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Observations on
Podophyllin and its Source

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Few of the important remedies employed in treating human disease are found in those countries where medical science has been most cultivated. This is not to be wondered at when we consider the narrow limits of this country and the rather ingenuous character of the climate. But it is strange that the inhabitants of the American continent, which has such a varied climate, such broad plains and vast prairies, deep valleys and towering mountains, should have to seek in foreign lands remedies for most of their pains and aches.

Even professional and scientific men seem infected with the feeling that objects at a distance, and substances coming from a distance are most worth seeing and possessing.
It is true that many of our most valued necessaries come from other lands. Medicinally this is very true, and we could not do without such remedies. But how few are the Indigenous remedies in our Pharmacopoeia America probably has the most, as she ought; but how little have they been investigated. This is shown by the little that was known of the subject of this Paper until within a few years, though the Plant has been in use ever since the settlement of the Country. Even now the regular Profession must thank a Seeding Body for the investigation made regarding it, provided Experience is found to confirm the result of those investigations.

We should surely not refuse to take advantage of any remedy from whatever source it originates, provided that remedy prove a valuable one. Men only find out what Nature provides. My task can only be to give an account of the Plant, the limited use of the powdered root, regular Practice, and of the Merits claimed for the prepared Root by the "Electric"
History - The Botanical Name of the plant is Podophyllum Peltatum. It is commonly called Mandrake. Various other names have been applied to it, such as the May Apple, Wild Lemon, Raccoon-berry, etc.

The first writers on the Vegetable Materia Medica who noticed the plant were Schoepf and Rehm, and they speak of it as an emetic, though its emetic action is scarcely more marked than is true of some other active purgatives. But if used in too large doses, it is very apt to induce vomiting.

Among the American Indians it was long a favorite medicinal plant. Prior to the settlement of the country by the Whites it
was had in common use, and was by them considered a most energetic purgative.

In consequence of this action it has long been used in the Medical practice of America, and in efficiency has been considered little, if at all, inferior to the most certain cathartics in use, as Salk, cathart, and also. As a remedy in Bilious and intermittent fevers it has also received some amount of praise.

But since the discovery of its resinoid, Podophyllin, more important actions have been claimed for it. The same

reason from which these assertions emanate must cause us to hesitate to receive them as facts before experience has fully proved their existence. Yet they are too important to be allowed to pass unnoticed.
Natural History. The Podophyllum Peltatum is a native of North America, it is found throughout the states bordering on the Atlantic, and ranging from New England to Georgia. But it flourishes most in the interior. And even there it is found in greatest luxuriance in damp and shady woods. It flowers from March to June, the period being naturally somewhat later in the more northern states. It fruit ripens in September or even earlier after which the leaves wither and fall off.

Lindley places the plant in the Natural Family Ranunculaceae. According to Linnaeus it should be placed among the Ruscades. Griffith in his Medical Botany ranks it among the Berberidaceae, though it is objected to this arrangement...
that it has more stamens than the 
plants of this order, and also differs from 
them in the absence of the peculiar deliscence 
of the Anther—

According to Bigelow, only one species 
strictly belonging to the order is known. 
Rafinesque however recognizes three species 
the Podophyllum Peltatum — Podophyllum 
Montanum — and Podophyllum Calceiferum. 
but Torrey and Gray think the latter a mere 
variety of the first —

Linnaeus describes the plant as a one 
flowered stem — leaves peltate, palmated — 
crenate and necised — Sepals true, deciduous — 
Petals 6-9, ovate — Stamens 6-18, with linear 
anthers — Fruit fleshy, indehiscent, and 
containing numerous seeds, in several rows in a pulpy placenta —
The plant has a long, creeping root which spreads widely in rich soils – it is of a dark brown color externally and somewhat corncob, but internally it is yellowish white. Numerous fibres of a somewhat pale color spring from it.

The stem is simple, upright and smooth, and about one foot in height. At the top, the stem divides into two petioles, from three to six inches long, which support two leaves, of a yellowish green color above and slightly glaucous beneath – the leaves are large, peltate, and divided into five or six lobes which are incised at their tops. In the angle, formed at the apex of the stem by the branching petioles, is a round peduncle supporting a solitary white flower. The flower is large, nodding, fragrant, and is succeeded by an oval fruit, of a lemon yellow color, containing a thick somewhat
mucilaginous pulp in which the seeds are
immersed, all being connected to the
tetralateral receptacle by fibres —
Bigelow thus describes the flower and
fruit — "In the fork of the stem is a solitary
flower on a broad nodding peduncle, one or
two inches long — calyx of three oval, acute,
concave leaves, cohering on the bud by their
scarious margins, and breaking off at the base
when the flower expands — Petals from six
to nine — Linnaeus makes them nine in
his generic character, but in this climate I have
found them more frequently seven in Linnaean
specimens growing in very rich soils — They are
obovate, entire, concave, smooth, white with
slight transparent veins. Stamens shorter
than the petals, and curving upwards; the
anthers olong, twice as long as their filaments.
Fruit oval, compressed, obscurely angular - Stigma nearly sessile, convex, its surface
rendered irregular by numerous convolutions
and folds - The flower is succeeded by a
large, ovate yellowish fruit, which is one-celled,
many seeded, and crowned with the stigma.
Its early period of ripening has given it
one of its names, May-Apple -

The fruit is edible, acid and very agreeable
to some persons - Its acridity and color have
given it the name of "Wild Lemon" - They are
said to resemble in taste, and even in
external appearance, the fruit of the Passiflora
Pedules of the West Indies - It is very slightly
aperient, and may therefore be largely
partaken of without any unpleasant effects.
The Indians are very fond of it, and are
even said to consider it medicinal -
The leaves are said to be narcotic and poisonous; but no direct experiments have been made to ascertain whether they do really possess these properties. The Botanical Relations of the Plant would certainly render the possession of such properties probable; though we should expect to find them in the root as well. But Professor Bigelow says that he has been able to detect no such property after repeated experiments with the root.

Chemical History. The official part of the Plant is the root. When dry it is fragile and easily reduced to powder. The powder is of a light yellowish grey color. Its odor is not unpleasant. Griffith likened it to the odor of Powder of Quercus. I have noticed only a slight imitation of the mucous membrane of the nose. The taste is at
first a peculiar sweet, but afterwards is very bitter and nauseous. the bitter taste remains at the base of the tongue for a considerable time.

Both the decoction and tincture are intensely bitter. Alcohol is said to be the best solvent of the active matter. When water is added to the alcoholic solution the mixture becomes very gradually turbid and at length opaque. On the other hand, alcohol is said to disturb both the infusion and decoction, especially the latter, in which it produces after some time a pearly whitening. (Begleis)

William Hodgson of Philadelphia separated from the root a bitter substance, which consists of pale brown shining scales, malleable in the air, very sparingly soluble in cold water, much more soluble in boiling water, soluble also in
Ether, and freely so in boiling alcohol—Nitric acid dissolved it with effervescence, producing a rich deep red colour—its taste, at first not very decided in consequence of its sparing solubility, became at length very bitter and permanent, and its alcoholic solution was intensely and permanently bitter.

This bitter principle was obtained by boiling the root with quick-lime in water, treating the decoction—precipitating the lime with Sulphate of Lime— evaporating the clear solution to the consistency of an extract—treating this with cold alcohol of a density 0.817—filtering and evaporating this alcoholic solution, and treating the residue with boiling distilled water, which deposited the bitter principle on cooling.

According to the Analysts of John R. Lewis,
the root yielded albumen, gum, starch, extractive matter, tannin, gallic acid, fixed oil, traces of a volatile oil, salts of potassa and lime, and two resinoid principles, one soluble in alcohol and ether, and the other soluble in alcohol only—both of these principles were found to possess the active properties of the root—while the substance obtained by the process of Dr. Hodgson acted with much uncertainty and only in much larger doses.

In account of the inactivity of the latter principle prepared by the process of Dr. Hodgson, that of J.R. Lewis seems the most eligible. Mode of obtaining the resinoid for actual medicinal use—His process was briefly this: A quantity of the coarsely powdered root was boiled a few minutes in diluted alcohol.
and when cold was displaced — the reddish brown liquor was then evaporated to dryness. The dry extract was reduced to powder and again treated with alcohol — the solution was then treated with purified charcoal, filtered and evaporated — The residue, which had the appearance of a light brown resin, was redissolved in alcohol and precipitated by water — which operation left a large quantity of colorless matter in solution. The precipitate was next separated, washed with distilled water, and left to evaporate after having been again dissolved in alcohol — In this state it has but little colour, and in form was said to be analogous to tannin. The active principle thus separated from the root has received the name of Podophylline — When pure it is insoluble
in cold water — neither is it acted on by dilute nitric acid or very dilute alkalis.
It may therefore be considered a neutral proximate vegetable principle of a resinous character — it is insoluble in oil of turpentine, but is readily soluble in ether and alcohol — In its chemical characteristics it would therefore appear to resemble very much those of the resin of the Galap. root — On account of its insolubility in aqueous fluids, it is important to administer it medicinally that it should be finely pulverized, or triturated with some other powder or some solvent, so that its particles may be readily and intimately diffused in the stomach. Otherwise there is much danger of its producing local irritation and severe griping.
Actions and Uses. In the American Pharmacopoeia, into which alone the Podophyllum has been introduced as a medicine, its action has been considered principally, if not only, cathartic; and of course applicable to all those diseased states which experience has proved purging to be beneficial. In activity and efficacy it is considered equal, if not superior, to Saltp. "We have hardly any native plant," says Professor Bigelow, "which answers better the common purposes of Saltp, Aloes, and Changth, and which is more mild and safe in its operation." Though always safe, it is mild in its operation, yet frequently it has a tendency to produce violent griping pains and a depressing nausea with vomiting.
The same objection does not apply in as equal degree to the aspinoid; it very seldom gives rise to gurgling pains. But in full dose nausea is frequently present, though a result less objectionable from the absence of the severe depression which accompanies the similar action of the powdered root.

"Podophyllum" ought therefore to be the best form in which to administer this medicine. Its leaf, if well should also be a recommendation. But more important still are the new indications for the use of this root, which have been pointed out since the discovery of the aspinoid. In the United States Dispensatory, it is said to diminish the frequency of the pulse, and to relieve cough, in account of which it is sometimes used.
in Cataract, and Pulmonary Affections. 
But those who have recently paid more particular attention to the actions of this remedy, have given to it a much wider range — the value of their experiments and deductions can only be tested by a longer experience.

Physiologically, they ascribe to it various actions, as a Catheretic, Physagogue, Emmenagogue, and Stimulant, and even assert that it produces a sharp Phlegm.

Therapeutically, they say it acts as an Antiphlogistic, Alterative, Antihelmentic, Anti-siphilitic, Deobstinate, and Sedative.

Some of these actions are granted to it by all Practitioners; but those which would be most important, if true, are claimed for it by a body of Practitioners whose assertion
we may hesitate to put implicit confidence in until they are confirmed by those facts which a wider experience may eventually furnish. It is well to know the claims presented in its favor, though we may be for the present unable either to confirm or refute them.

At first we will mention those actions which are certain, and which are more readily accounted for. Then we can refer to the many important assertions made by its advocates. Its operation as a cathartic is generally allowed to be efficient and certain. It acts in some form or other in the system, producing several pretty copious and moderately consistent discharges, which are very frequently charged with bile. In some instances a longer period will elapse before its
operation begins—But in nearly every case it leaves the bowels in a gently lax condition for several days after its immediate operation is over—Hence its efficacy in some cases of habitual constipation—

The resinoid very rarely causes griping but it occasionally produces nausea and full doses even vomiting—but when given in small doses these unpleasant actions are seldom noticed—but even when nausea and vomiting are excited, the death-like depression which accompanies the like action of the powdered root is wanting.

Previously to being employed medicinally, it should be finely pulverized—then it may be used in doses of one to three grains for an adult—it should be given in a little simple syrup, or made up into a pill with
Castile soap—Its activity is said to be increased by the addition of a small proportion of balsamum.

As a cathartic, it may be given so as to produce a powerful hydroxygogue action, or only as a gentle laxative.

An experienced physician has informed me that in bowel complaints generally, and especially in cases of dysentery, he finds the podophyllinum and guareaunqua powder a most useful combination—thus acting its efficacy when used alone. The value of the combination may be accounted for by the fact that guareaunqua possesses of itself some peculiar power of restoring a healthy action to the intestines in dysentery. For many years it was employed for this purpose in the East Indies, but for some
In Cholera Infantum and common complaints of children, the Podophyllin is said to act very satisfactorily, but must be given in very small doses. In a child three years old, from one-eight to one-fourth of a grain is considered sufficient, repeated every six or eight hours.

In the treatment of some forms of dyspepsy, its value is generally acknowledged. It should be administered in combination with the Bitartrate. Doses of half a grain of the Podophyllin to half a grain of the Bitartrate are recommended, the dose to be repeated every three or four hours until they have produced half a dozen copious watery discharges from the bowels. In a case
treated thus, with a repetition of the dose after an interval of two days, the patient was soon relieved completely of the deranged effusion — Some consider it as efficient in General Purposes, as in — Dissey of the Serosa Cavities —

As a Cathartic, its application to the treatment of various forms of disease need not be gone into — But it is probable that some of the other actions ascribed to may depend upon its efficiency either as a Hystagogue or Cathartic Cathartic — It is certain that, acting in one or other of these ways, it may produce a certain amount of Physiological or Therapeutic Action — As a Cholagogue it may act through the irritation caused in the Anodenum and on the Mouth of the Common Bile-Duct, and
if it really possesses any emmenagogue action at all (which is very doubtful), this may depend upon a similar sympathetic irritation—this is the only way of accounting for the influence of cathartics upon the menstrual flow. Its antiphlogistic, antihelminthic, sedative, and alterative action may be due to some extent to its evening as a cathartic. But the influence ascribed to this resin as an antiphlogistic, sedative, and alterative is too great to be wholly ascribed to this action, if experience is found to confirm the strong statements made by the friends of the drug.

When given in frequently repeated small doses, 1/10 to 1/4 of a grain, it has no effect on the bowels, but is described as producing a slight salivation which soon passes
away without leaving any disagreeable
secondary result—No importance should
probably be attached to this property, which
it possesses in common with other medicines
of various actions—But some of the
important results of actions, to which we
must refer, follow its administration
in these small and frequent doses—
Its action as a cholagogue may be due,
as we have already stated, to the stimulant
effect of cathartic doses on the mouth of
the Common Bile-duct—In regular practice,
the increased flow of bile is always considered
to result from such irritation—
But its action in frequently repeated
small doses would imply a specific
influence over the secreting or excreting
power of the Liver—Its advocates
Sheniously maintain that it does not
such a controlling influence — and they
assert its peculiar aptitude in every
variety of case which is characterized by
much Hepatie torpor and congestion of
the Portal Circle — alleging that it will
awoke the torpid energies of the Liver and
cure promptly its Suspended Function.
They recommend it in chronic and acute
Hepatitis and Jaundice, to be given in doses
of one-quarter to a whole grain, and to be repeated
every night for two or three weeks. The writer
states that he used it in this way for nine
weeks with a very favorable result.

This property, combined with its cathartic
action, will account for the efficacy of this
Medicine in those cases marked by a
strong determination of Blood to the Brain.
Causing congestion or incipient inflammation in that important organ. The writer says that, in several cases of this description, he was actually surprised to find every trace of congestion disappear before one or two thorough operations of the tongue. Such a result can be accounted for by the derivative influence of the medicine, which, acting as a powerful stimulus to liver and bowels, draws away the blood which is exciting and fermenting food for the pathological changes just beginning in the brain. A favorable result, so sudden as that referred to above, could only be effected at the very earliest stages of the disease. In head-ailments, especially those of children, the action of Calomel alone or combined with saltpar, some otherResolvedjuice, is the same—
It is said also to exert a powerfully controlling influence over the condition of the cutaneous as well as upon the action of the heart and arteries, producing in these cases a moderately powerful purgation—this follows upon the administration of cathartic. This action is developed in a more marked degree when full doses causing nausea and vomiting.

The powder probably has no special action as a diaphoretic apart from its nauseant action—full cathartic doses.

As an anthelmintic, it succeeds consider that it has few superior in effecting the expulsion of reccidiv from the intestines. this result follows upon the administration of full cathartic doses, and may depend upon the violent purgative action
Excited more than upon any specific destructive influence upon the worms. As a Sedative and Antiphlogistic, it has a more or less limited use among our regular Practitioners in America. It produces a depressing influence on the circulation, quickly diminishing the rapidity of the pulse and reducing its strength. It has also a soothing influence upon the Brain and Nervous System, an influence which may account for its alleged efficiency in cases of disease of the Brain, but which must be taken in connection with its cathartic action. In possessing this property, it would seem to resemble the powder of the Root of the Belladonna Major, which belongs to the same natural Family. Its use in the treatment
of the Remittent and continued forms of Pern will depend upon its action as an antiphlogistic. It is considered especially applicable to the Bilious form of Pern. From three doses of from two to four grains are stated to have arrested the progress of a severe attack of Bilious Remittent Pern, requiring only tonic and restorative means to complete the cure, with subsequent avoidance of the exciting causes.

The efficacy of this powder in the treatment of Dysentery ought probably to be ascribed to its sedative effect. It acts thus in very small doses. The similar action of Calomel is noticed after the administration of very large doses, such as twenty grains or even more.
Many years it has been used to a considerable extent in the intermittent forms of fever which are so prevalent in some parts of America and it has been much praised by a few for its efficiency. But the wonderful controlling influence exercised by quinine over this form of fever renders it unnecessary to have recourse to another drug possessing a similar property in a very doubtful degree if at all. A cheaper substitute would certainly be desirable, but only on condition it was equally efficient. I don't think anyone would pretend to assert that Muriatic acid was in any respect a specific in intermittent fever, as I am most assuredly is allowed to be. Though that is still transmitted for it without this...
The most important properties ascribed to Podophyllin by those who advocate its extensive use, and at the same time those which are most likely to be questioned by others, are its influence in promoting the absorption of glandular enlargements, in causing the breaking-down of inflammatory adhesions, and in effecting that diuretic action, called Alteration, caused by the stimulating operation of certain medicines upon the secreting surface and glands, and on the Absorbers. In account of these alleged actions, Podophyllin has found a wide application in the various chronic diseases, as the Venereal, Syphilitic, Ulcers, and Dyspepsy. It would seem to have the same wide range of action which an regular Practice ascribes to Mercury.
It is only just to allow that its advocates do not claim for it the power of breaking down inflammatory adhesions, unless it be employed in combination with another powder.

I probably cannot give a better idea of the preceding high claims presented in favor of this resinoid by the leaders of the "Eclatists" than by quoting the words of Dr. Cleveland, who is a Professor in an Eclatist School — Ohio. — The following is a summary of two strong statements as forwarded to me by a friend — "As a glandular stimulant, the Podophylline alone, or combined with blood-letting, will be found equal to Calomel; and as a Cholagogue Cathartic, it is superior to, more safe, and more certain than the Mercurials; but it
is not a solvent, and therefore cannot be relied on to supply the place of the Mercurials in those cases where the solvent property is demanded, as in inflammatory adhesions of the tissues of the eye, or in pleural or other adhesions of the Serous Surfaces. Neither do I think it will remove deposits of inflammatory exudations following upon Syphilitic infection as Mercury will do. But while I do not find Podophyllin to possess these properties, I esteem it the more highly from their absence, as we can administer it in many cases, when, did it possess the solvent property, it would inadvisable. But its merits in that important class of diseases where Solvents are indicated can be wholly remedied—combined with very small proportions of the
Hydrochlorate of Ammonia, it possesses solvent properties fully equal to the Mercurials. So that in inflammatory adhesions of Serous Surfaces, in particular, we have a valuable agent without being obliged to fall back upon Mercury. Therefore, Podophyllin, as a glandular Stimulant, and a Solvent, can supply the place of Mercury, then we reduce the necessity of using that mineral to very narrow limits, and supply its place with a simple remedy that can be used to the fullest extent necessary, without any risks to the Subsequent health and even life.

I regret that it is not in my power to prove or disprove the strong statements in the above paragraph. All will be ready to acknowledge their great importance.
Such are the claims made in favor of the use of Podophyllin by its most ardent advocates.

In our own ranks it has its acknowledged and very important actions in all cases where fungation is useful as well as achieving from aseptic collections in promoting the flow of the bile, in alleviating congestions in the Brain and its efficiency in the treatment of some forms of Rheumatism and Dysentery is pretty generally granted.

Of those very important actions accorded to it of late, I would not venture to give an opinion. It is very strange however that the most urgent claims upon our credulity are generally made by those out of the regular ranks of the Profession. We can only wait and have our incredulity.
cleared away by the light which experience must throw over these assertions. We ought not to deny, and we cannot believe before experience has supplied its test. All must allow that there is great difficulty in estimating the value of investigations and deductions made by men, who, influenced by an inveterate hostility to a long tried and well proved remedy, attempt to introduce a substitute. Their enthusiasm may lead them into error at the very time that they honestly think they are seeking for and have even discovered a great and important fact. We cannot help distinguishing the accuracy of observations made by such men. This must be acknowledged to be the character of those observations which have been referred to.
in this Paper — Their accuracy is maintained by the “Electrics,” who seem to have taken their name from a fancied prominence over the regular Practitioners as regards their freedom of choice. The Founders of the Body made their selection from the Materia Medica of the Regular Practice, and may with more justice be called “Electrics.” But no such choice remained to the poor misguided disciples — banishment from the pale of the Elect must be their lot on the first use of any of the proscribed remedies — This rejection of some of the most valued medicines of the Regular Practice seems to form the dividing line between them and the Electrics.

Mercury is among the most important of the Prescriptions — The words quoted
From one of their Leaders will show with what confidence they look upon Podophyllin as a Substitute. And if there is any truth in the bold assertions they so confidently make, we must allow that a very important discovery has been made — a substitute for Mercury, perfected of so many of its valuable actions, must be considered a great acquisition in those cases in which an idiosyncrasy exists rendering its administration unadvisable; for no one can deny that the action of Mercury is often troublesome and even at times dangerous — still less can its efficacy in many forms of disease, acute as well as chronic, be denied —

The attested experience of all physicians in this country, and in others, proves too satisfactorily the value of Mercury in various
Morbid states (as in breaking down and promoting the absorption of the plastic effusion in ulcers, &c.), to allow of any reasoning man yielding to the "dictum" of those who maintain that mercury either produces no salutary action, or is always troublesome and sometimes dangerous.

The experience of the first Men in the Profession is opposed to such a supposition.

It is true that many assertions are of no value, except in exciting investigation. Deliberate observation and experience must be presented in support of assertions. Several important indications for the use of Podophyllin have been acknowledged in the competent authority of the regular Practice. But the only claim upon our confidence in some of its more important actions
are the assertions and interested observation of partial interference.

I would that it had been possible for me to render this paper of some real value by direct experiment and observation—but such investigations have been impossible.

Still the alleged importance of the subject, together with the interest which startling novelty gives, may be sufficient to cloak its otherwise imperfect treatment.

Confirmation or refutation lies with the future.