MEDICINE-PHARMACOLOGY

Isolation of Strychnine

"A Classic of Science"

The Poisonous Alkaloid Occurs in Three Related Plants And Was Discovered by a Famous Team of Pharmacologists

MEMOIRE sur un nouvel alcali végétal (la strychnine) trouvé dans la fève de Saint-Ignace, la noix vomique, etc. Par MM. Pelletier et Caventou. (On a new vegetable alkali, strychnine, found in Saint Ignatius' bean, nux vomica, etc.). Published in Journal de Pharmacie et des Sciences Accessoires, Vol. V, April, 1819. *Translated for the* SCIENCE NEWS LETTER *by Helen M. Davis. This is a literal translation of extracts from the original publications.*

LINNAEUS thought that plants of the same family, and, even more, those of the same genus, were very frequently endowed with analogous medical properties. Murray and Gmelin shared this opinion: this is also the belief held by the most celebrated botanists of our day.

If, as we cannot doubt upon such authority, the action which the plants are able to exert upon the animal economy is connected with their essential constitution, in such a way that plants of the same family usually possess the same medical properties, is it not because they contain the same *immediate substances,* and through these there acts upon the animal economy a common principle, stronger, more energetic, seeming to impress its character upon all parts of the plant which contains it? And if Gleditsch, Cullen and several others contend that it is not possible to judge the properties of plants from their exterior forms and their botanical characteristics, it is because they take in too literal a sense the expressions which their opponents use. But by stating the question thus:

Plants owe their medicinal properties to the immediate substances which constitute them; plants of the same family very frequently contain the same substances or immediate principles; the characteristic medicinal property, in every plant, is chiefly due to one of these bodies; the intensity of this property is proportional to the quantity of the principle which determines it, and if this principle happens to be wanting in one species, the medicinal property characteristic of the family is also lacking in it; perfect accord upon the subject will be found to reign among botanists. It was with the object of establishing these truths in an incontestable manner that we undertook chemical researches upon the most active plants of the materia medica.

The Genus Strychnos

Among these there was reason to select several species of the genus *strychnos,* in particular nux vomica and St. Ignatius' bean (*Strychnos nux vomica* and *Strychnos ignatia*). These two seeds have, in recent times, attracted all the attention of physiologists, and the first has given rise to dissertations of the savants read in the bosom of the Academy. The effects of the second have also been observed; but the difficulty of procuring its seeds has made these observations less numerous. Several chemical studies have also been undertaken upon nux vomica, and there are two analyses of its seeds; one published by M. Desportes, and the other, little different, by M. Braconnot. The composition of St. Ignatius' bean, on the contrary, had been entirely ignored, until the time that we, having got a certain quantity of this substance, submitted it to analysis. It was while occupied with this work that we were able to isolate the active principle of this material and of the other poisonous *Strychnos.* We have obtained it in crystalline form, perfectly white, and with all the characteristics of a pure and entirely distinct substance, endowed with the particular and characteristic properties of salt-forming bases, that is to say, with the faculty of uniting with acids, of saturating them by forming with them true neutral salts, soluble, transparent and crystallizable.

Encouraged by this success we tried again the analysis of nux vomica, and we were not long in finding in this material the alkaline principle of St. Ignatius' bean. In nux vomica, it constitutes, by its combination with an acid and its mixture with coloring matter, the yellow bitter principle described by MM. Desportes and Braconnot. It exists, also, in a wood known by the name of *bois de couleuvre* [snake wood], the naturalists place with the strychnos (*Strychnos colubrina*).

The explanation of the chemical properties of the active material of strychnos and of its action upon the animal economy is the subject of this memoir.

The presence of an active material in three species of plants of the same genus authorizes us to derive the name which it is necessary for us to give such a new substance, from the name of this genus itself: consequently we propose to call *strychnine* the substance which is the principal subject of this memoir.

We would first have named it *vauqueline,* in honor of the famous chemist who first demonstrated an *organic alkali;* but we have followed the advice of the commissioners of the Academy, who thought *that a cherished name should not be applied to a poisonous principle.* We shall not discuss all the experiments which we made upon St. Ignatius' bean and nux vomica, to separate the different immediate principles which make up these substances. But we think we should report the experiments which we conducted in the discovery of strychnine, this publication being able to offer something of interest from the point of view of the history of organic analysis.

Extraction of Strychnine

The horny texture of St. Ignatius' bean, and the quantity of fatty matter which it contains, not permitting it to be reduced to powder, we divided it by means of a grater. In this state, it was subjected to the action of sulphuric ether in a valved digester. In this way we obtained a sort of butter or oil of thick consistency, of a slightly greenish color, transparent while it is in the state of fusion. This oil, which we at first regarded as a pure substance, had the characteristic action of St. Ignatius' bean

upon the animal economy, and made the animals die in an attack of tetanus. We thought afterward that this property did not belong to the oil, but to a body which it contained, and which we had not at that time suspected.

The St. Ignatius' bean, yielding nothing further to ether, was treated with boiling alcohol. The numerous alcoholic decoctions which we were obliged to make to remove from the St. Ignatius' bean all that seemed to be soluble in that medium, were reunited after having been filtered twice; the first time, boiling, to separate them from the material of the seeds; the second time, after being completely cooled, to obtain a small quantity of waxy material which separated on cooling. They were then subjected to evaporation, and yielded a yellowish brown material, very bitter, soluble in water and in alcohol. This material was most active and violent in its action on the animal economy.

Paralleled Earlier Observations

Thus far our analysis ran parallel to the analysis of nux vomica as carried out by MM. Desportes and Braconnot. Like those chemists, we found a very active fatty substance, and a yellow-brown very bitter one, not less active than the other. Although we were unwilling to admit that two such different bodies in their chemical composition as the fatty material and the yellow bitter material might have a similar effect on the animal economy; and always regarding the fatty material as a pure and homogeneous substance; having, on the contrary, strong reasons for considering the bitter colored principle as of more or less complex composition, our attention turned to the latter, and supposing that it would retain the fatty material in combination, we varied our attempts to separate it entirely. We succeeded, it is true, by many means, in separating from it a slight amount of fatty material; but it always retained its activity. Solutions in water and alcohol, the action of ether, of salts, of metallic oxides, were tried in vain, and we always remained in the same uncertainty. Finally, we perceived that the fatty material was susceptible of being saponified, we tried an attack upon the colored, bitter principle by employing alkalies, hoping to find greater facility in effecting the separation of the fatty material when it should be in the state of saponification. Having then mixed a solution of caustic potash with a fairly concentrated solution of the bitter yellow material obtained from St. Ignatius' bean, there immediately formed an abundant precipitate. This precipitate, washed by cold water, in which it was insoluble, showed a white, crystalline material, of excessive bitterness; the alkaline liquor retained all the coloring matter, and an acid, to which we will return later.

After having thus obtained the white material, we hastened to examine its properties. We soon perceived that it possessed that of restoring to blue vegetable colors reddened by acids, although it was impossible to recognize the least traces of potassium in the last washings of the white material. Nevertheless, to remove the least doubt, we prepared new quantities of crystalline material, by treating several grams of the bitter yellow material with very pure magnesia, with the aid of prolonged boiling for several minutes. The whole was cooled and thrown upon a filter which retained the magnesia and the crystalline material as a mixture, the coloring matter was entirely washed away by washing with cold water, which has but slight effect upon the bitter crystalline principle; the latter being, on the contrary, very soluble in alcohol, it was separated, by this means, from the magnesia, and obtained in a great state of purity. In this state, it displayed its alkaline properties in a very marked manner.

Frightfully Energetic Action

The frightfully energetic action which this material exercised upon the animal economy, action confirmed by a great number of experiments reported at the end of this memoir, allowed us to hesitate no longer in considering this substance as the active principle of St. Ignatius' bean; but then it ought to be found again in the fatty material, and that material, upon being deprived of it, ought to lose its poisonous properties. Experiment confirmed our idea. By dissolving the fatty material in ether in the cold, we obtained a certain quantity of crystalline material, and we were soon able to deprive the fatty material of all action on the animal economy, by boiling it for a long time in water acidulated with hydrochloric acid, which took up the last portions of alkaline matter.

The bitter, alkaline, crystalline material from St. Ignatius' bean, or, no longer to make a periphrasis do, strychnine, should be found in nux vomica: experiment soon confirmed our suspicions; but obtained by the same process, it was neither white nor crystalline like that furnished by St. Ignatius' bean, and it was rather difficult to recognize. If we had not been prejudiced in favor of its existence by our experiments upon St. Ignatius' bean, it would have escaped our researches as it did those of the chemists who preceded us in the analysis of nux vomica. It was colored, sticky, lumping, forming a mass. We recognized that it was contaminated with a large quantity of fatty material which it failed to get rid of. The quickest and most economical process for obtaining pure strychnine from nux vomica consists in making an alcoholic extract, which is dissolved in water; then add to the liquid a solution of lead sub-acetate, just to the end of precipitation. By the lead acetate there is precipitated at one time the acid combined with the strychnine, the fatty material, as well as the greater part of the coloring matter and the gum which make up the alcoholic extract of nux vomica.

The strychnine remains in solution, combined with the acetic acid. The liquid contains beside a part of the coloring matter not precipitated by the lead acetate, and sometimes an excess of lead acetate. The lead is removed by hydrogen sulphide; filter and boil the filtrate with magnesia which removes the acetic acid, and precipitate the strychnine; wash it with cold water, redissolve it in alcohol to separate it from the magnesia added in excess, and by evaporation of the alcohol it is obtained in a state of purity. If it is still not perfectly white, it is necessary to redissolve it in acetic acid or hydrochloric acid, and precipitate it anew with magnesia. It is by using this procedure that we have been able to obtain strychnine from *bois de couleuvre* (*Strychnos colubrina*).

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ASTRONOMY

Ammonia Gas Detected In Atmosphere of Jupiter

GASEOUS ammonia has been detected in the atmosphere of the planet Jupiter, by Dr. R. Wildt of the astronomical observatory of Göttingen University. Dr. Wildt made his discovery through a study of the infra-red spectrum of the planet's light. He has also found methane, or marsh-gas, in the atmosphere of Jupiter, Uranus, Saturn and Neptune.

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