

potatoes, apples or medicinals, there must be a market for the produce. The next factor to consider is, from which crop can we realize the greatest returns for the capital invested? Hence the grower must first acquaint himself with the market conditions and then, after careful calculation, determine which crop will be most profitable. If medicinal plants have been decided upon as the crop to be grown, and all the prerequisites, capital, market, satisfactory market price, skill, equipment, proper soil, etc., are at hand for the production of such a crop, then the grower must take into further consideration that if too many individuals engage in growing the same crop, the market price will drop below the figures on which he based his profits, and a financial loss will be the result. Under commercial conditions in order to warrant the cultivation of medicinal plants they must yield a greater return than other agricultural crops.

Five medicinal plants have been considered in this paper. Prices for the crude drug of two of them, namely, belladonna and hyoscyamus, are to-day lower by half than those paid for them in December, 1917, at which time the prices for crude drug materials had reached the high mark. We have not been importing any of these five drug plants within the last year, and our consumption—hence the demand—has been much greater than a year and a half ago. This clearly demonstrates that the United States has met the original so-called possible crude drug crisis, and all the demands have been and are being met, by products from plants grown here on a commercial scale.

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THE PREPARATION OF PHENYLCINCHONINIC ACID.*

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The cancelling of patent rights on synthetic preparations made in Germany and the issuance of licences to American manufacturers able to produce these

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products according to standard requirements as to physical, chemical and physiological tests, led chemists throughout the country to efforts along this line of work which heretofore had received very little attention.

The following is the result of work by the writer on phenylcinchoninic acid (former trade name Atophan), taking into account first the preparation of the products entering into it:

Benzylidin-Anilin.—This is made by mixing molecular quantities of anilin and benzaldehyde, the anilin being added slowly to the benzaldehyde. The result is the splitting off of one molecule of water when the two combine, leaving $C_6H_5N.C_6H_5CH$. It may be crystallized readily by pouring the mixture into shallow vessels, and within a few minutes crystals form and in the course of a half hour it becomes a crystalline mass from which the greater portion of the water may be poured and the rest removed by drying *in vacuo* at the temperature of the water bath. The crystallization, however, is not absolutely necessary, as the water formed will collect on the surface of the benzylidin-anilin and may be separated mechanically, the subsequent drying being done as with the crystals.

Pyroracemic or Pyruvic Acid.—This is made preferably by the destructive distillation of tartaric acid. The tartaric acid is mixed intimately with an equal weight of potassium acid sulphate and the mixture subjected to distillation at a temperature not exceeding $220^{\circ} C$. This is best done by the use of an oil bath, the distillation being continued four or five hours or until no more distillate is received. The process is very slow and the tartaric acid is broken down into carbon dioxide, water and pyroracemic acid, the acid being purified by redistilling from an oil bath, the portion between $130^{\circ} C$. and $180^{\circ} C$. being saved. The tendency is very strong for the acid to retain the water, some of it even above 130° , unless the distillation is conducted very slowly, raising the temperature not faster than 1° per minute from $100^{\circ} C$. to $130^{\circ} C$. The yield in acid is stated by some authorities to be 25 percent of the tartaric acid, but in working with small quantities the yield was found to be slightly below that figure.

Pyroracemic acid is a syrupy liquid, miscible with all ordinary solvents, is of light straw color and has a specific gravity of about 1.280.

A great deal of trouble was experienced in making the distillation from the tartaric acid, due to excessive foaming, and several preventive measures were tried with varying results. Cerasin was added, but owing to the extreme viscosity of the mixture it did no noticeable good. A method is suggested of charring the acid in an open vessel and after cooling the fused mass is broken into pieces and subjected to distillation. This plan has objectionable features owing to the loss of pyroracemic acid during the charring. Another effective means was tried, that of continuous stirring in the flask until it became charred after which it boiled quietly. This was attended with less loss of acid, as the greater portion condensed on the sides and neck of the flask while the water with a lower boiling point passed off. It is quite possible that a mechanical stirrer within the distilling chamber might be used with success in making distillations in large quantity.

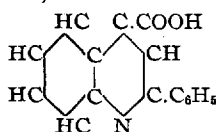
It was first thought that the presence of carbon was the chief factor in allaying the foaming, but on using the same potassium acid sulphate repeatedly, and which carried with it considerable carbon, no decrease was noted, so it is concluded that the formation of water in the decomposition of the tartaric acid is directly

responsible. The use of fused potassium acid sulphate tends to lessen the foaming, but does not eliminate it.

The method for the combination of these products is the same as that outlined in the patent which follows: According to this invention 2-phenyl-quinolin-4-carboxylic acid is made by boiling an alcoholic solution of benzylidin-anilin and gradually adding pyroracemic acid to the boiling solution. From the rather indefinite statements regarding the percentage yield it would seem that the latest patentees obtained a yield of about 135 percent of the pyroracemic acid used. By the above process I obtained a yield of 85 percent in one case and 90 percent in another, the variation being due largely to the presence of water in the pyroracemic acid used as otherwise the experiments were carried out under the same conditions.

Procedure.—The benzylidin-anilin is boiled in dehydrated alcohol (reflux condenser) for fifteen or twenty minutes and the pyroracemic acid added slowly to the boiling solution. The mixture assumes a cherry-red color and should be boiled for about two hours after all the acid is added. The excess alcohol is then distilled from the mixture until a portion of the phenylcinchoninic acid is noticeably separated, after which the mixture is cooled as rapidly as possible, then placed in an ice bath, when it becomes a crystalline mass. Cold alcohol is then added, after which it is filtered with suction and washed with cold alcohol or ether until the tarry matter is completely removed. The use of ether as the final wash liquid facilitates the drying of the crystals, the tarry residue being very soluble in it. The residue is spoken of in the patent as "residue insoluble in soda lye," but it may as well have been spoken of as insoluble in acids, as it is insoluble in either strong acids or alkalies and might well be used as a varnish for laboratory ware on which acids or alkalies have a corrosive action.

Pyroracemic or acetyl formic acid, $\text{CH}_3\text{CO}\cdot\text{COOH}$, combines with the benzylidin-anilin to form phenylcinchoninic acid, $\text{C}_6\text{H}_5\cdot\text{C}_9\text{H}_5\text{N}\cdot\text{COOH}$, which is, as stated, 2-phenylquinolin-4-carboxylic acid,



Inasmuch as there are four uncombined hydrogens as a result of this union, it is quite probable that the acid acts as an oxidizing agent, thereby eliminating it.

The Ninth Revision of the United States Pharmacopoeia states that the melting point should be about 210°C ., but samples of Atophan taken from the open market had melting points from 208° to 209°C ., corrected. It was found that the presence of water in the pyroracemic acid materially lowers the melting point and the product on melting decomposes at a lower temperature (noted by darkening). On observing the aforementioned precautions in redistilling the acid to eliminate the water a product was obtained with a melting point of 209.5°C . and no noticeable decomposition at its melting point.

In summing up the difficulties encountered it might be said that the destructive distillation of the tartaric acid and the subsequent distillation of the pyroracemic acid to eliminate the water were the chief ones.