

An Inquiry into the comparative effects of the Opium officinarum, extracted from the Papaver Somniferum or White Poppy of Linnaeus; and of that procured from the Lactuca Sativa, or common cultivated Lettuce of the same author

John Redman Coxe

An Honorary Member of the Philadelphia Medical Society; and a Senior Member of the Chemical Society of Philadelphia

Transactions of the American Philosophical Society, vol. 4, pp. 387-414, 1799

Read, Nov. 24, 1797

Gentlemen,

In the boundless fields of inquiry which the book of nature opens to our view in the extensive regions of America, much remains to be investigated. Our forests, our fields and rivers, our mountains, and the bowels of the earth, alike invite attention from the philosophic mind. Too long has a supine inactivity prevented our benefitting by the bounty of nature. She is not coy; yet she requires pursuit from those who wish to secure her; those alone who seek her, will she meet with a smile, and conduct them to the temple of honour and fortune. Proteus-like she assumes every form, and thus suits herself to the most fantastic imaginations.

The rugged aspect of the entrance to the various avenues of knowledge has deterred many from its pursuit, who if they had made the least advance, would have perceived a speedy termination to the labyrinth before them, and a luxuriant prospect unfolding to their view, and growing more delightful in proportion as they proceeded.

Among the various objects which nature holds up to our view, none are more deserving of investigation than the vegetable Kingdom. - Here we discover, plants sited to nourish and to preserve life; whilst others serve, by their grateful fruits and odours to gratify the sense of taste and [388] smell; or by their brilliant colours, the eye of man. By the noble discovery of the art of dying, many of these colours have become tributary to taste by their transmission to, and fixation in, other bodies; nature is thus improved upon, by rendering permanent and fixed these her fugacious and transient ornaments. In medicine, many of the most valuable articles of the *Materia Medica* are derived from this source; witness the ipecacuanha, jalap, rhubarb, gamboge, bark, and opium, with many others which might be mentioned, of less note.

Wherever we look, we find nature tributary to the labours of man. Her luxuriance is increased; she seems anxious to remunerate our fatigue, and to diminish as far as in her power the curse inflicted upon the human race, in the persons of our first parents, of "eating their bread with the sweat of their brow."

Though the bounty of nature is thus variously extended throughout the regions of the earth, it is not the less our duty and interest, to endeavour to discover such articles in our own country, as are similar or analogous to those which we obtain by importation from distant places; or at least to draw from other countries those riches which will prove equally productive, when naturaliz'd to our soil and climate. In the immense extent of United States, may be found almost every climate from the

torrid to the frigid zone. Let us not then despair of ultimately possessing among ourselves, all those invaluable sources of health and nutrition which are drawn from the vegetable creation in every part of the globe.

The potatoe is not a native of our climate, nor of the European countries in which it is cultivated; yet it is one of the most useful of the vegetable tribe, and grows among us as luxuriantly as in its native soil of South America. The rheubarb, though not natural to the climate of Great Britain, by cultivation, has there become tributary to the wants [389] of man. Let us not then longer than is necessary be dependant upon foreign countries for the production of such substances as our own will afford us: let us seek in our extensive regions those treasures of the vegetable world, which now droop unnoticed, "and waste their sweetness in the desert air;" and which by cultivation may become such articles of commerce as amply to repay any labour expended upon them. We have too long lavished our treasures upon foreign productions; let us now in turn render foreign countries tributary to us.

Having said thus much, I shall now proceed to treat of one of the most valuable articles of the *Materia Medica*, in a cursory way, as an introduction to the subject of the following paper; and which I trust from its importance will be found worthy to the attention and particular notice of your respectable body.

The substance I propose to consider, is Opium; emphatically styled by some authors, "*Magnum Dei Donum*," and in the class of stimulants regarded as the principal.

The plant which has hitherto yielded for the shop this invaluable drug is the papaver somniferum or white poppy; in the class polyandria and order monoginia of Linnaeus.

It is an annual plant; from the heads or capsule of which, the opium is obtained in Persia, Arabia, and other warm regions of Asia. Both the smell and taste reside in a milky juice, which is most copious in the cortical part of the capsules; though the leaves and stalks possess it in a less degree. This milky jouce in a concrete state, forms the officinal opium. Kaempfer and others have long ago described the manner in which it is collected: but the most circumstantial detail of the culture of the poppy, and the method employed to procure the opium from it, is that given [390] by Mr. Kerr, as practiced in the province of Bahar* [* See Woodvill's Medical Botany. Vol. III. p. 505].

The purest kind of opium is chiefly retained for the use of the inhabitants of those countries in which it is prepared; who being debarred by their religion, from wine or ardent spirits; accustom themselves to a still more pernicious luxury, by raising their ensebled ideas with the stimulus of opium.

The quantity taken by some in the space of twenty-four hours is truly surprising. It is true, that the use of it in the commencement is very moderate; but like dramdrinking become more necessary each day, to the existence of those who are accustomed to its influence.

According to Mr. Boumé opium consists of an extractive matter soluble in water; a resin; a volatile concrete oil; and a peculiar salt; existing in the following proportions.

4 lb of common opium yielded	lb	33.	3.
of Insoluble matter,	1	1	0
Extractive matter,.....	1	15	0
Resin,	0	12	0
Oil,	0	3	7

Saline matter 0 0 1
 Equal to 64 33. or..... lb 4 0 0

In the history above referred to, of the cultivation of the poppy, previously to obtaining from it this invaluable drug, may be remarked the extreme labour and attention requisite to its production. If then this time and labour can be saved, it must certainly prove beneficial to mankind, by diminishing the price of this useful remedy. Nor is [391] there any danger that this diminished price should tend to increase the number of those unfortunate wretches, who blindly seek to bury their faults of their misfortunes with them in the grave, by the impious and cowardly act of suicide. The avenues of death are too numerous, and the price of this balm to human misery (when properly applied) is much too inconsiderable to deter from his purpose a person, intent on terminating his existence.

The *lactuca sativa*, or common cultivated garden lettuce, is ranked by that great naturalist Linnaeus in his class syngenesia, order polygamia equalis, and is thus described:

"*Lactuca*. Receptacle naked. Calyx imbricaterd, cylindric, with membranous margins. Pappus simple, stiped. Seed polished."

The genus *Lactuca* comprises according to Linnaeus seven species, of which this is the second, and is described thus, "*lacutca sativa*, with leaves rounded on the stem hearted, stem corymbed."* [* System of Vegetables of Linnaeus, translated by a Botanical Society of Litchfield. London 1783]

Since the time of this great man several other species have been enumerated; it is not however my intention to speak of any other than the one above mentioned.

The lettuce had long been known to possess narcotic properties. None however had extracted from it a substance possessing all the properties of opium in the fullest degree: it was chiefly from tradition that its effects were known, and by observing that people were rendered sleepy by eating old lettuce. It is the more remarkable, because, as we shall see presently, some has arrived at the very threshold of the discovery, but have stopped from the pursuit.

As far back as the years 1792, and long before I had perused any author, upon the subject of lettuce, it occurred [392] to me to try some few experiments, to determine the quality and nature of that milky juice which exudes from this plant in copious streams when wounded; and this I was induced to do, from the well known effect of the plant in causing sleepiness when old; as well as from its peculiar smell and taste.

These experiments, at that time few in number, convinced me of the truth of the analogy which I had drawn between the common officinal opium, and the milky juice of this plant; for with a small quantity of extract obtained by inspissating this juice, I found similar effects induced upon myself when taken internally in the same doses with opium of the poppy. The most pleasing sleep was brought on by one grain of the extract, or by fifteen drops of the tincture made with proof spirit. By similar experiments since tried upon myself in England, I found the same effects; and a repetition of them within a few months past, proves them strictly the same. I have occasionally removed in myself a slight cholic, with twelve or fifteen drops of the tincture; and a series of comparative experiments upon frogs, & c. which I shall here detail, assure me by their uniformity of the identity of the opium extracted from the poppy and of that procured from lettuce.

Before I proceed to relate the experiments, I have made upon this subject, I must be permitted to show, by quotations from several authors, how nearly they had reached the discovery of this fact. JONES, a celebrated author, who published in 1701 his "*Mysteries of Opium revealed*," in speaking

"of the election (or choice) of opium," says: "3. It was mixed with juice of *Lactuca sylvestris*, or wild endive leaved lettuce."

"This made it of a duller colour, and not to smell so perfectly and rankly of the poppy." He soon after, adds, "but *lactuca sylvestris* being of the nature of opium, made the loss of its virtue less discernible." See p. 13. [393]

Dr. CHARLES ALSTON, in the 5th vol. of the Edinburgh Medical Essays and Observations, p. 105, in his dissertation on opium after mentioning several articles with which it is reported to be adulterated, adds, "I know not the glaucium of the ancients, nor did I ever see any opium that I had reason to suspect as adulterated with gum or suet; but the wild lettuce, that is, the *lactuca sylvestris*, odore viroso, C.B. Pin. 123 abounds more than any poppy I know, with a milk of the same taste and smell; perhaps therefore this, if it can be more easily collected, may still in some place mixed with opium, and the medicine be nothing the worse for it, the milk of even the common lettuce being anodyne and somniferous, as well as that of the poppies." See also his 57th lecture in the 2nd vol. of his *Materia Medica*, p. 153 et seq.

HILL in his British Herbal, p. 436, under the head of *lactuca*, has the following: "Division F. I. Great wild lettuce. *Lactuca sylvestris major opii odore*."

"The root is long, thick and whitish; and when cut, it yields abundantly a yellow juice, of a very unpleasent smell, resembling that of opium; and of a bitter, nauseous taste." "C. Bauhine calls it, *Lactuca sylvestris odore viroso*. Others, *lactuca sylvestris major odore opii*."

"This is one of those English plants which deserves to be more known in medicine. It has been called poisonous, and men have from that been frightened from its use; but it is a very gentle and a safe opiate. The best way of giving it is in a syrup made from a decoction of the fresh leaves and stalk. This way it greatly exceeds the common diacodium, and may be given to tender constitutions with more safety. This I wrote from experience."

DALE has described the lettuce also in his *Pharmacologia*, p. 80. In this the different characteristic names of various authors are brought together. I. Bauhine calls it "*lactuca sylvestris lato folio, succo viroso*." I.B. ii. 1002. DIOSCORIDES [394] has said, according to Dale, that it mitigates pain. DALE has also made a second species or variety of the *lactuca sylvestris*, under the distinguishing mark of, "*L. sylv. costa spinosa*, or jagged leav'd wild lettuce." I shall here quote his own words.

"*Lactuca sylvestris sativae similis est (ut scribit Dioscorides) sed longior caulis, et folia graciliora, et asperiora; maro gustu est. Quae de viribus lactucae sylvestris veteres prodiderunt, quod scilicet semen ejus non minus quam sativae libidinum imaginationes in somno amolitur, et venerem arcet; cui huic plantae convenient, dubitat D. Raius. Narcoticam eam esse et soporiferam, adeoque (ut rectè observat) viribus papaveri similem, ut Dioscorides et Plinius tradunt, opii vehemens et virosus odor abunde convincit,*" et seq.

These quotations will sufficient to prove that however analogous their authors might suspect the officinal opium and the juice of the lettuce to be; they had not to put it to the test of experiments. I now proceed to state those which I have made.

LETTUCE OPIUM EXPERIMENT 1.

July 1ft, 1791
To one ounce of rain water, I added 5 grms.

COMMON OPIUM EXPERIMENT 2.

The same day I added a similar quantity
of rain water to 5 grms. of the opium of

of the opium of the lettuce in the vial
marked A.

the poppy, in the vial marked B.

I frequently agitated both vials, and on the 21st of the month, I found by filtration, only one grain and a half, left on the filtre of the vial A. whilst 2 grains were left on that of B. This difference of half a grain I at first described to the common opium being much more dry than that of the lettuce which was freshly made; and hence, in an equal weight not containing so great a proportion of fixed matter. [395]

The colour of the solution A. was however much deeper than that of B. and succeeding experiments convinced me that the quantity of extractive matter in the lettuce opium, is considerably greater than in the common. By the aid of my ingenious and worthy friend Dr. Cooper, of this city, I obtained a larger quantity of the lettuce opium, with which I was enabled to make the following.

**LETTUCE OPIUM
EXPERIMENT 3.**

July 1st, 1791

August 14th. I put 20 grains of this opium thoroughly dried, into two ounces of filtered rain water, in the vial A. and after repeated agitations, I filtered it on the 18th. When dried, there were left on the filtre, 10 grains, so that one half, was pretty accurately held in solution. The filtered solution was of a dark brown colour, possessing much of the taste and smell of opium.

To both of these solutions I added about a drachm of alkohol, to prevent putrefaction.

**LETTUCE OPIUM
EXPERIMENT 5.**

July 1st, 1791

August 19th. I put the 10 grains remaining on the filtre of A. (experiment 3) into an half ounce of alkohol. I filtered it on the 29th, and found 7 grains left on the filtre, which when washed and dried, was devoid of taste or smell. The quantity of resinous matter than was 3 grains, or rather more than one 7th of the whole mass.

Neither of the above solutions possessed to any considerable degree the peculiar smell or taste of opium; probably from the large proportion of alkohol. The resin was precipitated from the solutions in alkohol, by the addition of water. That of the lettuce appeared to me whiter than the other; but not so copious: the opium taste, & c. was more evident in the water. Its resin was more evident by standing some days.

**LETTUCE OPIUM
EXPERIMENT 7.**

August 19th. I put 20 grains of the lettuce

**COMMON OPIUM
EXPERIMENT 4.**

August 19th. I put 20 grains of common opium into a similar quantity of rain water in the vial B. On the 24th, I filtered it after frequent agitations. There remained on the filtre, when dried, grains 11, which consequently leaves but 9 twentieths, dissolved by the water. The filtered solution was not nearly of so deep a colour, as that of A.

**COMMON OPIUM
EXPERIMENT 6.**

August 26th. I put the 11 grains remaining on the filtre of B. (experiment 4) into the same quantity of alkohol. I filtered it on the 29th, and found 8 grains left on the filtre; devoid of taste and smell, when washed and dried. Here than the proportions agree. The colours of this solution in alkohol was much deeper than that of experiment 5. [396]

**COMMON OPIUM
EXPERIMENT 8.**

The same day, I put a similar quantity of

opium into the vial A. and added to it one ounce of a mixture of equal parts of alcohol of rain water. On the 29th, after repeated agitation I filtered it and found that 12 ½ grains had been taken up, as 7 ½ remained on the filtre after washing and drying. The solution eminently possessed the smell and taste of laudanum; and was of an higher colour than that of the following experiment.

The mass left on the filtre A. was of a more gummy feel than that of B. and not of so high a colour; the smell or taste of opium was not very evident in either of them. With the solutions of experiments 3 and 4, I proceeded now to make the following.

LETTUCE OPIUM EXPERIMENT 9.

To a solution of sugar of lead, I added 30 drops of the aqueous solution of the opium lactucae, a copious brown coloured precipitate instantly formed. The opium smell was evident.

EXPERIMENT 11.

To a solution of sulphate of iron (green vitriol) I added 20 drops of the aqueous solution. A brownish coloured precipitate was formed; but not very copious. The supernatant liquor upon the subsidence of the precipitate was of dirty green; as was also the precipitate itself upon standing.

The opium smell was retained.

EXPERIMENT 13.

To a solution of hepar arsenicum (made with orpiment and quicklime) I added 20 drops of the above aqueous solution; a brown and pretty copious precipitate was here formed. The supernatant liquor appeared clear. The hepatic smell seemed to be augmented by the union of the two solutions.

EXPERIMENT 15.

To one drachm of lime-water. I added 20 drops; a brownish precipitate was formed. The opium smell remained.

EXPERIMENT 17.

To one drachm of lime-water. I added 20

common opium into the vial B. and added the same quantity of the mixture of the alcohol and water. By filtration on the 29th, seven grains were left upon the filtre; or 13 grains were suspended in the solution. This difference I regard as proceeding from a small allowance not being made in the weight of the opium of the lettuce, which had not dried thoroughly; and hence not containing as much solid matter in the whole mass.

COMMON OPIUM EXPERIMENT 10.

A similar effect took place with the acetite of lead, and the aqueous solution of common opium. The precipitate was not as dark as the former; the opium smell was evident. [397]

EXPERIMENT 12.

The precipitate here was of a darker colour, but in the same proportion apparently. The solution was itself of a brown colour, and retained the opium smell.

EXPERIMENT 14.

The precipitate here, was of a light green colour, and very small in quantity, until after standing a considerable time, when the cloud began to subside of a brownish or dirty green colour. The hepatic smell seemed increased.

EXPERIMENT 16.

I added 20 drops, to 15 drops of nitrate of silver, diluted with rain water; a light coloured cloud gradually formed itself after standing some time.

EXPERIMENT 18.

The same effect, but in a less degree, took

drops; a brownish precipitate was formed.
The opium smell remained.

EXPERIMENT 19.

I added 20 drops to a solution of carbonate of ammonia; a brownish coloured precipitate took place. The peculiar smell of both solutions, was evident.

EXPERIMENT 21.

I added 20 drops to a diluted solution of nitrat of copper. The green colour of the latter, predominated; but a very lightish brown coloured precipitate gradually subsided.

LETTUCE OPIUM EXPERIMENT 23.

A copious lightish brown colour precipitate was produced by adding 20 drops to a diluted solution of nitrat of mercury.

EXPERIMENT 25.

Alkohol, diluted with water, produced no effect when added to the above solution.

As in the above related experiments, the general effects of the two species of opium were pretty nearly similar, with chemical texts. I thought a set of comparative experiments made upon frogs, would be proper to illustrate still farther this identity. I therefore submitted several to the action of the opium in the manner following.

EXPERIMENT 27

July 1st. In a vial (C.) I put 8 grains of the opium lactucae, and added by measure half an ounce of good brandy. On the 14th of August, I filtered it, and found 2 grains left upon the filtre. This I put into the same vial C. and added half an ounce of filtered rain water. The mass was of a gummy nature, possessing nothing of the peculiar taste of opium, and but little of the smell. On the 16th, after filtering it, I still found 2 grains remaining. The water had [399] acquired an evident bitter taste, and a slight smell; which was doubtless owing to my neglect of washing the mass previously to the addition of the water.

EXPERIMENT 28

August 20th. At 12 o'clock, I injected a portion of this aqueous solution (experiment 27) between the skin and muscles of the right lower extremity, of a fine lively bulfrog. At the same time I also injected between the muscles and the skin of the left lower extremity, a mixture of one part of alkohol, and two of water. He did not appear sensible of pain at the introduction of either, but leaped about in the receiver, in which I confined him, with great vigor. At 10 minutes after 12, he appeared equally vigorous; as he did at the expiration of 15. I now injected some more of the same solution under the skin of the right extremity, but found no alteration evinced at the end of 10 minutes. I therefore introduced a third portion, at the distance of 25 minutes from the first; but without any alteration, excepting a slight convulsion, in drawing the leg to the body, and which probably was occasioned by the irritation of the instrument used in injecting the solution. Finding no effect

place in this experiment.

EXPERIMENT 20.

In this experiment the same effects took place. [398]

EXPERIMENT 22.

In this experiment the brown colour of the solution of opium predominated, and a beautiful clear solution remained which did not become cloudy after standing 10 minutes.

COMMON OPIUM EXPERIMENT 24.

A similar effect took place in this experiment. [397]

EXPERIMENT 26.

This experiment proved the same.

produced by the solution upon the muscles of the extremities, I injected a portion into the stomach at 30 minutes after 12. At 35 minutes after 12, the right leg was moved with considerable difficulty; and generally remained in an extended position, unless struck or otherwise irritated; when it was drawn forwards pretty forcibly. The frog could use it very well in the action of jumping; and he did not seem affected by what was taken into the stomach, except that respiration appeared to be increased at the end of 10 minutes. A portion injected into the rectum, produced no effect; and his legs had regained their perfect use. [400]

At 10 minutes before one o'clock, I introduced between the skin and muscles of the left leg (which had had the alcohol and water injected into it at the commencement of the experiment) a portion of the aqueous solution of the opium lactucae, of the vial A. (experiment 3.) at this time the frog was very lively. Much of the solution was discharged by the motion of the leg in placing him under a receiver; in 5 minutes he moved about briskly; in 10 his left leg began to drag. At this period of the experiment, something occurred to carry me away, and I put the frog into the water.

EXPERIMENT 29

August 21st. The frog, the subject of the preceding experiment, had perfectly regained his liveliness and animation. At 30 minutes after one o'clock, I injected a few drops of the aqueous solution A. (experiment 3.) into his stomach. In 3 minutes, considerable contractions of his abdomen appeared, and continued at intervals; with an opening of the fauces, as if to obviate the difficulty of respiration. By agitating him, he was made to move with considerable briskness. At 15 minutes before 2, he appeared very lively. Neither of these appeared to affect him. At 25 minutes after 3, I injected a portion, through a small incision, into the abdomen; a considerable part of it was rejected; but his lower limbs were paralyzed to a certain degree in 5 minutes. He could not jump, but drew his legs after him with much difficulty. In 12 minutes he could jump slightly. At 45 minutes after 3, I injected more, and retained it by keeping him upon his back. At 4 o'clock he jumped pretty well. At 30 minutes past 4, he continued lively. I now put him into the water, but found him dead the following day. [401]

His death arose, in all probability, from inflammation, induced in the abdomen, by the incision made into it for the introduction of the solution; at least it must have had some influence.

EXPERIMENT 30

Neither the aqueous solution A. (experiment 3.) nor alcohol and water, appeared to affect this frog when dropped upon the naked eye.

EXPERIMENT 31

Several drops of the aqueous solution A. (experiment 3.) were dropped into my right eye. It gave me some degree of pain, which was not so long duration. I felt no other inconvenience from it; but a slight inflammation for some hours was evident in it.

EXPERIMENT 32

After separating by inflation the skin and muscles of the right inferior extremity of a fine active frog; I injected, at 20 minutes before 4, several drops of the aqueous solution of opium lactucae, A. (experiment 3.) In 5 minutes little effect was induced. In 10 he experienced some difficulty in moving it, and it was accompanied with a dragging motion. In 15 minutes still greater difficulty. Upon extending the leg it was retained in that position; whilst the left was quickly drawn up to the body; yet when the right leg was irritated, it was exerted with considerable facility.

In 20 minutes the sense of feeling seemed to be in some degree impeded; for it did not appear to

evinced by any contractions, that it felt pain from a pointed instrument in this leg, though in the left, it was very evident. [402]

At 5 minutes past 4, I introduced some of the same solution beneath the skin of the left leg. At 10 minutes past 4 there was considerable difficulty in moving this leg; and his motion seemed now to be performed by pushing himself on with his fore-legs. If he wished to jump, he was compelled to push his body back upon his hind legs, instead of drawing them up to his body. The jump was only the length of his hind legs, which then remained extended as before. A silver probe introduced into the opening made to inject the solution, produced convulsions in both legs, by the aid of zinc. At 15 minutes after 4, both his legs appeared perfectly paralytic. At 20 minutes after 4, I injected some of the same solution under the skin of the abdomen, which seemed in some degree, after a short time to paralyze his fore-legs.

The solution applied to the naked eye of the frog did not seem to affect in the least, as it did not cause it to cover it with the lids.

At 30 minutes after 4, I injected some drops into the stomach, which seemed at first to convulse it considerably; it appeared to strive to vomit, opening its mouth to the utmost extent, and making repeated convulsive motions of the oesophagus. It could not now move its lower limbs, though they were occasionally convulsed; and violent convulsions were induced by zinc and silver.

At 20 minutes before 5, it seemed to have expired, but by introducing a few more drops into the stomach, a slight convulsion was induced in about a minute. At 15 minutes before 5, it was completely dead.

Ten minutes before 5, I opened the thorax and abdomen. The heart beat 80 pretty vigorous pulsations in a minute. After removing the pericardium, I put a drop of the solution upon the heart, which did not appear to diminish its frequency. I now removed it from the thorax, and put it into some drops of the solution, which seemed soon to check [403] it, for at 5 o'clock it beat only 50 pulsations in a minute, and at 10 minutes past 5, only 18, and chiefly of the auricle. A pointed instrument scarcely increased its vigour. The stomach was corrugated, and contained the solution mixed with a slimy matter.

EXPERIMENT 33

At 15 minutes before 2, P.M. I injected a few drops of the aqueous solution A. into the abdomen of a lively frog, the greatest part of which escaped. Though the frog was stifly contracted before the introduction of the solution; yet the abdominal muscles relaxed and elongated themselves the instant it was introduced.

At the expiration of 5 minutes no effect was produced. At 10 minutes being equally lively, I introduced another portion and retained it there for some time.

In 10 minutes he lay upon his abdomen, not as usual resting upon his legs. Irritation with a pointed instrument, did not now cause his extremities to contract; they appeared perfectly paralyzed. When placed upon his back, he lay without motion. His eyes were sensible to irritation.

In 20 minutes he began slowly to move his lower, and soon after his upper extremities, and gradually elevated himself upon them as usual. Contractions were produced by zinc and a silver probe passed into the abdomen.

In 5 minutes from this time he appeared to be nearly dead, and was completely so in two or three minutes longer. At 3 o'clock his limbs were nearly stiff.

On opening the thorax the heart was beating 60 vigorous pulsations in a minute. I removed it from the body, and in 15 minutes it pulsated only 32, and chiefly of the auricle. In 30 minutes after 3, it beat only 10 times. At 45 minutes, it was excited to a few weak pulsations by a pointed instrument.

[404]

The length of time in which contractions may be induced by metallic substances, in the frog, is much diminished by the application of the opium. In 20 minutes after the death of this frog I could not produce any; now they may be induced at the expiration of 48, 72 and even a greater number of hours, in a frog by cutting off, or crushing the head; as the experiments of Dr. Fowler on animal electricity evince.

EXPERIMENT 34

August 22d. At 10 minutes after 3 o'clock, I exposed to vie a brain of a frog, and put a few drops of the aqueous solution A. upon it. By a want of attention to the motions of the frog, the greatest portion of it was speedily lost. In 5 minutes he was very lively. In 10 minutes the same. At 30 minutes after 3, I introduced a second portion with greater care, which almost instantly seemed to affect him; for instead of supporting himself as usual upon his legs, he lay upon his abdomen. In 5 minutes his left leg seemed paralyzed, and he tumbled about with a sort of convulsive motion. In 10 minutes he was more affected. A pointed instrument scarcely causing him to move; and his motions were chiefly confined to his upper extremities.

In 20 minutes he appeared to be quite dead. On opening the thorax I found the heart pulsating vigorously 56 times in a minute. In 15 minutes from this time it beat 48. In this frog, the contractions produced by zinc and silver were by no means so vigorous, as in those killed without the application of opium.

EXPERIMENT 35

By way of a comparative experiment, on the 26th of August, I injected some drops of the aqueous solution of [405] common opium, B. (experiment 4.) beneath the skin of the right inferior extremity of a lively frog, at 15 minutes before 1 o'clock. At 1, he was quite lively. By means of a probe, I now detached the ligamentary union of the skin at the knee, and passed a second portion of the solution down to the ankle joint. In 20 minutes he was as lively as ever. I now injected a third portion and retained it some time. A prolapsus ani occurred during the introduction of the solution by the sole exertion of the animal, as no force was employed. In 5 minutes his leg began to drag, and in 10 minutes he could not move it. The left was used with violence when irritated.

At 20 minutes before 2, I injected a portion into the stomach, which almost instantly convulsed him, in a manner resembling the contractions produced by zinc and silver. His irritability was so highly increased from the effects of the opium, that the slightest touch produced convulsions in all his extremities. After some minutes more had elapsed, a sudden noise or even blowing upon him, would produce them, and they became more frequent by degrees. At 2 o'clock they were less considerable, and at 10 minutes past 2, he appeared dead, as irritation produced no contractions.

On opening the thorax, the heart beat 48 vigorous pulsations in a minute. The stomach was filled with a slimy mass, possessing the smell of opium, and it appeared to have contracted upon itself about the middle. The vessels on its surface were distended with blood. Contractions induced by zinc and silver, were very inconsiderable; being confined chiefly to the toes of the right leg, even when the silver was placed in contact with the large sciatic nerves; and in the left leg, similar contractions extended no farther than the foot. At 3 o'clock neither would contract. The auricle was still pulsating 27 times in a minute. Having shewn by the preceding experiments that there exists a great similarity between the effects of the aqueous [406] solutions of common, and of the lettuce opium; I next proceeded to some few experiments with the spirituous tinctures, A. and B., described in experiments 7 and 8.

EXPERIMENT 36

September 2nd. At one o'clock, P.M. I injected between the skin and muscles of the right inferior extremity of a lively frog, a few drops of the spirituous tincture of opium lactucae, A. (experiment 7), and at the same time, I introduced beneath the skin of the left leg some of the spirituous tincture of common opium, B. (experiment 8). At the moment of introduction both tinctures gave pain, and by the efforts which the frog made to escape, a considerable portion of the tinctures was lost. In 5 minutes he hopped with great difficulty; or rather, his motions seemed to be performed by quickly and repeatedly pushing himself on by his lower extremities. Considerable inflammation was speedily induced in both thighs, and blood was even effused. In 10 minutes his motions were more difficult; and his jumps more circumscribed. Both legs seemed equally affected.

A drop of the tincture put upon his eye appeared to give pain, as he immediately closed it. In 20 minutes I injected a few more drops below the skin of the inferior extremities. In a few minutes, both legs appeared immovable. In 5 minutes from this time, the inflammation was seen extending itself with considerable speed, down the legs; as many small vessels before invisible to the naked eye, were now distended with red blood. His legs lay motionless in any position they were placed; and no irritation, except that produced by zinc and silver, caused them to move. These metals caused strong convulsions in both. [407]

For nearly 20 minutes he seemed to be dead. After which a very slight touch convulsed him, and by this time the inflammation had extended to his toes.

Some business carried me away at this period. I did not return till nearly 3 o'clock, when I found the frog laying as I left him; but the irritability of his system was so highly increased, that a very slight touch caused strong convulsive motions. I now placed him in a tumbler of water, and at 20 minutes after 3, the merely making a noise, as in the motion of a chair along the floor, and even only touching the glass in which I placed him, caused such strong convulsions, as nearly to project him from it. By degrees this effect ceased; and by 4 o'clock he was quite dead.

On opening the thorax the heart was beating 45 moderate pulsations in a minute. The right leg exhibited stronger marks of inflammation than on the left; as the vessels were more turgid, and one or two considerable effusions had taken place into the substance of the muscles.

EXPERIMENT 37

Fifteen minutes before two o'clock, I introduced a few drops of the spirituous tincture, A. (experiment 7) into the stomach of a fine lively bullfrog. A violent and instantaneous projection of the tongue shewed a disposition to vomit it up. He jumped about under the receiver with great vigour. In 10 minutes he began to breathe more quickly, and his jumps appeared more languid. When placed upon the ground, he could not jump above twice or thrice his length. About 3 o'clock he appeared to have recovered considerably from the effects of the tincture.

At 10 minutes past 3, I injected a few drops below the skin of the right lower leg, which caused considerable pain. A portion of it was lost, and a slight effusion of blood took place, which probably washed away another portion of the [408] tincture. At 20 minutes past 3, he moved with considerably agility, and seemed very brisk. In 30 minutes he appeared quite well. I now injected a second portion under the skin of the leg. At 35 minutes after 3, he moved it very briskly. At 40 minutes after, the right leg began to drag, although he could draw it to his body, and he lay with his head upon the table, instead of supporting himself upon his legs as usual. I now put him into some water, which revived him considerably; so that at 4 o'clock he moved his legs with ease, and by 20 minutes after, he used them vigorously, though still he was unable to leap to any distance.

At 20 minutes before 5, I introduced some more of the tincture into the stomach. In 10 minutes, he appeared very languid. Five minutes before 5, his legs remained motionless in any position in which they were placed, and were insensible to irritation. At length he gradually began to mend, and at 6 o'clock could move his limbs with great ease. I now put him into the water, and the next day found him quite lively.

EXPERIMENT 38

September 5th. At one o'clock, P.M. I laid bare the brain of the frog, the subject of the preceding experiment. He had perfectly recovered from the effects of that experiment, and was extremely lively. I injected some drops of the spirituous tincture A. down the spinal canal, which seemed instantly to affect him, as his fore legs were considerably paralyzed. He appeared somewhat recovered in 10 minutes, but breathed quick. The greatest part of the tincture was discharged and washed away by some blood which oozed from the wound. At 15 minutes after one, with more care, I introduced a second portion, which passed to all appearance, lower than the first. In a moment the whole [409] muscular fabric, became motionless and relaxed. The eyes closed; respiration ceased; and a slight pulsation of the heart, evinced by the motion of the thorax, alone rendered it probable that any vitality remained. No contractions of the extremities followed the application of a pointed instrument; but zinc and silver caused strong convulsive motions of the limbs. If the brain was touched with a silver probe, and brought into contact with the zinc on which the frog was placed, strong contractions of the body and limbs succeeded. When the probe was introduced to some distance down the spinal canal, the frog moved. At 25 minutes past one, he opened his eyes; and drew up soon after, his extended lower extremities to his body. At times the muscles of his upper limbs appeared strongly contracted, and they generally remained in the same position unless irritated.

At half past one, he suddenly became most violently convulsed; writhing his body and limbs, in every possible direction; and he even threw himself with considerable force from the table on which he was placed, although at least six inches from its edge. During the period of these violent convulsions he uttered a croaking noise. The convulsions were induced by the slightest noise, extending even to the toes; and they were more evident in proportion to the suddenness of the cause producing them. In 5 minutes this effect diminished considerably, and his limbs when extended were slowly drawn up again to the body.

At 20 minutes before 2, I left him feebly supporting himself upon his legs; and did not return till about 5 minutes before 3, when I found him under the receiver, and lying upon his back, as if from a renewal of the preceding convulsions. His eyes were open, and he moved slightly when touched. A probe passed down the spine caused his extremities to move. In 10 minutes from this time, very little effect was produced by passing the probe down the [410] spinal canal; and in a minute or two, he appeared completely dead. Convulsions produced by zinc and silver were still strong. The heart on exposing it to view was pulsating moderately 42 times in a minute.

EXPERIMENT 39

At 30 minutes past 4, I injected a few drops of the above tincture A. into the stomach of a young frog; which caused it to gag, and a considerable portion was rejected. In 5 minutes he remained under the receiver pretty quiet; though before this he had been striving violently to escape. When touched he did not jump, but lay in the position in which he was placed. Ten minutes before 5 o'clock, his respiration was quick, being 66 times in a minute. His hind legs were moved with difficulty, and he lay with his head upon the table.

At 5 minutes past 5 he began to move about, and seemed to have recovered considerably. Business

now calling me away, I put him into the water. At 10 o'clock he was very active and vigorous, and continued so till I threw him out some days after.

The following very interesting experiments, were made at my request at the Pennsylvania Hospital by my very ingenious and worthy friend Dr. Samuel Cooper, to whose kindness I am much indebted. "Jeremiah Smith, 34 years old; puls beating 96 strokes in a minute, took 30 drops of the lettuce laudanum, (A. experiment 7)

In min.	2	5	10	15	20	25	30	35	40	45	55	60	70	80
Pulse beat	96	96	94	95	98	98	100	101	100	101	101	103	102	102

His face was now evidently flushed, and his skin was warmer. He said that he felt very agreeable. His puls seemed increased in force as well as frequency." [411]

"Upon taking 30 drops of the same preparation, I felt as if I had swallowed a glass or two of wine, or a small quantity of opium.

"It was given in the following diseases, viz. heart-burn, chronic rheumatism; the pain of which occurred In the night; Diarrohoea; and in a pectoral complaint attended with a periodical cough. It seemed to destroy the disagreeable sensation of heart-burn, and hindered the occurrence of the pain of rheumatism. It checked the frequent stools accompanying diarrhoea, and occasioned the evacuation of much flatus. It allayed the cough attending the pectoral complaint. In all these cases it seemed to be precisely analogous in its operation to the tincture of opium; and like opium it increases the frequency and energy of the pulse."

In any person reads the foregoing experiments with attention, he cannot hesitate in allowing the most perfect identity to the two species of opium. The experiments of Whytt, of Alston, and of others, strengthen in the highest degree the evidence of the fact.

The milky juice from which the opium is prepared, exists in the stalk and in the leaves of the plant. It is not indiscriminately deposited throughout, but is placed in appropriate vessels running longitudinally in the woody or fibrous part of the stalk. The internal or medullary part of the plant is soft; and perfectly bland to the taste, abounding in a transparent mucilaginous juice; which has not the smallest analogy to the above-mentioned one.

The best time for collecting the juice, is when the plants are beginning to seed. If we take it before this, it has not sufficiently acquired its medical properties; and if a later period, the quantity is by no means so considerable.

It is best procured in the manner described for collecting it from the poppy, viz. by incisions; with this difference, that in the poppy they are longitudinal, but in this must be circular. A very moderate depth suffices. It exudes free[412]ly in milky drops, which may be either immediately collected; or suffered to dry on the stalk, and then scraped off and deposited in proper vessels. If we obtain it by pressure from the plant, and than inspissate; the other juices seem to alter it considerably: the colouring matter of the vegetable is taken up, and the smell of the opium no longer exists; at least this was the case with 30 grains of an extract procured thus, from 10 drachms of the plant, by Dr. Cooper. It possessed none of the peculiar smell or taste of opium, and when I put it into a mixture of equal parts of alcohol and water, it readily yielded the green colouring principle, but nothing further. Probably more attention to the subject will lead to a method of separating the opium from the other principles united to it. Exposure to the sun and to the air, may possibly produce this effect; the smell of the juice when first extracted by pressure is strong of opium. The extract above alluded to was inspissated in a sand bath, the heat of which may have been too considerable for it.

Having said thus much upon the juice of the common lettuce, I must observe that all the species contain it in a larger or smaller proportion. The *lactuca sylvestris*, or *virosa* of Linnaeus, contains it most abundantly. That from which I obtained my opium, was, I observed before, the *lactuca sativa*; it abounds in juice, and will serve the double purpose of cultivating for the table as well as for the shop.

I cannot avoid contrasting the superior advantages of the opium extracted from the lettuce, above that procured from the poppy.

Some judgment may be formed of the labour and experience attendant upon the cultivation of one acre of the poppy, by the account given by Mr. Kerr. He says "an acre yields in the East Indies, 60 lbs. of opium, which, at 9 shillings sterling, (2 dollars) per pound, is £ 27 an acre." Now, [413] at a moderate computation, it may be presumed that one half of this sum is employed in the necessary expences of ploughing, manuring, sowing, watering, and collecting, &c. &c. Say then that £ 13. 10, are clear gain, (which must be allowed to be a large proportion). Now the poppy cannot be employed as an article of diet; whereas the lettuce, which grows here in the most luxuriant manner, will amply repay the labour and expence (which at most is trifling) attending its cultivation, by the sale of the supernumerary plants taken up at an early period for diet, long before the development of the opium principle. Here then the very labour employed has the double advantage of thinning the plants, thereby rendering the remainder more perfect; whilst it collects for the market such as have arrived to sufficient maturity for the table.

The sale of these supernumerary plants would, I conceive, at least repay the labour, &c. attending their cultivation: and if the rest yielded per acre only 60 lbs. of opium, double the profit would arise from its cultivation, above that of the poppy. The great abundance of the juice however, and the luxuriance of the plant, render it highly probable, that double that quantity, if not more, might be procured from the acre of ground.

The price of this valuable article of the *Materia Medica*, leads me to hope that farmers and others will attend to the cultivation of the lettuce, in order to obviate one source of the annual expenditure of money from the United States; and as Dr. Crumpe observes in his valuable treatise upon opium, "if any overplus remained after our own demands, a ready market would be found for it in the East Indies, where its consumption is very considerable, and price generally high."

The medical virtues of opium would appear from the experiments of authors, to reside more particularly in the extractive principle. If this be certainly the case, the opium [414] of the lettuce, would prove far more valuable to the *Materia Medica*, than the common opium: for by the comparative experiments 3d and 4th, ten grains of extractive matter were taken up from one scruple of the lettuce opium; whilst only nine grains of the common opium were taken up from the same quantity. This in a pound weight, will give a very decided advantage of six drachms, one scruple, four grains, to the lettuce opium, above the common; for in one lb. of the lettuce opium, one half, or 8 oz. are extractive matter, whilst of the common opium only 7 oz. 1 fc. 1 dr. 16 grs. are extract.

As I conceive the foregoing facts may prove serviceable to my fellow citizens, I have taken the liberty of drawing them up in the form of a paper, addressed to your respectable Body, as the surest mode of obtaining their promulgation.

I have the honor to be,
With the greatest respect,
Your obedient humble servant,

JOHN REDMAN COXE.