, probably are contributing factors in the differential results obtained.

Leprosy, like tuberculosis, is a malady that claims most of its victims from the homes of poverty. The individual whose nutrition is normal rarely contracts the disease regardless of the exposure to infection. In past ages leprosy was of frequent occurrence in all lands, but as social conditions improved with the lapse of centuries, it became less and less common until today it is a rarity in civilized countries. Whatever the treatment in the disease, the value of hygiene, good food and an open air life is emphasized by all clinicians.

Although results are being published almost daily which appear to indicate that derivatives of chaulmoogra oil may be almost specific in the treatment of leprosy, yet among the many clinicians who have recorded their experiences with these drugs there are none, apparently, with the possible exception of McDonald,[38] who have been willing to assert dogmatically that leprosy can be cured. Most of these writers are careful to state that it is as yet too early to exclude possible relapses in the seemingly cured patients. However, with numerous patients in whom the diagnosis of leprosy had once been positive by bacteriological and clinical tests, now on parole, bacteriologically negative and free from symptoms, the outlook for permanent cures would seem to be distinctly hopeful. It seems plausible to suppose however, that even if the most sanguine hopes of the present day investigators of leprosy be realized, there will always remain some cases which will prove intractable to the chaulmoogra treatment or to any other treatment which may be discovered. Some cases, too, will continue to escape segregation, so that the spread of the infection will not be stopped. Consequently the entire disappearance of leprosy from the earth will not be likely to be realized during the lifetime of any now living, and possibly not for many generations to come.

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DRUG TOPICS.*

No. 5. Curing of Japanese Burdock.

BY W. E. CLEOPHAS.[1]

Through the kindness of Mr. Susuki a small package of Japanese burdock seeds was obtained. The root of the Japanese burdock is also used as a vegetable. The roots are reported to acquire a large diameter.

Dr. Fischer reported that he had obtained large plants, and late in October dug up roots almost an inch in diameter or a little more. When cooked and prepared with a white sauce they reminded him of the taste and flavor of the egg plant.

For the purpose of comparing them as a drug with American burdock, the plants raised by Edward Kremers in 1909 were utilized. The Japanese seeds had been sown in spring in the same place where the year before American burdock had been raised. Unfortunately, for an exact comparison, the plants were not thinned out as early as they ought to have been. As a result the plants did not develop as finely as did those of the previous year.

FALL COLLECTION. For the purpose of curing, roots were dug up from time to time after the middle of October. Following the method of the previous year, part of the roots were cut longitudinally, *i. e.*, the conventional way, and partly into cross sections. Some were dried at room temperature, others at different temperatures in drying ovens. It having been found that 70° apparently was the best temperature for curing the roots, a beginning was made with this temperature, other temperatures being selected both upwards and downwards at intervals of ten degrees.

Drying at 70°. In a preliminary experiment no hourly record was made of the loss of water due to drying. At the end of about 9 hours, 92.49 grammes of cross sections weighed 25.32 Gm., hence a total loss in weight of 67.17 Gm. or 72.6 percent. 139.88 of the longitudinal sections weighed 37.75 Gm. at the end of about seventeen hours, hence a loss in weight of 102.05 Gm. or 72.9 percent.

* From the Laboratory of Edward Kremers.

[1] Walter E. Cleophas, "The Curing of Burdock," Thesis, University of Wisconsin, 1910.