

1860.

On *Gyoseyanus Niger*.

Gyoseyanus is mentioned by Dioscorides both as a white and black variety, and has been known from his time to the present as a drug in common use.

The Genus *Gyoseyanus* of which *Gyoseyanus Niger* is the only native species belongs to the Natural Family Solanaceae (Lindley) and to the division Atropaceae.

Though various Authors do not recognise this division there are good reasons for establishing it both botanically and physiologically; these reasons in fact have appeared sufficiently strong to lead Miers to erect them into separate natural orders.

Botanically the Atropaceae differ from the Solanaceae by the corolline aestivation being more or less imbricate, never valvate, the lobes of the corolla somewhat unequal, Stamens 5 of which one, (rarely 3.) is sterile, with anthers

The Solanaceae on the other hand have the aestivation valvate, or in duplicato-valvate, the corolline lobes nearly equal, the stamens, 5 of which very rarely one is sterile, the anthers opening by slits or holes.

They are still more distinguished physiologically by the fact that the juice of the Atropaceae ^{which} are generally narcotic

1. 'Annual of British Botany'.
2. Elements of Materia Medica. Vol. 2. p. 139.
3. Pharmaceutical Journal. Vol. 3. p. 578. 1864.

Maracotie, powerfully dilate the pupil whether taken internally, or applied to the eye, while the Solanaceae have no such action.

Botanical History

Hyoscyamus niger. to which I intend to confine my remarks, as being the only one of the Hyoscyami officinal in this country, is met with both as an annual and biennial plant. 1. Babington mentions varieties A. & B. but gives no characters by which we can distinguish them. 2. Pereira who follows Babington's description almost verbally, gives as the character of the varieties, the difference between their annual and biennial growth. 3. W. Boulton who complains of the discrepancies in the description of this plant suggests that the differences of these varieties are well worthy of being investigated, as he found in no book on the subject, an account of this plant sufficiently careful and accurate for pharmaceutical purposes. Various authors he says, state that it is annual others that it is biennial, others that it is both, and some that there are 2 varieties of the annual. W. Boulton himself thinks that there is an annual variety of the biennial, and another variety which is annual and never biennial, After very careful examination conducted for years, he finds that the plant is usually biennial, both in the wild and cultivated state.

The differences between the Annual and biennial varieties are

The first year's leaves of the biennial variety rise by a petiole from the crown of the root. In the second year they rise from the stem, are more foetid and clammy, and yield more extract than those of the first year.

They are long, varying a good deal in the wild and cultivated varieties, pinnatifid though not necessarily deeply so - the lower leaves are stalked the cauline leaves are subamplexicaul, the decurrent lobes being of a finer texture than the general mass of the leaf.

The Annual variety cultivated for medicinal purposes is smaller, has an annual root, a stem simple or dividing into nearly equal branches, leaves glabrous, sinuately toothed, flowers sessile corolla reticulate, the whole plant less clammy, and less foetid than the biennial variety.

There is a more thoroughly developed kind, larger, more clammy and more foetid which Boulton regards as a sub-variety of the biennial but these differences do not seem sufficiently marked to constitute a distinct sub-variety.

The Annual variety flowers in July and August the biennial before this period. According to Boulton the leaves of ^{the} biennial variety should be gathered in May or June, soon after the flowers have blown, as they are then at their best, having a more clammy feel and a strong foetid odour, somewhat like that

of

1. Christian on Poisons.

of the black Currant leaf. This however seems to be a mistake, as the leaves gathered in August yield more juice than those gathered in July. If they are allowed to remain till the seeds are ripe, the best leaves will be withered and much extract will be lost.

The seeds of Byoscyamus niger are small, about the size of a large pin head, slightly biconcave, round, smooth, and finely dotted, oily to the touch when ground, bitter and oleaginous to the taste.

Other species of the genus Byoscyamus are stated to have the same properties as Byoscyamus niger (viz) Byoscyamus albus, lureus, Physaloides, and scopolia. (Orfila)¹.

Pharmaceutical Preparations

The leaves are the part of the plant used for making the Extract and Tincture which are its only official preparations in the Edinburgh Pharmacopoeia. The Tincture is ordered to be prepared from the dried leaves, the proportions being 5 ounces of the leaves to 2 pints of Proof Spirit. The use of the dried leaves is convenient, as it enables the druggist to work by the process of percolation, and to prepare his tincture at any season of the year. It is more than probable however, that this convenience is obtained at some sacrifice of the activity of the tincture, and it

it appears to me that the expressed juice with a certain amount of strong alcohol added, to preserve it and separate albuminous matters, as has been proposed by Mr. Bentley, would give a more efficient preparation; for the fresh juice of these plants is unquestionably of great activity, and by such a process we avoid all the risks connected with drying and keeping, which with a plant whose active principle is so unstable, cannot fail to produce some deterioration.

The average dose of the tincture for an adult is commonly stated to be a dram, but full hypnotic effect is seldom produced by less than double this quantity.

If the dried leaves are to be used, too great care cannot be taken to prevent them from being spoiled. For this reason they should be gathered in dry weather, placed in thin layers on the floor of a dark room, through which a free current of air passes turned frequently to dry them quickly and kept in the dark, otherwise they lose their green odour.

The Extract which is generally supposed to be the more variable preparation, should, if carefully prepared be quite equal to the tincture as regards certainty. The Extract of the British Pharmacopoeia is an insus-
sated juice and is prepared by evaporating the expressed and filtered juice to the consistence of a firm extract either in a vacuum with the aid of heat or spontaneously

1. British and Foreign Medical Review, 1837. Page 229.

by in shallow vessels exposed to a strong current of air freed of dust by gauze screens. (Pharmacop. Sibirica)

According to M. Soubeiran the expressed juice deposits a flocculence of a brownish colour which has considerable activity. If prepared by filtering and washing with water, this flocculence when administered in small doses, gives rise to weakness of vision and agitated sleep. If procured by boiling, filtration, washing and drying in a stove, it is more apt to give rise to irritant symptoms.

A young lad received a dose of it daily augmented by two grains per diem. until ten grains were administered, his sleep was disturbed; after fourteen grains he slept more, but complained of pain in the legs; eighteen grains produced nausea, heaviness of the head and disturbed sleep; when the medicine was stopped these symptoms ceased.

These symptoms are not to be desired in the action of Hyoscyamus, as they partake in no respect of the soothing narcotic quality of the drug. If M. Soubeiran's statements are correct therefore, though it must be admitted that they require confirmation, the filtration of the expressed juice is a more important part of the process for the preparation of the extract, than at first appears.

The amount of juice contained in the leaves, and therefore of extract yielded by them varies according

1. *Periera* page 1401.

2. Dictionary of *Materia Medica*. page 312.

3. *Pharmaceutical Transactions* page 97.

according to the period at which they are gathered. Thus

July 21 th	2	but gave 21.	Imperial Quarts of Juice
July 28 th	2	but —	22
August 3 rd	2	but —	25

those in August yielding most.

The quantity of Extract yielded according to Brand is from 4 to 5 lbs from the 112 pounds.

According to Squire. 5 lbs. 9 ounces is the yield of this quantity of good leaves picked free of waste leaves and dirt of which there were 3½ lbs.

The dose of the extract as a Hypnotic, is commonly stated to be about 5 grains, but it is by no means an energetic preparation, and to produce full effect, the dose should be about One Semple.

The leaves which are stated to be powerfully Narcotic, in doses of from 3 to 10 grains, would perhaps form an efficient preparation if used in the state of Electuary, which would preserve them from spoiling, and give the pure action of the drug, by avoiding any chance of injuring them by heat or other chemical agency.

The Root varies greatly in its activity according to the season of the year in which it is taken, being in fact nearly inert in Spring, — the juice of three pounds of root collected at the end of April. taking nearly two days to kill a dog. while a decoction of about an ounce and a half of root collected at the end of June. proved fatal in two hours and a half. This variation

1. Christison on Poisons. 4th Page 74b.

variation however does not appear to be true of the
biennial variety, however it may be with the annual,
as Wilmer "On the poisonous vegetables of Great Britain"
mentions a case of poisoning by them in "winter time."
the Root is not used in British Pharmacy.

Chemical History

Although many scientific men of eminence have written chemical memoirs on Strychnos, and some of them profess to have isolated its active principle, it must be confessed that its chemical history is in a very unsatisfactory position. - Brandes in 1822 described its active principle, under the name of Strychnamine, as a crystallizable body with an acid taste, yielding Ammonia when heated. Its physical properties are stated to be almost identical with those of Atropia, only differing in the fact of its being more soluble in water. Brandes' experiments were repeated and his statements confirmed by Seiger and Hesse, as well as by Mein.

The process followed by Seiger and Hesse was the following.

Freshly dried Strychnos roots or seeds were powdered and exhausted with spirit of 96 Per cent (Density 814). to which a small quantity of sulphuric acid had been previously added. The alcoholic fluid was mixed with slaked lime to the amount of a 24th part of the materials employed, and after repeated agitation, allowed to stand for 24 hours. It was then filtered and sulphuric acid in excess added to the filtrate, which was refiltered to separate impurities. The greater portion of the alcohol having been recovered by distillation, and some water having been added to the residue, it was evaporated in an open capsule at

at a gentle heat, till the last traces of spirit had been drawn off. - It was again filtered and the fluid evaporated to about the weight of one twelfth part of the roots employed. - To the cooled fluid a concentrated solution of carbonate of potash was added to separate the Hyocyamine. - The mixture was then ^{agitated} ~~agitated~~ with ether, till all that was soluble in ether was taken up, the ether distilled off and the residuum of the evaporation treated with water which dissolved the Hyocyamine. - The watery solution was mixed with alcohol and ether, and decolorized by animal charcoal. - The addition of alcohol and ether to the water was rendered necessary, because a watery solution used alone, was decomposed by the charcoal. The fluid was filtered, the alcohol and ether distilled off at a gentle temperature, and the watery residue evaporated over sulphuric acid, *in vacuo* to obtain the Hyocyamine.

According to the same authorities it may be got from the fresh plant by the following process.

The expressed juice is boiled and filtered, the filtrate mixed with lime, then refiltered, the fluid mixed with excess of carbonate of Potash, and then agitated with ether as long as it takes up any thing. The ether is distilled off, the Hyocyamine remains behind and is to be purified in the manner described above.

1. Journal de Pharmacie. Vol. 20. Page 93.

Here authors advert to the unstable nature of Cyanamine, which is easily decomposed when in contact with water and alkalis, or even when in contact with water and exposed to the air, - they therefore advise all the above operations to be done rapidly, avoiding all excess of heat. - The following according to Mein are its properties when pure. It is slowly crystallizable in star like groups of colourless transparent silky needles which are inodorous and, according to him, little soluble in water, but readily soluble in Alcohol and Ether. In Löwig's description of it which seems to be taken from Seiger & Besse, it is stated to be readily soluble in water and when impure to be soluble in all proportions. When anhydrous it gives a neutral reaction, but when moist it is strongly and persistently alkaline, when carefully heated it volatilizes undergoing very little alteration being equally alkaline and physiologically active after sublimation. It is however easily decomposed by a higher temperature and gives off ammoniaical fumes, the same being the case when it is heated along with alkalis. It is stated that Cyanamine may be distilled in small proportions, along with water, the resulting fluid having an alkaline reaction and dilating the pupil.

Cyanamine is stated to form with acids neutral salts. In a watery solution tincture of Iodine produces

1. *Idem* *ubi supra*

2. Taylor on *Poisons*. Page. 760.

produces turbidity and strikes a brown colour as it does with other alkaloids. Hyocyamine gives an abundant white precipitate with tincture of Sassa, a yellowish white with chloride of Gold, but more with chloride of Platinum. It is further stated that Hyocyamine when dry is odourless, but when moist and impure has a highly unpleasant stupefying odour like that of Tobacco. - its taste is strongly unpleasant and very acrid. - In minute doses it is a deadly poison and dilates the pupil.

2. Professor Schreff of Vienna performed some experiments on himself and a friend with small doses of Hyocyamine. The symptoms produced, were giddiness, unsteadiness of gait, with great dryness of the mouth and throat, so that nothing could be swallowed; there was headache, with impairment of the senses of tasting and smelling, and after a time a strong tendency to sleep, - the pupils were dilated, - With regard to this symptom it was observed that by local application, a solution of Hyocyamine produced intense and continued dilatation. - The medicinal dose is assigned by him to be from one sixtieth to one twentieth of a grain.

Its poisonous operation begins to be manifested with one tenth of a grain. - These effects are not distinguishable from those of Atropine, the chief difference being that Hyocyamine if it were pure, which it probably was not in these experiments, must be a very

very active poison compared with Atropine, the dose of which when pure is estimated at from a thirtieth to a sixth of a grain.

The above statements as to the chemical and physiological properties of Hyoscyamine, which are to be found in standard books, and are quoted as authoritative by successive writers are so circumstantial, that it appears that, although some care is required in the operations, Hyoscyamine ought to be procurable without any very great difficulty. - Under this belief, I undertook a series of experiments, with a view to preparing it, and observing for myself its chemical and physiological properties. - Accordingly with this intention, I procured from London several pounds of the seeds, and taking Seiger and Besse's process as a basis, I proceeded to prepare the Alkaloid from them.

ment I. The seeds were ground in a coffee mill and extracted with Alcohol, acidulated with Sulphuric Acid, the fluid saturated with lime, filtered to separate the Sulphate of lime, Sulphuric Acid added in excess, and the spirit in great measure distilled off, a considerable amount of water being added to the residuum, to separate the oil, of which the seeds contain a large quantity. - The fluid was strained through a wetted filter, on which the oil was retained. The fluid having been concentrated by

by gentle evaporation, Carbonate of Soda was now added, the fluid being rendered decidedly alkaline and letting fall a considerable precipitate of a dark green colour. - The fluid was now agitated with successive portions of Ether, which were drawn off and exposed to spontaneous evaporation. - The Ether which at first was nearly colourless, gradually as it concentrated, acquired a darker tint, until on its complete evaporation, nothing was left, but a small amount of a brown Nicotianic smelling extract, freely alkaline to test paper soluble in water, but not diluting the pupil, when a drop of the solution was put into my eye. The quantity of seeds used in this experiment was twenty Ounces.

As this process was complex and troublesome and resulted in a complete failure to obtain any thing with the active properties ascribed to Syzygamine. - I resolved not to repeat it. - It seemed to me probable that the amount of oil dissolved in the spirit, and the long continued evaporation of the water required to be added to separate the oil, had led to the decomposition of the active principle. Indeed by Seiger and Besse's original plan, it would I think be impossible to obtain Syzygamine free from fatty matter, for it is exceedingly difficult to separate it from the spirituous solutions except by the addition of a large quantity of water, as the fluid portion of the

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1. Edinburgh Medical Journal 1852 page 313

The oil is soluble to a considerable extent, even in weak spirit. - I therefore resolved to try the well known process of Stuf now so commonly employed in medico legal researches for strychnia and other organic bases, - And in order to get rid of the annoyance connected with the oil in the seeds, I determined to operate upon the ordinary Pharmaceutical Extract of the leaves.

Experiment II. Two ounces of the extract obtained from Lunan and Stockhart, (a sufficient guarantee for its purity), were diffused through half a pint of rectified spirit containing about half a drachm of oxalic acid, and were left in contact with the spirit for upwards of a week. - It was filtered and yielded a rich green tincture, leaving on the filter a copious brown residue of albuminous and other impurities perfectly insoluble in alcohol. The acid tincture was evaporated to about one half its volume, over the vapour bath at a gentle temperature, and then to avoid the further exposure to heat, was left for a fortnight to allow the remainder of the spirit to disappear by spontaneous evaporation. - At the end of this period, a thick semi-fluid extract remained, which was freely treated with Ether in successive quantities, to dissolve out the Chlorophyll. - The residue amounting

amounting to rather more than two drachmas of very soft brown extract, was dissolved in water, supersaturated by carbonate of ammonia, and agitated with ether in successive quantities. - so long as it seemed to dissolve any thing. - The greater part of the ether being recovered by distillation, during which process a large quantity of a brown matter separated which was removed by filtration, a clear fluid was obtained and left for spontaneous evaporation, in the hopes that it would yield something like a pure product. But the only product I obtained from it was a thick brown extract, with the mechanic colour as before, but also smelling strongly of ammonia, the total quantity being about eight grains. It was too obvious that this was merely a product of decomposition, ether obstinately retaining the ammonia used in its preparation, or what was more probable, developing ammonia from itself. For these reasons, I did not try its physiological action on my iris.

The ether employed to extract the chlorophyll was evaporated, the residue treated with water containing a small quantity of acetic acid to combine with any tyrosamine which might be present, - again treated with ether, to dissolve out the colouring matter, and the residue having been dissolved in water, was left ^{for} spontaneous evaporation in

In the residue of evaporation there was left some
zeolite = like tufts of crystals consisting of thick
needles grouped in a cruciform arrangement. - I
picked out some of these crystals with a needle,
dissolved them in a drop of water and introduced
it into my eye, but without producing the least
effect upon the iris. I think it probable that these
crystals were nothing more than a trace of oxalate
of ammonia dissolved up by the ether.

The poor success met with in the above
experiments, which agreed so little with the manner
in which Pyoseyamine is mentioned in text books
precluded the expectation of procuring it in any thing
like quantity sufficient for studying its effects. -
I therefore now devoted myself to the simple enquiry
whether such a thing as Pyoseyamine was to be
procured at all, and in this view, though much
discouraged, I continued my experiments.

Experiment III. Twelve ounces of the ground seeds were
moistened with six ounces of water containing
about two drachms of oxalic acid, and after being
left in a covered vessel for three days were expressed
in a strong screw press. - I thus separated about
three ounces of an emulsive mixture of oil and
water. - The process of maceration and expression
with water and oxalic acid was repeated until I
obtained

obtained about nine ounces of fluid altogether, which I passed through a wetted filter, and then agitated with ether to remove the whole of the oil. The watery fluid, which contained some albuminous flakes, was again filtered, neutralized with bicarbonate of soda, agitated with ether, and the ether allowed to evaporate spontaneously. Seeing however that some experiments already quoted, seemed to show that Hoxycyamine may, at least in part, be volatile, and more especially seeing that in my own Experiment No. II the product which had been attempted to be got in the state of free base had undergone decomposition during evaporation, I thought it best now to get it in the form of a salt. I therefore before allowing the ether to evaporate added to it a few drops of acetic acid, I preferred this to oxalic or any of the mineral acids, as an excess of oxalic acid might form crystals of the acid itself, and so give a deceptive appearance to the product, and an excess of any of the mineral acids would act upon the product when it evaporated, whilst an excess of acetic acid would itself evaporate and do no harm. It is to be noted that in the above process no heat was applied to the substances from first to last.

The product of the evaporation of the ethereal acetic solution was very small, not amounting in all to more than half a grain. To the naked eye

It looked like a thin layer of resinous matter lining the watch glass, it was nearly white with a faint greenish tinge. Under the microscope it was seen to be a transparent nearly colourless varnish-like substance with here and there a few greenish nodular looking masses dispersed through it, but in no part did it present the least appearance of crystallization. It was evidently not homogeneous, and therefore not pure Hyocyamine, though perhaps it approached as near to it as any product that has yet been obtained, if I may judge from the following test of its activity.

I dissolved it in about a drachm of water and put one drop of the solution into my eye. - It occasioned no smarting or irritation. - I proceeded to wipe a microscope slide, and by the time I had done so, which could not have occupied more than a minute, I became conscious that my vision was confused, and on going to a mirror, I found the pupil so much dilated that the iris was reduced to a very narrow ring. - This was on Saturday morning, and on the following Wednesday the difference between the contractibility of the pupils of my two eyes was appreciable in a bright light.

Having thus obtained what I considered to have been Acetate of Hyocyamine not quite pure, I endeavoured to separate the Hyocyamine from it. For this purpose the impure acetate was dissolved in a small bulk of
Water

water. It formed a clear solution, with a faint greenish yellow tinge, Ammonia was added to it, in slight excess, a faint white precipitate was produced, but from the rapidity with which it settled to the bottom, and from its not dissolving entirely in Ether, it is clear that this precipitate was in part due to a trace of inorganic impurity. - The Ether with which I agitated the fluid was allowed to evaporate spontaneously and left behind a residue having the following properties

It formed a homogeneous colourless transparent varnish on the watch glass, presenting under the microscope in some places a somewhat granular aspect but no traces of crystallization. - It had a feebly bitter taste without the least acrimony. - It was readily soluble in Ether, Chloroform and Spirit, and slowly soluble in water, its watery solution having a feebly bitter taste.

A drop of the watery solution put into my eye in about ten minutes produced confusion of vision, and in five minutes thereafter the pupil was fully dilated, the effect of this on the iris was still perceptible after the lapse of three days. I think there can be little doubt that what I got here was Hyocyamine, and although its homogeneous appearance is strongly in favour of its being pure, the minute quantity which I obtained rendered it impossible for me to prove this chemically. I have ascertained this however, that this Hyocyamine does not decompose if kept dry, and free from the contact of

of chemical agencies, for that which I have described above remained in a watch glass for six months after its preparation, and still retained its power of dilating the pupil. Its watery solution operated less rapidly, though not less powerfully than its solution in Acetic Acid.

Believing that probably I had not succeeded in taking up the whole of the active matter from the watery fluid by means of Ether, I determined to examine it further. - For this purpose, the watery fluid was freely super-saturated by Acetic Acid, and tincture of Gallic added, which threw down a copious precipitate of a dark purplish colour. This precipitate was collected on a filter, washed with water and triturated when moist with Hydrated protoxide of lead. - It gave off during the trituration, an ammoniacal odour which gradually gave place to a smell resembling that of Nicotine. It was clear that it had undergone some decomposition; perhaps the protoxide of lead had not been completely washed free from the potash with which it was precipitated. I now agitated it with Ether which on spontaneous evaporation left a residue which powerfully dilated the pupil when freshly prepared, but gradually became brown and in a few days lost its nicotine-like smell.

It results from this experiment that the watery fluid had retained a portion of the active matter
of

of the *Hyoscyamus*, and that this had become decomposed, though not at first completely, in the attempt to separate it by oxide of lead.

Experiments IV. and V. I do not need to give these experiments in detail as they were both unsuccessful. - In both instances the seeds were extracted with methylated spirit, the spirit distilled off, the residue taken up in water and precipitated by tannin; - the tannin precipitate was decomposed in the one case with carbonate of soda, and in the other with hydrated oxide of lead, and Ether employed as the solvent in the same manner as before, but in both instances a brown product was obtained, which had no effect on the iris.

Experiment VI. Having in all the previous trials with the seeds, experienced much annoyance from the difficulty of separating the fatty oil. I endeavoured to extract *Hyoscyamine* from the juice of the plant. - For this purpose I procured from London several pints of the expressed juice of biennial *Hyoscyamus*, to which a small quantity of spirit had been added to preserve it. With the juice I made several trials, operating on quantities of two pints at a time. Lime and Carbonate of Soda were the decomposing agents used, and Ether the solvent as usual; but in all these trials the product which I got was brown and evidently decomposed, as it did not dilate the pupil.

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1. ¹⁰Pereira Vol II Page 1339.

In one of the experiments where carbonate of soda was used, there were some groups of imperfect prismatic looking crystals formed in the residue of evaporation. - Some of these I picked out, dissolved in water and introduced into my eye. The result was much pain and irritation at the time, followed by a smart attack of conjunctivitis, but no dilatation of the pupil. It is clear that these crystals had nothing to do with Hyocyamine, but were probably some compound of the soda, or an acid product of decomposition. - It was clearly some such product as this which made Seiger and Besse state that Hyocyamine had an acid taste, and which Reisinger found to cause irritation, when a strong solution was introduced into the eye.

Having found that Hyocyamine can be obtained by a process in which heat is entirely avoided, it appeared to me probable that the well known property which animal charcoal possesses of combining with some of the vegetable bases, might afford a means of extracting Hyocyamine, without the employment of heat or chemical agents likely to decompose it, & therefore made the following trial.

VII. An ounce of extract of Hyocyamus was triturated with water till nearly thoroughly dissolved the solution filtered, mixed with freshly burnt animal charcoal, and agitated thoroughly from time to time for two or three days. - The charcoal was collected on a filter

filter, washed freely with water, allowed to dry in the air, and agitated with ether. The ether on being allowed to evaporate spontaneously, left a small quantity of a greenish brown granular residue, nearly entirely soluble in water. A single drop of this solution dilated the pupil powerfully, the dilatation continuing for nearly two days. It was clear therefore, that by this means, I had obtained Hyocyamine in a state of impurity, I had not time to attempt its purification but the result was enough to show that animal charcoal affords a means of separating Hyocyamine without the aid of heat.

It appeared to me worth while to endeavour to ascertain, whether the ^{nicotine} ~~moisture~~ like residue, obtained as a product of decomposition in my former experiments, possessed any poisonous properties. - For this purpose I collected together, the residue of my former experiments, which, including impurities, amounted to about six or eight grains, and having dissolved it by the aid of a little spirit, injected it into the cellular tissue of a healthy rabbit. - The effect produced was, that the pupils became much dilated, and insensible to a bright light, the animal became still and stupified the ears and body cold, the heart beating 102 in a minute. - These symptoms however gradually went off, and the animal was quite well in twelve hours.

It would appear from the effect on the pupils that there

these products retained a portion of Hyoscyamine in the undecomposed state. I had expected however, that they would have manifested more decidedly poisonous properties, like the volatile product obtained by Dr. Murray from Hyoscyamus and Digitalis by destructive distillation, and which when administered to Animals speedily proved fatal with coma and convulsions.

I made a few experiments with the fixed oil of Hyoscyamus extracted from the seeds, and found that after saponification it yielded two distinct fatty acids, one solid at about the comparative of 80° - the other fluid, but becoming thick at 32° - this was probably a mixture of oleic and inorganic acids. - The seeds also yielded a dark coloured resinous matter soluble in Alcohol and Ether.

The conclusions which I draw from my experiments are.

I - That the products obtained by Brandes and Seizer and Oberse, are not Hyoscyamine, though they may have retained traces of this active principle, for the methods they used, as my own experiments show, were inconsistent with its production. - This has been conclusively established by the experiments of Chevallier, who made several attempts to procure it but unsuccessfully, and by a memoir of M. M. Brault and Poggiale, who not only failed to obtain Hyoscyamine by these processes but

1. Journal de Pharmacie 21. Page 134.

2. Pharm. Journal. March 1858. Page 462.

but showed that the crystalline products were entirely mineral, being a mixture of Acetates, Muriates, Sulphates, and Phosphates, of lime, Magnesia and Potash. They obtained the same results, on repeating a process given by Purge, which they quote, but the original of which I have not seen, for detecting the Solanaceous principles. Purge's product they found to be mineral matter also.

II. That the numerous trials hitherto made to separate Hyocyamine, and which have led to the conclusion that it cannot be isolated, have failed from imperfections in the method of working.

III. That the substance separated by me was Hyocyamine though from its uncrystallizable nature, it was probably not obtained in a state of purity. - That in order to obtain it, it is necessary that no heat should be employed in the process, and that to detach Hyocyamine, the alkaline bicarbonates or Ammonia should be employed. The caustic alkalis certainly decompose it as has been shown by Dr. Sarron 2, and the neutral carbonate of Potash and Soda appeared in my experiments equally to do so although Dr. Sarron thinks that they have no such action. As my later trials, (vide experiment III) were directed solely to the attempt to prove the existence of Hyocyamine, comparatively little attention was paid to economy in working, otherwise I have no doubt a larger product

product might have been obtained.

I think myself however entitled to hold that I have indicated a method by which Strychnine may be produced.

Strychnine has not, as far as I know been employed criminally as a poison, but should any case arise in which medico-legal researches for this poison would require to be undertaken, - the following process would probably be found to answer.

The contents of the stomach should be agitated in the cold with a considerable excess of Acetic Acid and passed through a wetted filter. To the filtrate Ammonia is to be added, until its odour is feebly but permanently perceptible, and the fluid agitated with twice its volume of pure Sulphuric Ether. The Ether being withdrawn by a pipette is to be left for spontaneous evaporation which will be much expedited, if the operator make use of any available current of cool dry air. The residue of evaporation is to be treated with a very small bulk of cold water, and a feeble excess of Acetic Acid, and passed through a filter, by which means fat will be separated.

The process of separation by Ammonia and Ether, is to be repeated as above, and the Alkaloid obtained by allowing the Ether to evaporate in a watch glass. - A single drop or two of Acetic Acid, in a small quantity, say half a dram, of water, should be employed to dissolve the Alkaloid, and the fluid exposed to spontaneous evaporation, until the smell

of

1. Brewer's "Medical Jurisprudence for India." Page 121.

of the excess of Acetic Acid has disappeared. - We have now the Hyocyamine if present, in the soluble and active form of acetate. - It is now to be dissolved in the smallest possible quantity of water, and a single drop of the solution placed upon the conjunctiva of the eye. - The occurrence of confusion of vision, and dilatation of the pupil, will indicate that a Solanaceous narcotic has been detected. It would probably not be safe for the Analyst to assert anything more precise than this. - If the residue of evaporation of the second ether in the watch glass had distinctly the appearance of a crystalline organic body, it would afford a strong probability that the poison was Belladonna or Datura. - The latter of which (D. Fastuosa) is very commonly used for criminal purposes in Bengal.

If on the contrary, the product obtained were a totally uncrystalline, transparent varnish-like substance, dissolving slowly in water, but readily soluble in Acetic Acid and the solutions of which, confused vision and dilated the pupil, the evidence of the presence of Hyocyamine would be tolerably strong.

Physiological Actions

The Physiological action of Hyoscyamus is that of a Narcotic possessing however certain peculiarities common to it and others of the Solanaceae such as Belladonna and Stramonium, the more conspicuous of which are, the tendency to produce Delirium and Mydriasis. (dilatation of the pupil). For these reasons it has by some been classified as a Deliriant narcotic (Meadland). by others as a Mydriatic. (Perera) some Authors have regarded it as a Narcotic-acrid, but it has no claims to be regarded as such. For the production of dry throat, and occasionally of Diarrhoea in cases where large doses have been taken and which have been cited as instances of its acrimony, are not so generally attendant upon its action as to be characteristic of it. - In ordinary Medicinal doses, these effects are not observed, dryness of the throat is more frequently seen after even moderate doses of Opium, which is certainly in no sense acrid and as regards the bowels the most that can be said is that Hyoscyamus, does not constipate as Opium does

1. Edinb' Medical Journal. April 1860.

doses. In moderate doses it has a calming and soothing effect, especially in cases of nervous irritability and often produces sleep, not so much by narcotically affecting the brain as by allaying praeternatural sensibility of particular organs, preventing sleep. It is perhaps in this way that it acts when it allays the maniacal paroxysms accompanying cases of general paralysis. Dr. Haas who finds it useful in such cases, gives it in large doses such as from a scruple to half a drachm of the extract. 1.

It seems to have a particular power in allaying the undue muscular contractibility in the Abdominal and pelvic viscera, as several of its most common practical uses seem to show. Thus, the use to which it is applied perhaps more frequently than any other is to moderate the griping tendency of the compound Colocyath pill which it does without impairing its purgative action. This use of Hyoseyamus was first made known by the late Professor Hamilton of this University. The Pilula Colocyathidis et Hyoseyami of the Edinburgh Pharmacopoeia which consists of two parts compound Colocyath mass with one of Extract of Hyoseyamus being commonly known as Hamilton Junior's pill. Another of the uses of Hyoseyamus showing its power over muscular action of the Abdominal and pelvic viscera is its effect in Chronic cystitis and irritable bladder in which affections it is very often employed conjoined with Lymph or Pareira in cases of severe after pains, I have frequently administered

Hyoseyamus

1. Journal de Médecine Vol. 1. Page 297.

Oporeganus both in the form of tincture and extract and have found that patients who had suffered severely in previous deliveries were perfectly relieved after a few doses, whilst by avoiding the use of Opium the subsequent employment of laxatives was rendered unnecessary. As examples of its relieving morbid irritability and muscular spasm may be mentioned its employment in cases of chronic catarrh with dyspnoea, by allaying these symptoms it frequently produces sleep. It is not so powerful as Opium, but it has the advantage over it of not constipating the bowels or checking secretion. Large doses sometimes produce sleep. Fouquier however denies its hypnotic power, saying that though it produces more or less of sleep, it does so only after a certain amount of its poisonous action has been developed (viz) giddiness, headache, dilatation of the pupils with dimness of sight and painful delirium. These he says are in some cases followed by thirst, nausea griping, and either purging or constipation, and in a few instances febrile heat and irritation of the skin.

Dr. Pereira however states that he has frequently seen it produce sleep, though its hypnotic effects are neither powerful or constant. It frequently fails to produce any effect when given to people accustomed to the use of Opium.

The physiological action of dilating the pupil which it possesses in common with other Solanaceae has been the subject

subject of considerable discussion

Two hypotheses have been propounded - The one supported by Mr Benjamin Bell of Edinburgh, the other by Dr Harley of University College London, Mr Bells view is that Atropine, and the same remarks may be applied to Hyoscyamus, produces dilatation of the pupil by stimulating motor filaments connected with the sympathetic and thus exciting the radiating fibres to contraction - Dr Harley's view is, that its dilating power depends on its paralyzing the ciliary branches of the third pair of nerves, and thus depriving the circular fibres of the iris of their power of contracting. The subject is one which still admits of physiological experiment and discussion. - It is not my intention to consider the question in detail here, and although Dr Harley's experiments can perhaps hardly be said to be conclusive, yet the general action of Belladonna and Hyoscyamus upon other muscular fibres, seems so opposed to all ideas of stimulation, that it appears more probable that it acts by a relaxing effect on the circular than by a stimulating effect on the radiating fibres.

Dilatation of the pupil may be produced either by the topical application or by the internal administration of Hyoscyamus. When topically applied it probably operates by the absorption of its active principle by the skin or conjunctiva, when swallowed it operates like other poisons by passing into the blood. It will operate on the eye when applied to the skin of more distant parts of

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of the body. Wislizenus mentions a case in which a lady was affected with deep stupor, dilated pupils, flushed face, loss of speech and full hard pulse, with swelling of the abdomen, from several ounces of the leaves having been applied as a poultice to the abdomen to relieve stranguary and tympanitis. One case of severe after pains - where the woman requested me to give her something to relieve them as they had been very painful in her previous confinements I tried the effect of local application of Hyoscyamus - For this purpose I ordered two ounces of extract spread upon plaster to be laid over the abdomen. The effects were to procure sleep, and to diminish the number of after-pains, but it did not prevent them altogether - There was no dilatation of the pupil, nor did any bad consequences follow, ^{unless} when a slight attack of Diarrhea which supervened, is to be regarded as having been produced by the Hyoscyamus.

All the recorded fatal cases of poisoning by Hyoscyamus have been accidental, and as already stated Hyoscyamus has never been used for purposes either of Suicide or Murder.

As a guide to the diagnosis of this form of Narcotic poison, it may be well shortly to contrast the poisonous actions of Hyoscyamus with that of Opium - Hyoscyamus generally produces delirium - Opium rarely does. Hyoscyamus causes dilatation of the pupils, Opium most generally but not invariably, causes them to contract to the utmost. Opium binds the bowels, and checks all the secretions, except that

1. Edinb^r Medical Journal. 1854. Page 377.

2. Report of Edinb^r Medico. Surgical Society (re-published.)

that of the skin. Corymbium does not constipate, and does not affect the other secretions. - These symptoms might enable a Medical Practitioner to affirm that poisoning had been produced by a Solanaceous vegetable, but it would not be possible unless portions of the vegetable were got, so as to identify them botanically, positively to state whether the poison were Belladonna, Corymbium or Datura.

The fact of the action of Opium and of the Solanaceae especially in the pupil being to a certain extent antagonistic, led Dr. Thomas Anderson of the Indian Army to propose Belladonna, as a remedy in poisoning by Opium, and conversely Opium as a remedy in poisoning by Datura.

There are no Post Mortem appearances characteristic of poisoning by Corymbium - cerebral and pulmonary congestion have been observed, and in some instances florid blood in the ventricles of the heart showing paralysis of this organ, but all these appearances have been observed in the case of other Narcotics.

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May. 1860.