Allspice is sometimes dried by placing the berries on drying-frames over heat. When thoroughly dried, they are placed in bags and sent to market.

Allspice of commerce is a fruit, varying in color from brownish-gray to grayish-brown, to reddish-brown, to reddish-black. All the fruits, with the exception of the reddish-black ones, which are at first sweet, then sweet-aromatic, and finally slightly astringent, are first aromatic and then aromatic-astringent. The surface is granular in appearance and rough to the touch. The outline of the fruit varies from indistinctly four- to indistinctly three-sided. The upper part of the fruit is crowned either with the four-parted calyx or its fragments, or by the remains of the cohering calyx-tube, which appears as a gray ring around the rim of the tube. In the center of the small depression, there is a persistent style of variable length. The base of the fruit is either marked by a slightly depressed scar, or attached (rarely) to a short stalk.

On cross-sections the pericarp is about 1 m.m. in thickness. The septa is thin and membraneous. The fruit is two to three-celled, and from one to three-seeded. In the one-seeded form, fragments of the septa are visible. In each cell there is a solitary seed. In the two-celled fruits, the seed is slightly reniform, two-sided, concave on the inner face, and indistinctly beaked. The seeds of the three-celled fruits, are indistinctly three-sided, and slightly angled. The seeds of the two and three-celled forms vary from astringent to astringent-aromatic. Most of the tannic acid is contained in the seed,—at least judging from the taste, one is led to believe that.

The structural variation of allspice is not of recent origin, for I found a similar variation when I examined a sample of allspice which had been placed in our museum many years ago.

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THE PHARMACOGNOSY OF THE MEDICINAL RHAMNUS BARKS.

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INTRODUCTION.

The European Group of Rhamni:—For centuries the bark of a wild shrub, known in England as Alder Buckthorn or Berry Alder, has been used in Europe as a purgative. This bark is now recognized in most of the leading pharmacopœias of the world, under the name of FRANGULA *or* FRANGULÆ CORTEX. The plant yielding the drug, RHAMNUS FRANGULA, (*Linnæus*), ranges along roadsides and in thickets over all of Europe, except the very northernmost parts and east over northern Asia.

Associated with RHAMNUS FRANGULA is RHAMNUS CATHARTICUS, (*Linnæus*), a thorny shrub, named in England, Buckthorn or Waythorn. This plant is also found in northern Africa, India and eastern United States. The fruit, especially, has been employed for many centuries in Europe as a cathartic. It is now official in a few of the European pharmacopœias. As a medicine the fresh, ripe berries are made into a decoction or the abundant juice is expressed and made into a syrup. The juice of the partially-ripe Buckthorn Berries is yellow and

has been used for staining parchments, etc., while the juice from the ripe berries, is of a greenish-purple color and, when evaporated to dryness with lime or alum, produces the well-known water-color pigment, "sap-green." The bark, also, possesses purgative properties, which, in the fresh bark, are said to be more drastic than Frangula.

Among the other European Rhamni may be mentioned RHAMNUS INFECTORIUS, (*Linnæus*) yielding "French Berries"; RHAMNUS SAXATILIS, (*Linnæus*), RHAMNUS TINCTORIUS, (*Waldstein et Kitaibel*) and other species yielding "Persian Berries"; and RHAMNUS CARNIOLICA, (*Kern*) (possibly identical with RHAMNUS SAXATILIS), the bark of which has been found admixed with Frangula. These plants grow wild in southern and eastern Europe and Asia Minor. From French Berries a valuable yellow dye for textiles is prepared and from Persian Berries is obtained the dye used in staining Morocco leather.

The American Rhamni:—Another group of Rhamni furnishing medicinal barks, is found along the western coast of North America. With the settlement of California by the Spaniards, the new-comers noted that the native Indians used the bark of a certain kind of shrubby-tree, as a cathartic. The Spaniards named this plant and its bark Cascara Sagrada (Sacred Bark). The early American settlers used the name "Chittem Bark" (Chittam, Shittem, Shittim, Sittem), the origin of which is unknown. This drug is now official in nearly all the pharmacopœias of the world. It is obtained from the plant RHAMNUS PURSHIANA, (*DeCandolle*), which ranges over the west slopes of the Cascade Mountains, from central California well up into British Columbia, and forms extensive low forests on the valley and mountain sides.

Associated with RHAMNUS PURSHIANA, though ranging more to the south, is RHAMNUS CALIFORNICA, (*Eschscholtz*), locally known as Wild Coffee, found in central and southern California and northwestern Mexico, a shrub or small tree. Probably the bark of this plant was that originally introduced as cascara bark. It was gathered for years along with the RHAMNUS PURSHIANA bark.

RHAMNUS CROCEUS, (*Nuttall*), a shrub of central and southern California, also furnishes a bark with cathartic properties.

Another American Rhamnus which has furnished a medicinal bark is RHAMNUS CAROLINIANA, (*Walter*), of southeastern United States, commonly known as Southern or Carolina Buckthorn.

Foreign Medicinal Rhamni:—Little mention is made, in medical or pharmaceutical literature, of the medicinal use of Rhamnus barks from other countries. The bark of RHAMNUS WIGHTII, (*Wight and Arnott*), of India, is described by Hooper, (1888), who states that it is commonly sold in the shops of Bombay. The plant is included by Tavera, (1892), in a list of the medicinal plants of the Philippines. It is a tall shrub or small tree ranging over the higher hills and valley slopes in the forests of Western Bombay and Madras; is also found in central Ceylon and in Batangas, Philippines. The bark possesses cathartic, also tonic and astringent properties.

A specimen of the bark of RHAMNUS CHLOROPHORUS, (*Decaisne*), from China, was exhibited, in a collection of rare drugs, at the World's Columbian Exposition in 1893. Whether other lots of this bark have ever been received into the United States is not known. This plant, with another species, RHAMNUS UTILIS,

(*Decaisne*), was described and named by Decaisne, from specimens sent to Europe in 1854. Hemsley, however, claims that RHAMNUS CHLOROPHORUS is identical with RHAMNUS TINCTORIUS and that RHAMNUS UTILIS is the same as RHAMNUS DAVURICUS. Fortune, in an account of his travels in China, states that the bark and twigs of these species, mixed together, furnishes the dye long known in Europe as "Chinese Green." In China, the mixed barks are boiled with water, the liquor sopped up with cotton cloth coated with lime, and the resultant beautiful, green color washed out of the cloth. The plants were introduced into France and cultivated for the dye-stuff, but later the project was abandoned because of the high cost of production. The color is, apparently, very similar to sap-green.

LITERATURE AND HISTORY.

Botany:—The term *"ramnos"* used by the early Greek physicians and naturalists, is thought to be derived from the Celtic *"ram,"* signifying a tuft of thorns or branches. The name was applied to certain thorny plants by these writers, but from their meager or inaccurate descriptions it is impossible to establish that the plants mentioned by them were any of the Rhamni as we know them to-day.

Theophrastus mentions two kinds of *ramnos,* black and white, both thorny, thus shutting out RHAMNUS FRANGULA, which is not thorny. Dioscorides describes three kinds: one with long, flat, soft leaves; one with white leaves, and a third with round leaves. He states that the leaves should be used in the form of poultice for erysipelas and herpes.

Pliny, the Roman physician, under the name *"rhamnos,"* mentions two kinds, one whiter or lighter in color (*candidior*), and more shrubby (*fruticosior*), the branches terminating in straight thorns and with larger leaves. The other kind is darker, more of a reddish-color with curved spines and bearing a sort of pod. It is very evident that the second plant mentioned, is not a modern *Rhamnus* and while the first one has some characteristics of the RHAMNUS CATHARTICUS, one fails to see why it should be described as white, for the bark is black and even the flowers are greenish. Galen makes no further distinction than this one of color.

The early Anglo-Saxons were acquainted with the purgative properties of, at least, the RHAMNUS CATHARTICUS, for we find the plant mentioned in their medical writings before the Norman Conquest. The juice of Waythorn Berries is described as an aperient by Welsh physicians (Physicians of Myddvai), at the beginning of the thirteenth century.

Crescentius (1305), mentions RHAMNUS CATHARTICUS under the name *Spina Cervinæ* and describes RHAMNUS FRANGULA under the name *Avornus,* mentioning the use of the middle bark as an evacuant.

With the enlightenment appearing in natural science at the beginning of the sixteenth century, many important contributions were made to botanical and medical literature. Ruellius (1537), does not recognize RHAMNUS FRANGULA, but does refer to a thorny species of *Rhamnus,* probably RHAMNUS CATHARTICUS.

It is not until Matthiolus (1548), in his commentary on the materia medica of Dioscorides, that a good description of RHAMNUS FRANGULA, with mention of the purgative property of bark and berries, is found in literature. He first uses

the name "frangula" in connection with the plant; (*frango, frangere* meaning "to break," an allusion to the soft and fragile nature of its wood).

Among those who describe one or both plants or refer to their medicinal properties, after Mattiolus, one may mention Tragus (Hieronymus Bock) (1551), a Bavarian clergyman, who carefully illustrated and described several European Rhamni; Eucharius Rosslin (1569), a German physician, who called RHAMNUS FRANGULA "arbor fœtida," from which originated the present common German name for FRANGULA, "Faulbaum"; the Dutch physicians, L'Obell (1576),—to whom is credited the specific name "catharticus,"—and Dodoens (1583), whose writings have been translated into several languages, including English, and constitute a basis for modern pharmacognosy; Dalechamps (1586), a famous French botanist, who mentions the yellow staining properties of the fresh juice of the fruit and the production of green pigment by treatment of this juice with alum; Tabernæmontanus (1588), one of the creators of Germany botany; Bauhin (1596), a famous Swiss professor of botany who fully describes these plants and gives the name *"Alnus nigra baccifera"* to frangula; Camerarius (1598); Gerarde (1666), the author of an English herbal and history of plants; Ray (1696), an English botanist of note, etc., etc.

By this time the botanical characters of most of the European Rhamni were well established. Linnæus (1753), places them in the *Pentandria Monogynia.* He includes both RHAMNUS FRANGULA and CATHARTICUS as natives of Sweden, in his *Flora Svecica* (1745), and mentions as pharmaceutical products derived from them: *Spinæ Cervinæ Baccæ, Syrupus Domesticus, Frangulæ Cortex.*

Jussieu (1787), introduced the term *Rhamnæ* as a generic name and Willdenow (1806), established these plants in the natural system.

The California group of Rhamni was studied by many botanists during the first part of the nineteenth century. Pursh, in 1814, described the plant RHAMNUS PURSHIANA under the name RHAMNUS ALNIFOLIUS, and it was named as a new species by DeCandolle in 1825. RHAMNUS CALIFORNICA was described and named by Eschscholtz in 1823 from specimens sent to him. This plant is closely allied to RHAMNUS PURSHIANA, if not identical with it, as has been repeatedly pointed out from time to time. (Beckett, Rusby, True and Klugh, Brandegee.) RHAMNUS CROCEUS was described and named by Nuttall, from plants seen near Monterey, California, his manuscripts being published by Torrey and Gray in 1838.

About 1850, Mayer mentions the use of Chittem Bark as a purgative among the Indians and trappers in California. Probably the Yokia and Yuki Indians of Mendocino County, California, may be credited with the introduction of cascara bark to the American settlers. These Indians used the bark in decoction—a handful boiled in about a gallon of water—as a cathartic and a kidney-remedy. The Indian name for the plant in *Hosa-kala.*

In 1877, Bundy, in a short article about *Berberis aquifolium* mentions the cathartic qualities of cascara bark and in the following year published a description of the drug and suggested its more general use as a valuable medicine.

Collection and Commerce:—Within a few years after 1877, Cascara Sagrada established a reputation as a tonic-laxative and peristaltic that placed it in the

foremost rank of purgative medicines, and its collection became an established industry in the regions where cascara trees were abundant.

The bark, stripped from the trees during the season (April to August), when it "peels" easily, is laid, outer-side upwards, over racks placed in the open and when dry, it is broken into smaller pieces, sacked, sold to local dealers and shipped out by the car-load.

The trees soon die after the removal of the bark, and the dried wood, either of the tree cut down or standing, has been an added fire-menace to the forests.

The exact amount of frangula and cascara barks entering commerce yearly, is hard to estimate, though it is stated by Henkel that probably more than two million pounds of dried cascara bark, is consumed annually. The total consumption of frangula bark is far less in amount.

Cultivation:—The Cascara plant has been cultivated in Washington, D. C. (True and Klugh), in Michigan (Farwell), in Kew Gardens and in Ireland, but nowhere, as yet, for the commercial production of bark. While there have been very extensive areas of the wild growth in California, Oregon, Washington and British Columbia (Zeig), the annual destruction of trees has also been very large, so that the district of bark-collection has been gradually driven north, until now apprehension has arisen lest the entire natural growth of Cascara trees be destroyed. (True and Klugh.)

Pharmacopœial History:—The fruit of RHAMNUS CATHARTICUS was recognized in the London Pharmacopœia of 1650 and in later pharmacopœias, until the present day. It was official in the U. S. Pharmacopœia, only in 1820. The fresh fruit is now official in the pharmacopœias of Belgium and Greece and in the French Codex, and the Syrup, made from the juice of the fruit, in the pharmacopœias of Belgium, Germany and Switzerland and in the French Codex.

The bark of RHAMNUS FRANGULA has been recognized in the pharmacopœias of central Europe since the middle of the last century, including the Danish, (1868), Norwegian, (1870), Swedish, (1871), German, (1870), Prussian, (1862), Hanoverian, (1861), and Dutch, (1871). It was recognized in the Austrian Pharmacopœia first in 1889, in the French Codex in 1908, in the U. S. Pharmacopœia in 1880, and in the British Pharmacopœia in 1885, though it was omitted from the last edition. Neither is it mentioned in those of Croatia, Hungary, Italy, Roumania, Servia and Spain, but otherwise it is at present recognized in all the pharmacopœias of Europe and in those of the United States and Japan.

The bark of RHAMNUS PURSHIANA, first made official in the U. S. Pharmacopœia of 1890, is now recognized in the pharmacopœias of the United States and Japan, and in all those of Europe except the Finnish, and that of Portugal, which has not been revised since 1878.

None of the other Rhamnus barks have been made official in any pharmacopœia nor do any of them appear in the commerce of Europe or America except, possibly, as adulterants.

Adulterations:—The fruit of RHAMNUS CATHARTICUS and also the juice from the fruit, have both been repeatedly reported as adulterated. The early Edinburgh Dispensatories mention the adulteration of the fresh fruit with fruits of the Dogberry (*Cornus*) and of the Black Alderberry (*Frangula*). The juice of

the fruit was very frequently diluted with water by those who prepared it. (Quincy's English Dispensatory.)

Van Pelt, (1874), points out that the juice of RHAMNUS FRANGULA berries is substituted in Belgium for that of RHAMNUS CATHARTICUS berries. As the former juice is much inferior as a cathartic, the substitution is very reprehensible.

Umney, (1874), states that the freshly prepared juice of Buckthorn Berries has a specific gravity of 1.070 to 1.080, which, after the juice has stood for a year, is reduced to 1.035. However, four commercial samples of fresh juice gave a specific gravity about 1.005, indicating the addition of water to the extent possibly of 500%.

Adulteration of Frangula has apparently never been extensively practiced. The bark of RHAMNUS CATHARTICUS has been found admixed with Frangula bark, and Moser, also Mitlacher, reported in 1905 the presence of RHAMNUS CARNIOLICA bark in Frangula. The barks of several species of *Alnus,* especially of ALNUS GLUTINOSA (Wuerffel, 1907), have been mentioned as adulterants.

Cascara bark has been reported adulterated with RHAMNUS CALIFORNICA bark, but in view of the facts that the species are nearly if not quite identical; that unquestionably the RHAMNUS CALIFORNICA bark was the one originally employed by the Spaniards and named by them Cascara Sagrada; that the chemical constituents cannot be differentiated and that the gross characters of the barks as also their histological structure are very similar, it seems hardly correct to name the one an adulterant of the other. Moss in 1888, and Squibb in 1899, complain of the poor quality of the Cascara of those dates, but attribute it to bark gathered out of season and improperly cured, on account of the heavy demand and high price created for the drug. Rusby, (1890), mentions the bark of CORNUS NUTTALLII, as an adulterant of Cascara bark. Perrot, (1901), mentions the admixture, in Europe, of RHAMNUS FRANGULA bark with powdered Cascara. Miller, (1912), finds in a large consignment of Cascara a spurious bark rather uniformly mixed and present to a considerable extent. In 1913, a large consignment of bark from Europe labeled "BUCKTHORN," received at Chicago, was found to consist entirely of this same *non-Rhamnus* bark. It resembles cascara quite closely, in size, shape and external markings, but, upon closer examination, was found to be the bark of a *Prunus.* The taste is quite astringent, somewhat bitter and has a decided flavor of hydrocyanic acid and benzaldehyde. The structure is much like that of PRUNUS VIRGINIANA bark and the external markings also closely resemble those of unrossed wild cherry bark.

Histology:—Moeller, (1892), places accurate illustrations of the structure of FRANGULA *and of* RHAMNUS PURSHIANA in his *Pharmakognostischer Atlas.* Cabanes, in 1895, refers to the histology of *Frangula* and, likewise, do Sayre, (1897), Wuerffel, (1907), Mitlacher, (1905), and Moser, (1909.)

The bark of RHAMNUS PURSHIANA was first described histologically, by Prescott in 1879, who mentions the presence of "thick-walled' yellow cells.'[1] Later, it was more carefully and fully described by Moeller, (1882), who differentiated it from *Frangula,* pointing out the presence of "stone-cells" in the Cascara, and their absence from the Frangula.

Beckett, (1889), refers to the histology of Cascara, and so do Rusby, (1890), and Sayre, (1897), who attempt to differentiate the Cascara barks from RHAMNUS

PURSHIANA and RHAMNUS CALIFORNICA. They find, however, but slight points of difference, principally some distinctions in the characters of the medullary rays.

Perrot, (1900), and Miller, (1912), refer to the structure of Cascara bark in connection with certain adulterants thereof.

Kraemer, (1912), discusses and illustrates the number of cells in the medullary rays of Cascara bark, and Farwell, (1914), compares the medullary rays of RHAMNUS CALIFORNICA bark with those of RHAMNUS PURSHIANA bark, differentiating between the barks by the differences in the rays.

Chemistry:—The chemistry of the *Rhamnus* barks presents much of interest because from the first analysis of frangula bark by Gerber in 1828, it has been observed that the active principles are resinous in nature, difficult to separate from one another and to determine their true constitution. Even at the present day, these analyses are far from being in a satisfactory condition.

Gerber obtained, among numerous other vegetable constituents, 2.7% of yellow resinous coloring matter and 4.6% of bitter-acrid extractive, which he considered contained the active constituents. He noted that the yellow coloring matter became dark-red with alkalies.

Hubert, (1830), analyzed the juice from the fruit of RHAMNUS CATHARTICUS. He found a bitter substance, apparently the active constituent, and closely resembling the *cathartin* of senna leaves, a green coloring matter, which, in the ripe fruit is purple-red, due to the action of acids in the ripening fruit and a brown material, insoluble in alcohol but easily soluble in water.

Fleury, (1842), obtained from the unripe berries of RHAMNUS CATHARTICUS, *rhamnine* in pale yellow crystals.

Kane, (1843), isolated *chrysorhamnine* from unripe Persian berries and *xanthorhamnine* from the ripe berries. *Chrysorhamnine,* ($C_{23}H_{12}O_{11}$), extracted with ether, formed golden-yellow, silky, stellated needles, sparingly soluble in cold water, soluble in alcohol and ether and in alkalies, (though much altered), and by boiling in water is changed into xanthorhamnine, ($C_{23}H_{12}O_{14}$). This latter substance is extracted from the ripe fruit with boiling water and is olive-green in color.

Winckler, (1849), obtained *rhamnine* from the unripe fruit of RHAMNUS CATHARTICUS and *cathartin* from the ripe fruit. He considered that *rhamnine* by the ripening process is converted into *cathartin* and glucose. (This is the first published evidence of the glucosidic nature of these resinous constituents of the *Rhamni.*)

Binswanger, (1849), found in frangula bark the crystallizable yellow coloring principle which was named (by L. A. Buchner) *rhamnoxanthin,* an ether-soluble amorphous resin, one or more alcohol-soluble resins, a bitter substance of resinous nature in which the purgative properties of the bark seem to lie, sugar, gum, tannin, plant acids, extractive, etc. He compared the bark of RHAMNUS CATHARTICUS with frangula bark, and found that the constituents were similar, but included also a bitter, water-soluble, crystallizable substance to which he attributed the greater hydragogue properties of the RHAMNUS CATHARTICUS bark. This principle was differentiated from the *cathartin* of senna leaves and named *rhamno-cathartin.* He found *rhamno-xanthin* also in the seeds of RHAMNUS CATHARTICUS and RHAMNUS FRANGULA. The juice of the ripe berries contained

a violet coloring-matter turned red with acids and green with alkalies, a bitter extractive, etc. The unripe berries and those also of RHAMNUS INFECTORIUS contained only the *rhamnin* of Fleury.

Buchner, (1853), who worked with Binswanger at Munich in 1849, obtained from the root-bark of RHAMNUS FRANGULA, *rhamnoxanthin* in sublimable, golden-yellow needles, very slightly soluble in water, but easily so in alcohol or ether, (especially hot), readily in solutions of ammonia and the fixed alkalies with a fine, purple-red color and in concentrated sulphuric acid with a red color. By neutralization of the alkaline solution, the *rhamnoxanthin* was thrown out as a yellow powder and by dilution of the concentrated sulphuric acid solution with water it was likewise separated out.

Casselmann (1857), obtained the resinous constituent from Frangula in crystalline form, designated it *frangulin* and decomposed it with the formation of glucose and an acid product he named *frangulinic* or *nitro-frangulic* acid.

Phipson, (1858), found *rhamnoxanthin* in the branches of RHAMNUS FRANGULA and of RHAMNUS CATHARTICUS and corroborated Buchner's description of it.

Gellatly, (1858), obtained from Persian berries, a substance which corresponded with Kane's *xanthorhamnin,* but to which he ascribes the formula, $C_{48}H_{28}O_{28}$, and which, hydrolyzed, yields grape sugar and *rhamnetin,* ($C_{22}H_{10}O_{10}$) in yellow needles nearly insoluble in cold water but soluble in alcohol or ether.

Kubly, (1866), separated from frangula bark the glucoside, which he named *avornin,* an amorphous resin and a principle similar to cathartic acid, which he had a short time previously isolated from senna leaves. The *avornin* he split into *avornic acid* and glucose.

Lefort, (1866), named *rhamnine* and *rhamnegine* as the coloring constituents of RHAMNUS CATHARTICUS berries.

Stein, (1868), indicated that the *rhamnine* of Fleury, the *chrysorhamnine* of Kane, the *rhamnetine* of Gallatly and the *rhamnine* of Lefort, to be the same substance in different degrees of purity, while the *xanthorhamnine* of Gellatly and the *rhamnegine* of Lefort were also identical, but the *xanthorhamnine* of Kane and that of Gellatly, were not the same substance. He stated that, undoubtedly, *rhamnetin* was identical with *quercetin.* He named as the coloring principles of Persian berries *rhamnin,* soluble in water and *rhamnetin,* insoluble in water. The *rhamnin* upon hydrolysation with dilute acids, or with the ferment present in the fruit, yielded *rhamnetin* and a sugar.

Schutzenberger, (1868), revised the formula of the *rhamnegine* of Lefort and decomposed it with the formation of *rhamnetin* and a sugar isomeric with mannite.

Faust, (1869), stated that the *frangulin* of Casselmann, and the *avornin* of Kubly, are identical, and assigned them the formula $C_{20}H_{20}O_{10}$. He named the acid-resin from the decomposition of this glucoside, *frangulic acid.*

Liebermann and Waldstein, (1876), identified *emodin* (trioxymethylanthroquinone) from frangula bark and stated that frangulic acid is probably *emodin.*

Liebermann and Hormann, (1878), found *rhamnoxanthin* in the pericarp of the berries of RHAMNUS INFECTORIUS and determined that, under the action of a ferment, it splits into *rhamnetin* and *isodulcite.*

Prescott, (1879), was the first to analyze cascara sagrada bark. He found

a brown resin of strongly-bitter taste, colored a vivid purple-red by potassium hydrate solution, sparingly soluble in water or ether, but freely so in alcohol, chloroform, benzole, carbon disulphide and solutions of caustic alkalies, though precipitated from the latter by acids. He found also some other resins, tannin, oxalic and malic acids, etc.

Limousin, (1885), noted that the scraped surface of Cascara bark, touched with strong ammonia or potash solution, gave a fine red coloration and considered it an incontestable evidence of *chrysophanic acid,* which he declared the "resins" of Prescott to be.

Ward and Dunlop, (1887), described the enzymatic action in the berries of RHAMNUS INFECTORIUS, but found that no such action took place in the fruits of RHAMNUS TINCTORIUS, CATHARTICUS, CAROLINIANA, etc.

Meier and Webber, (1888), mentioned in addition to other constituents found in RHAMNUS PURSHIANA bark, an enzyme, to which they attribute the griping effects and the epigastric pain sometimes accompanying the use of the drug, especially of the fresh bark.

Eccles, (1888), found minute quantities of an alkaloid present in Cascara fluid extracts.He also examined twenty prominent drugs by treating the ethereal extracts obtained from fluid extract, with ammonia water and found that the ethereal extracts from frangula and cascara barks alone assumed a red color. He did not distinguish between them.

Schwabe, (1888), found frangula to yield *frangulin* 0.04%, and *emodin* 0.1%. He corroborated the physical characters of *frangulin* as stated by Casselmann and Faust and amplified upon them. His proximate analysis indicated the formula $C_{21}H_{20}O_9$. *Frangulin,* by hydrolysis, yields *emodin.* He found in cascara bark *emodin* but no *frangulin.*

Hooper, (1888), examined the bark of RHAMNUS WIGHTII. He reported several resins, some ether-soluble, some alcohol-soluble, tannin, bitter principle, etc. From the published analyses of RHAMNUS PURSHIANA bark, he concluded that the two barks rather closely correspond chemically, though the former probably had a larger tannin-content. He mentions a yellow coloring-matter in the phloem layer of the bark, which assumes a brilliant red with potash.

Thorpe and Miller, (1892), corroborated Schwabe's formula for *frangulin* and determined that the sugar from the decomposition of *frangulin* was a true *rhamnose.*

Leprince, (1892), isolated a crystalline constituent from cascara bark which formed prismatic needles of a yellow color, insoluble in water, slightly soluble in chloroform but readily so in alcohol and in aqueous solutions of alkalies with a purple-red color. He named it *cascarine.*

Phipson, (1892), regarded the principle isolated by Leprince as identical with *rhamnoxanthin* described in 1858.

Perkin and Geldard, (1894), named the coloring principles of the fruit of RHAMNUS INFECTORIUS: *rhamnazin, rhamnetin* and *quercetin.*

Cabanes, (1895), reported that, in sections of frangula bark, treated with alcoholic potassa solution, the parenchyma of the cortex, medullary rays and bast, all acquire a strong red color, but that in cascara bark sections, only one or

two layers of the cortical parenchyma, the medullary rays and the five or six inner rows of bast parenchyma, take the color. Ammonia and soda solutions react the same as potassa.

Dohme and Englehardt, (1897), obtained what they declared to be the glucoside of cascara bark, *purshianin,* in dark, red-brown needles, not responding to the tests for *emodin,* nor identical with *frangulin,* but yielding, by hydrolysis, *emodin* and a sugar.

Sayre, (1897), proposed identity-tests for distinguishing between the barks of RHAMNUS CALIFORNICA and RHAMNUS PURSHIANA as follows: To 0.2 gm. of the powdered bark in a small test-tube add 2 cc. of potash, T. S. RHAMNUS CALIFORNICA gives a blood-red color at once. RHAMNUS PURSHIANA an orange-red color.

Leprince, (1899), reports cascara bark to contain *chrysarobin, emodin* and *chrysophanic acid.*

Aweng, (1899), presented a method for separating the glucosides of frangula, cascara and rhubarb into groups, by successive extraction with benzene, benzene and absolute alcohol, and 60% alcohol. He obtained a number of glucosides, in varying proportions, from each of the three drugs, most of them yielding, by hydrolysis, *emodin, chrysophanic acid* and *frangula-rhamnetin.*

Oesterle, (1899), found that *frangula-emodin* differs from *aloe-emodin.*

Perrot, (1900), stated that powdered frangula bark with alkalies, produces a deep-red color, but that powdered cascara bark gives a yellow-color and that the powders could be distinguished in this manner.

Tschirch and Polacco, (1900), analyzed RHAMNUS CATHARTICUS fruit and determined the presence of *emodin,* several coloring matters, a sugar, etc. The purgative action was ascribed to the *emodin.*

Jowett, (1904), found in cascara bark, *emodin,* glucose, an enzyme, fat, etc. His attempts to isolate the bitter principle, were unsuccessful, but he claimed that *emodin* was not the most important purgative principle. The enzyme, in one-gram doses, was not griping. There was practically no distinction in the chemistry of the barks from RHAMNUS PURSHIANA and RHAMNUS CALIFORNICA.

Warin, (1905), presented a colorimetric method for the quantitative determination of the *emodin* in frangula bark, by neutralizing the rose-red tint of a measured, alkaline, aqueous extract of the drug, with the green tint of a standardized, nickel-salt solution. Later, he pointed out that, before this method could be applied to cascara bark or its preparations, the same must be so treated as to hydrolyse the glucosides.

Tschirch and Pool, (1908), found that the *emodins* from frangula and cascara barks were identical, that neither of the barks yielded *rhein,* but that *chrysophanic acid* was present in frangula bark. They approved Warin's colorimetric assay.

Waljaschko and Krassowski, (1908), claim that the same coloring principles occur in the fruits of RHAMNUS CATHARTICUS as in those of RHAMNUS INFECTORIUS and RHAMNUS TINCTORIUS. In addition the fruits of RHAMNUS CATHARTICUS were found to contain about 2% of *emodin* bodies.

Tschirch and Bromberger, (1911), obtain from the bark of RHAMNUS CATHARTICUS, *frangula-emodin,* chrysophanic acid, *rhamnofluorin, rhamnosterol,* glucose, tannin, etc.

Oesterle, (1911), states, regarding the oxymethylanthroquinones, that *aloe emodin* reduced, forms chrysophanic acid, but oxidized, forms *rhein,* while chrysophanic acid oxidized, likewise forms *rhein.*

Tutin and Clewer, (1911), state that the anthroquinone derivatives from rhubarb,—*rhein, emodin, aloe-emodin, frangula-emodin, emodin-monomethyl-ether* and chrysophanic acid, are derived from medicinally inert glucosides; that only *aloe-emodin* and chrysophanic acid possess purgative properties, and that most of the purgative value of the drug, lies in a non-glucosidic resin which they isolated.

Rosenthaler, (1911), presents a list of anthroquinone drugs distinguished from one another by the physical characters of their micro-sublimates and the color-reaction of these sublimates in alcoholic solution with ferric chloride solution.

Schmidt, (1912), describes *frangulin, (rhamnoxanthin),* ($C_{21}H_{20}O_9$), as occurring in lemon-yellow, glistening, fine needle-crystals, odorless and tasteless, melting at 228° to 230° C. It is almost insoluble in water and in cold ether, but soluble in 180 parts of 80% hot alcohol. Concentrated sulphuric acid dissolves it with a dark-red color and with caustic alkalies it forms solutions of a purple-red color. By boiling with an alcoholic solution of hydrochloric acid, it becomes converted into *rhamnose* and *frangula-emodin,* ($C_{15}H_{10}O_5$), which forms bright-red, glistening needles melting at 255° C. It is insoluble in water, slightly soluble in alcohol and easily in chloroform and benzol In ammonia it dissolves with a red, slightly bluish color.

(To be continued.)

A NEW METHOD FOR THE ESTIMATION OF GLYCERIN IN PHARMACEUTICAL PREPARATIONS.

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Glycerin is one of the most common and generally used substances in pharmacy and yet its quantitative determination in pharmaceutical preparations presents many difficulties. On several occasions in our laboratory it has been necessary to attempt to assay for glycerin such preparations as elixirs, tooth-pastes, shaving soaps, liquid face creams, and essences of pepsin, and the results have been far from satisfactory. Several methods with necessary modifications to adapt them to the particular preparations were tried, but in some cases the duplicate results showed marked variations, thus making doubtful the reliability of the process.

The official methods for the determination of glycerin in wines are not applicable to all pharmaceutical preparations because of interfering substances and, to say the least, they are long and tedious. (See Allen's Organic Analysis, Vol. 1, page 167.)

It would seem therefore that a simple and reliable method for the estimation