14.—CORN SALVE

Salicylic Acid	2	oz.
Ammonium Chloride	2	oz.
Acetic Acid	4	fl. dr.
Lanolin	2	oz.
White Wax	2	oz.
Lard to make	1	lb.

Mix the acid with the ammonium chloride, add the lanolin, and, lastly, the lard and wax previously melted. Mix thoroughly, pour into ¼-oz. tin boxes, and allow to cool.

15.—WORM SYRUP

Fl. Extr. Spigelia	40	fl. oz.
Fl. Extr. Senna	24	fl. oz.
Oil Anise	80	drops
Oil Caraway	80	drops
Syrup	64	fl. oz.

Put up in two-ounce green glass panels, and sell for 25 cents.

16.—CARBOLIC SALVE

Petrolatum	16	oz.
Paraffin	1½	oz.
Camphor	1	oz.
Carbolic Acid	210	grn.
Oil Sassafras	30	min.

Rub the carbolic acid, camphor, and oil together until solution is effected. Add to the petrolatum and paraffin previously melted, and stir until cool.

This makes an excellent salve for general use. Put up in two-oz. tin boxes, with label and carton. Sell for 20 or 25 cents.

THE CHEMISTRY OF CANNABIS INDICA*

By John Humphrey

THE hemp plant, *Cannabis sativa*, Linné (N. O. Urticaceæ), is an annual dicœcious herb which acquires marked narcotic properties when grown in tropical countries, the effects being most pronounced in the case of female plants cultivated in India, where the dried and crushed leaves are known as "bhang" and the compressed flowering tops as "ganja." The leaves and bracts bear yellow glands containing a resinous secretion, the exudation of which renders them viscid to the touch. During the preparation of the flowering tops to form "ganja," part of the dried resinous exudation is said to separate in the form of a grayish powder, which is collected and mixed with an extract of the plant to make a preparation called "charas," used for smoking. The best "charas," however, is prepared by collecting the resinous exudation from the flowering tops and packing it in bags, an oily resinous mass being produced as the powder gradually consolidates. There are several varieties of "ganja," the best being produced in Bengal and consisting of the dried and compressed flowering tops of female plants which have not been been fertilized, great care being taken to remove all male plants before there is any chance of fertilization being effected, since it has been found that the secretion of resin is increased if the formation of seed be prevented. The drug —Bombay ganja—official in the British Pharmacopœia, under the name of Cannabis Indica, or Indan hemp, may consist of either flowering or fruiting tops, and is frequently of very inferior quality, since fruiting tops yield less resin—the constituent which has been considered the most important part of the drug—then flowering tops in which the development of seed has been prevented. In addition to the resin, the only important constituent of Indian hemp appears to be a volatile oil which occurs in small proportion, though several investigators have recorded the presence of alkaloidal matter in the drug.

*Pharmaceutical Journal.

ALKALOIDAL MATTER

The first announcement of the discovery of an alkaloid in hemp was made by Preobraschensky (*Pharm. Zeit. f. Russland,* 1876, p. 705), who obtained from "haschisch"—a kind of confection made from Indian hemp—a volatile alkaloid, apparently identical with nicotine, which he believed to be the active principle of the drug; but it appears probable that the "haschisch" which he examined contained a certain proportion of tobacco. Later, Siebold and Bradbury (*Pharm. Journ.* [3], 12, 326) gave the name cannabinine to an uncrystallizable volatile alkaloid, somewhat resembling coniine, which they obtained from "pure" Indian hemp, and Dr. Hay (*Pharm. Journ.* [3], 13, 998) arrived at the conclusion that the drug contained several alkaloids, one of which he named tetano-cannabine, because it resembled strychnine in its action. Denzel (*Pharm. Centralhalle,* 1885, p. 540) also reported the presence of a tetanizing alkaloid, but Warden and Weddell (*Pharm. Journ.* [3], 15, 574) were unable to obtain any such base, though they found indications of a nicotine-like principle in an oil obtained by destructive distillation of a freshly-prepared alcoholic extract of Indian hemp. The base was not identical with nicotine, however, and Kennedy (*Pharm. Journ.* [3], 17, 453) subsequently confirmed the presence in the drug of an alkaloid which differed from nicotine. Still later, H. F. Smith (*Amer. Journ. Pharm.,* 1891, 386) confirmed the results of Siebold and Bradbury, by separating from Indian hemp a coniine-like base, while Marino-Zuco and Vignolo (*Pharm. Journ.* [4], 1, 519) also obtained from the drug a substance of alkaloidal nature. But Jahns (*Pharm. Journ.* [3], 17, 1049) had previously detected the presence of choline in Indian hemp, and pointed out that this base, or a decomposition product thereof, was probably what some previous investigators had found. Choline or bilineurine is trimethyl-ethylol-ammonium hydroxide, a strong base which crystallizes with difficulty and is not uncommon in plants. By the action of caustic alkalies, as in the process employed by Siebold and Bradbury for the extraction of "cannabinine," choline can be converted into trimethylamine, which also occurs naturally in several plants, and there appears to be good reason for the belief that the various substances of alkaloidal nature obtained at different times from Indian hemp may have consisted of choline or some decomposition product, such as trimethylamine, in a more or less impure condition. Certainly the presence of no distinctive alkaloid has yet been proved in Indian hemp, and it is noteworthy that the most recent investigators —Wood, Spivey, and Easterfield—failed to obtain any alkaloid whatever from "charas."

VOLATILE OIL

The volatile oil of Indian hemp, as obtained by Personne (*Journ. de Pharm. et de Chim.* [3], 31, 46) congealed at 12°-15° C., and consisted of two hydrocarbons —cannabene, $C_{18}H_{20}$, and cannabene hydride, C_6H_{14}, the former being a liquid boiling at 235° to 240° C., while its supposed hydride, which probably consisted of paraffin, crystallized from alcohol in scales. Personne (1857) was of opinion that cannabene was the active principle of Indian hemp, and the effects produced by it, as described by him, were similar to those which had been recorded in 1840, by Bohlig, as having been produced by an oil of which he obtained 0.3 per cent. from the fresh herb. Subsequently, Valente (*Journ. Chem. Soc.* (Abst.), 40, 284) found that an oil (s. g. 0.9292) obtained from *Cannabis sativa* grown in Italy consisted chiefly of a sesquiterpene, $C_{15}H_{24}$; it boiled at 256°—258° C. and yielded nothing resembling the solid hydrocarbon mentioned by Personne. Still later, Vignolo (*Journ. Chem. Soc.* (Abst.), 68 [i.], 623) obtained an oil which boiled between 248° and 268° C. and yielded a sesquiterpene, $C_{15}H_{24}$, which boiled at 256° C. and left a stearopten behind when distilled over sodium. Cignolo was of the opinion that the cannabene obtained by Personne was a mixture, and that opinion was confirmed on purifying it, when it appeared to be identical with the sesquiterpene, $C_{15}H_{24}$, obtained by Valente from ordinary hemp. Finally, Schimmel and Co., (*Bericht,* 1895, p. 57) obtained, by distillation of the non-flowering herb, 0.1 per cent. of a mobile oil (s. g. 0.932) with a narcotic odor; but Roux (*Bull. Gén. de Thérap.,* 1886, p. 492) had previously proved, by experiments on animals, that the volatile oil obtained from Indian hemp is inactive, and no satisfactory evidence to the contrary has yet been brought forward.

RESIN

The resin, which constitutes the greater part of "charas" of good quality, was first separated from Indian hemp in a state of comparative purity by T. and H. Smith (*P. J.* [1], 6, 127 and 171), who named it cannabin.* As prepared by them, it was a soft, brown, neutral resin, soluble in alcohol or ether, insoluble in water or weak alcohol, and capable of producing powerful narcotic effects in doses of two-thirds of a grain. A resin obtained by Martius (*N. Rep. f. Pharm.,* 4, 529) was also soluble in alcohol or ether, as well as in volatile oils; it fused at 68° C. and dissolved with difficulty in aqueous alkalies or in acids. By treatment with nitric acid, Bolas and Francis (*Chem. News,* 24, 77) converted the resin of Indian hemp into oxycannabin, $C_{11}H_{11}NO_4$, a substance forming yellow needles which melted at 176° C., and Dunstan and Henry (*Proc. Chem. Soc.,* 1898, p. 44) have since obtained the same substance from "charas." It is a nitro-lactone and, when quite pure, occurs in colorless needles (m. p. 182° C.) which are insoluble in water, but dissolve in hot alcohol and crystallize out again on cooling. A substance to which the name cannabindon, $C_8H_{12}O$, was applied by Kobert (*Chem. Zeit.,* 1894, 741) resembled the resin of Indian hemp in narcotic power and in being soluble in alcohol, ether, or oils; but it was a dark red, syrupy liquid and, apparently, similar to

*MERCK (*Pharm. Journ.*) [3], **13,** 1052) described a preparation obtained by combining cannabin, a glucoside supposed to exist in Indian hemp, with tannic acid, and Bombelon (*Pharm. Journ.* [3], **14,** 965) claimed to have obtained the pure glucoside by decomposing the tannate; the supposed glucoside, which was described as a greenish-brown powder, probably consisted chiefly of resin. The name "cannabinon" (*Pharm. Journ.* [3], **17,** 685) was subsequently applied to the resin of Indian hemp, from which the supposed tetanizing alkaloid had been removed by treatment with tannic acid, and Leib Lapin (1894) proposed the name "cannabindon" for a similar resinous substance, prepared by a process of fractional precipitation from an ethereal extract of the plant.

the "cannabinol" originally obtained from "charas" by Wood, Spivey, and Easterfield (*Journ. Chem. Soc.*, 69 [i.], 539). Those workers obtained from "charas" a terpene (b. p. 160°—180° C.), a sesquiterpene (b. p. 258°—259° C.), a crystalline paraffin, $C_{29}H_{60}$, melting at 63°—64° C., and 33 per cent. of a toxic red oil (b. p. 265° C.), with the formula $C_{18}H_{24}O_2$, to which they gave the name cannabinol, the last-mentioned constituent being regarded by them as the only active constituent of the resin. It was soluble in alcohol, ether, benzene, glacial acetic acid, and organic solvents generally. The same red oil was found to constitute a large proportion of various pharmaceutical preparations of Indian hemp, and Dr. C. R. Marshall showed that it was extremely active, the symptoms produced by it being those peculiar to Cannabis Indica and not possessed by the terpenes or any other product of "charas."

CANNABINOL

Further investigation of the red oil or crude cannabinol by Wood, Spivey, and Easterfield (*Journ. Chem. Soc.*, 75, 20) proved that it was a mixture of at least two compounds having similar physical characters, and the name cannabinol has been retained for the only one of those compounds which has yet been isolated. The crude cannabinol obtained by fractionating an alcoholic "charas" extract, under diminished pressure, yielded a yellow crystalline substance—trinitro-cannabinol, $C_{21}H_{23}N_3O_8$—when treated with nitric acid under certain conditions. The trinitro-cannabinol was readily reduced by boiling with hydriodic acid and phosphorus, yielding the hydriodide of a base which has not yet been isolated, owing to the readiness with which it oxidizes. As the formula $C_{21}H_{23}N_3O_8$ represents the trinitro-derivative of a compound with the formula $C_{21}H_{26}O_2$, the presence in crude cannabinol of a body having the latter formula appeared probable, and its existence was definitely proved by the isolation of an acetyl derivative—$C_{21}H_{25}O_2.C_2H_3O$—from the red oil or crude cannabinol. The latter sets to a sticky, semi-solid, odorless mass when cooled below 60° C., but pure cannabinol, $C_{21}H_{26}O_2$, obtained by distillation of an ether extract under diminished pressure, is an almost colorless oil which sets, on cooling, to a transparent brownish resin. This pure cannabinol, when administered in very small doses, produces the toxic symptoms characteristic of Indian hemp, and there appears little reason to doubt that it is the active principle of the drug. Further, Dr. C. R. Marshall has shown, in a paper read before the American Medical Association, that the activity of cannabinol diminishes as the substance becomes oxidized by exposure to the air, so that—if, as appears extremely probable, cannabinol is the active principle of the Indian hemp—it is obviously desirable to protect the drug and its preparations from the action of the air as much as possible. This accords with Dr. Prain's observation (see *P. J. ante*, p. 342) that "ganja" does not keep; the deterioration of the drug being normally so rapid that its potency diminishes to one-fourth within twelve months, while "ganja" two years old is practically inert. The facts recorded by Dr. Marshall also seem to afford an explanation of the conflicting results obtained by different investigators, since the samples of Indian hemp or resin examined on various occasions probably differed as much in composition and potency as they doubtless did in age and physical characters.

SUMMARY AND CONCLUSIONS

To sum up, Indian hemp appears to contain no peculiar alkaloid, but the drug may yield a certain proportion of choline (bilineurine) or some decomposition product of that base, such as trimethylamine, formed during the process of extraction. The drug also contains a little volatile oil which consists chiefly of a sesquiterpene (cannabene) and paraffin, but the chief constituent of Indian hemp is apparently the resin, cannabin, of which "charas" mainly consists, and of which cannabinol is the active principle. Finally, since cannabinol, on exposure to the air, becomes oxidized and loses its potency, the loss of activity of Indian hemp and its preparations would also appear to be due to that cause. Hence, it seems desirable that Indian hemp used in medicine should be obtained as fresh as possible, and that, as suggested by Dr. Marshall, the drug and its preparations should be preserved in hermetically sealed packages if they are to be kept for any considerable length of time before use.

GLYCOCOLL, THE SOLVENT OF MANY METALLIC OXIDES AND HYDROXIDES*

By Theodore W. Schaefer, M.D., Kansas City, Mo.

GLYCOCOLL was first prepared by Braconnot in the year 1820. It belongs to the group of organic compounds known as the amido acids of the fatty series. These substances possess, more or less, an amphoteric function, exhibiting both acid and basic properties, forming combinations with a number of acids, as well as with a number of metallic oxides and hydroxides. Some of these amido acids have been found in a free state in the animal body. Most of these bodies possess a saccharine taste.

Glycocoll, $C_2H_5NO_2$, also known as glycocine, glycine, glycolamic acid, amidoacetic acid or sugar of gelatin, is obtained by the decomposition of various animal substances like hippuric acid, uric acid, glycocholic acid, gelatin, or glue, when they are boiled with alkalies or acids.

Glycocoll has not yet been detected in the human body in a free state, although Chittenden was successful in finding it in the muscles of *Pecten irradians*, the common edible scallop of the United States. Glycocoll as such has not been found among the products of pancreatic digestion, although the radicle is manifestly present in certain albumoses. It plays an important role in the nitrogenous metabolism of the body, and is intimately concerned in the formation of urea, hippuric acid, phenaceturic acid and glycocholic acid.

When glycocoll is taken internally its constituents are eliminated from the body through the urine in the form of urea.

Glycocoll is a whitish, crystalline substance, possessing a sweetish taste, sparingly soluble in cold, but very soluble in hot water and insoluble in ether and alcohol. It is slightly acid in reaction to blue litmus paper.

One of the most characteristic properties of glycocoll is the great solvent powers which it exerts upon many metallic oxides and hydroxides. It unites with the alkalies and alkaline earths, driving off the carbonic acid from their carbonates. I find that a hot aqueous solution of glycocoll readily dissolves the hydroxide of nickel, forming at first an apple-green solution, which turns bluish after some time. The hydroxide of cobalt is rapidly dissolved by a hot solution of glycocoll, a pink colored solution of considerable permanency resulting. Manganous hydroxide is at once dissolved by a hot solution of glycocoll. Ferrous hydroxide is very soluble in the same menstruum. Zinc hydroxide, freshly precipitated, behaves in a similar manner. Zinc oxide is also rendered soluble by a hot solution of glycocoll. Mercuric oxide is at once dissolved by glycocoll, forming a transparent solution, which, however, turns dark on boiling, metallic mercury separating, formate of ammonia being produced at the same time. Mercurous oxide is dissolved by a hot solution of glycocoll, forming a solution which is more stable than the one with mercuric oxide. Glycocoll, in a hot aqueous solution, dissolves anhydrous cupric oxide, forming a beautiful, blue solution. Antimonous oxide, Sb_2O_3, is slowly dissolved by it. The yellow oxide of bismuth, Bi_2O_3, is not dissolved by it and the hydroxide is not rendered soluble on boiling. Litharge or lead oxide, PbO, readily dissolves in hot solution of glycocoll. Cadmium hydroxide, $Cd(OH)_2$, is rapidly dissolved by a hot solution of glycocoll. Stannous hydroxide is not so readily dissolved by it. Uranic oxide, UO_3, dissolves very slowly in hot glycocoll solutions. Tungstic trioxide, WO_3, when boiled for some time in a solution of glycocoll, changes its yellow to a green color and the solution finally assumes a bluish tint. Auric trichloride, in solution, does not produce an important color change with glycocoll, and I find that auric hydroxide does not appear to be readily dissolved by it. Platinic chloride does not seem to be disturbed by it, no color effect being produced. Platinic hydroxide appears to be scarcely affected by a hot solution of glycocoll.

A hot solution of glycocoll dissolves freshly-precipitated cupric hydroxide, forming a liquid, possessing a beautiful, deep-blue color, from which cupric glycolamate crystallizes readily in dark-blue needles on cooling. If to a solution of cupric glycolamate some grape sugar be added, the copper becomes reduced to cuprous oxide when boiled for some time. The copper is not completely reduced to the suboxide, because the latter is somewhat soluble in boiling solutions of glycocoll. Cane sugar produces no such an effect.

Silver oxide dissolves in a boiling solution of glycocoll. The silver glycolamate crystallizes readily. I find that a hot solution of silver glycolamate is at once reduced to the metallic state by a solution

*Druggists' Circular.