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ON
THE INFLUENCE OF
LIQUOR POTASSÆ,
AND OTHER CAUSTIC ALKALINE SOLUTIONS,
UPON THE THERAPEUTIC PROPERTIES OF HENBANE,
BELLADONNA, AND STRAMONIUM.

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It was my original intention to have added a dated postscript to the first therapeutic communication, containing the results of some fresh observations and more recent experiments; circumstances,¹ however, have altered this inten-

¹ Among others, I may mention that, since the abstract of my paper appeared, Mr. France has published a paper in the *Lancet*, February 27th, 1858, in which he attempts to show that no destructive influence is exerted by potash upon the active properties of belladonna and henbane. If his communication is examined, it will be at once seen how he has fallen into error. In one of his experiments, the amount of potash employed was not more than half sufficient to neutralize the natural acidity of the extract; and a comparison of his results with those detailed in the present and first papers will show that his observations may be perfectly true, and my deductions at the same time absolutely correct. It is to be re-

tion, and induced me to bring before the Society a second paper on the same subject, in which it will be my endeavour :

First : To prove that the active principles of the plants under consideration, are absolutely destroyed by the influence of the caustic potash.

Secondly : To show the ratio which must exist between the different preparations of the plants and the alkali, for the neutralization to be perfect.

Thirdly : To ascertain the time demanded for the decomposition to be complete.

Fourthly : To illustrate clinically the influence of the alkali in preventing the occurrence of symptoms, when large medicinal doses of these solanaceous drugs are administered.

Before proceeding to discuss any of these different heads, it will be necessary, for the right understanding of the subject, to have a clear conception of the nature of the drugs employed in the various experiments. And, in the first place, it must be remembered, that although liquor potassæ is strongly caustic and alkaline in reaction, still it is a very dilute solution, containing but 6·7 per cent. of alkali, and, consequently, its power of neutralizing acids is exceedingly limited. Again, it will be found that the preparations of henbane, belladonna, and stramonium (the extracts and tinctures) are acid in reaction, as tested by litmus paper, and to such a degree is this the case, that two fluid drachms of the potash solution are not more than sufficient to neutralize the natural acidity of an ounce of the extracts. Nor must it be forgotten, that in the plants the alkaloids or active principles do not exist in a free state, but combined with acids in the form of salts, and that consequently, before any alkali can act upon them as a destructive agent, they must first be separated from such combinations ; and to produce this effect, a portion of alkali necessarily becomes

gretted that attempts should be made to throw a doubt upon the accuracy of an observer, before the experiments from which his results have been obtained are made known, and such must have been the case in the present instance.

neutralized, or rendered inert, as far as ulterior action is concerned; and, lastly, it must be borne in mind, that the most minute quantity of the active principles, or even of the preparations containing them, will cause dilatation of the pupil, and that the effect, at least for a time, will be much the same, whether $\frac{1}{100}$ grain, or $\frac{1}{10000}$ grain of atropine or daturine be put into the eye, and, therefore, we may sometimes neutralize $\frac{99}{100}$ ths of the power of a preparation, without being able to ascertain the fact by the local physiological action.

1. The active principles of the plants are absolutely destroyed by the caustic alkali.

In my first communication I did not attempt to show the manner in which the activity of the various plants became neutralized by the action of the caustic potash, resting satisfied with the mere statement of the fact. I have, however, since that period, made several experiments, which throw considerable light upon the subject.

The first consisted in making a solution of atropine in distilled water, with the aid of a few drops of rectified spirit, dividing it into two equal portions, to one of these adding a little liquor potasse, sufficient to effect the desired purpose, and, allowing it to remain for some hours; afterwards shaking each portion with chloroform, and, on the subsidence of this body, pouring off the supernatant fluid, washing the chloroform, and allowing the two quantities to evaporate spontaneously in glass dishes; from the solution to which the liquor potassæ had been added, a very slight white-looking residue remained, having a powerful odour; when moistened with water, and a drop of the solution put into the eye, no effect was produced, and it evidently contained no atropine; from the other quantity, however, to which no addition of potash had been made, a gummy residue remained, and a drop of the watery solution produced intense dilatation of the pupil, which did not recover its original size for a fortnight.

In the next experiment, I made a solution of atropine in distilled water, employing one grain of the alkaloid to two fluid ounces; to one half liquor potassæ was added, in the proportion of twenty minims to the ounce, to the other a strong solution of the carbonate of potash in the same proportion; after allowing each to remain during four or five hours, chloroform was employed in the same manner as in the first experiment, and the products exposed to spontaneous evaporation; in the case where the carbonate of potash had been added, the product was first gummy in nature, but afterwards became distinctly crystalline; the slightest particle dilated the pupil intensely, and, when a solution was made with water acidulated with hydrochloric acid, and chloride of gold added, a beautiful plumose crystallization of the double chloride of gold and atropine took place.

In the case where liquor potassæ had been used, a whitish product was found, having a peculiar odour, causing no action on the eye, even when applied in large quantities, and giving rise to no crystalline salt on the addition of chloride of gold. By these experiments it is proved, that liquor potassæ *destroys* the alkaloid atropine, even in very weak solutions, and at the ordinary temperatures of the air. The nature of the compounds resulting from such decomposition I have not ascertained, it being a subject purely chemical, and one which would probably take some months to investigate fully. Proof is, at the same time, afforded by the second experiment, that the carbonate of potash is devoid of this destructive power on atropine. It might perhaps be imagined that this action of potash on the alkaloids is common, and not at all confined to the group of solanaceous plants; that such, however, is not the case is easily proved, by performing the above experiments with quinine, cinchonine, strychnine, &c., in place of atropine or daturine, when it will be found that no alteration has taken place in the alkaloids, and that they can be recovered in their crystalline forms. It is also a well-known fact, that morphia, when dissolved in caustic alkaline

solutions, can be separated in its original state. Possibly, however, there may be a few of the alkaloids, besides those derived from the solanaceous plants under consideration, which are also broken up by means of dilute solutions of caustic potash.

2. The necessary ratio between the alkali, and the various preparations of the plants.

In my former communication I detailed the result of experiments made with certain definite quantities of the preparations of the plants, without determining the limit to the destructive power of the potash solution; since this time, I have endeavoured to arrive at something like quantitative determinations, which, if not absolutely correct, will still be found sufficiently so for all practical purposes; these results I have given in tabular form, and it will be observed, that the observations have been made upon the tincture and extract of henbane, the extract of stramonium, the tincture and extract of belladonna, and, lastly, upon pure crystallized atropine.

TABLE exhibiting the amount of *Liquor Potassæ* required to destroy the activity of the preparations of *Henbane*, *Belladonna*, and *Stramonium*, as determined by at least *Sixty Experiments*.

On Henbane.

Tincturæ Hyoscyami, ʒij.	} Dilated the pupil.
Liq. Potassæ, ℥v.	
Tincturæ Hyoscyami, ʒij.....	} Dilated the pupil.
Liq. Potassæ, ℥x.	
Tincturæ Hyoscyami, ʒj.	} No dilatation.
Liq. Potassæ, ℥x.	
A second tincture of same proportions	} No dilatation in two instances.

Extracti Hyoscyami, gr. v.	} No dilatation in two trials.
Aquæ Destillatæ, ℥j.....	
Liq. Potassæ, ℥xxv.	
Ext. Hyoscyami, gr. x. (<i>Hospital</i> <i>Extracts.</i>).....	} No dilatation.
Aquæ Destillatæ, ℥j.....	
Liq. Potassæ, ℥xxx.....	
Ext. Hyoscyami (Bell's Ext.) gr. x.	} A moderate amount of dilatation.
Aquæ Destillatæ, ℥j.....	
Liq. Potassæ, ℥xxx.	
Ext. Hyoscyami (Bell's Ext.) gr. x.	} No dilatation in seven cases.
Aquæ Destillatæ, ℥j.....	
Liq. Potassæ, ℥xl.	
Ext. Hyoscyami, gr. ix.....	} No dilatation in six cases.
Aquæ Destillatæ, ℥j.....	
Liq. Potassæ, ℥xxx.....	

On Stramonium.

Ext. Stramonii, gr. v.	} No action on five eyes.
Aquæ Destillatæ, ℥j.....	
Liq. Potassæ, ℥xx.	

On Belladonna.

Tincturæ Belladonnæ, ℥j.....	} Some (moderate) dilatation of the pupil.
Aquæ Destillatæ, ℥vij.	
Liq. Potassæ, ℥x.	
Tinct. Belladonnæ, ℥j.....	} No dilatation in five cases.
Aquæ Destillatæ, ℥vij.....	
Liq. Potassæ, ℥xv.	
Ext. Belladonnæ, gr. ij.	} No dilatation in two eyes.
Aquæ Destillatæ, ℥j.....	
Liq. Potassæ, ℥x.	
Ext. Belladonnæ, gr. v.....	} No effect on pupil.
Aquæ Destillatæ, ℥j.....	
Liq. Potassæ, ℥xxx.....	
Ext. Belladonnæ, gr. v.	} No dilatation in four cases.
Aquæ Destillatæ, ℥j.....	
Liq. Potassæ, ℥xxv.	

On Atropine.

No. 1. Atropinæ, gr. ½.....	} Dilated the pupil intensely.
Spirit. rect. ℥ss.	
Aquæ Destillatæ, ℥viiss.	

a.	The above (No. 1), with ℥xxv.
of Liq. Potassæ	} No action on pupil.
b.	The above (No. 1), with ℥xijss.
of Liq. Potassæ	
c.	The above (No. 1), with ℥vijss.
of Liq. Potassæ	} Some dilatation of pupil.
The same next day.
No. 2.	Atropinæ, gr. j.....
Spt. rectific., ʒj.
Aquæ destill., ʒvij.
Liq. Potassæ, ℥xxv.....	} In four cases produced no
dilatation.
a.	The same (No. 2), with Atro-
pinæ, gr. j½.	
b.	The same (No. 2), with Atro-
pinæ, gr. j½.	
c.	The same (No. 2), with Atro-
pinæ, gr. j½.	
d.	The same (No. 2), with Atro-
pinæ, gr. ij.	} Produced some dilatation of
pupil.
No. 3.	Atropinæ, gr. j.....
Spt. rectific., ʒss.
Aquæ destill., ad ʒj.
Liq. Potassæ, ℥xxv.	} No dilatation in two cases.
No. 4.	Atropinæ, gr. j.
Spt. rectific., ʒss.
Aquæ destill., ad ʒij.
Liq. Potassæ, ℥xx.	} No effect produced; tried in
two cases.

A caustic soda solution tried upon atropine and some of the preparations of henbane, was found to destroy their activity; but the requisite quantities were not determined.

From the above table it will be seen, that when atropine is operated upon by liquor potassæ, the destructive influence of the latter is so great, that less than 20 minims are required to neutralize one grain of the active principle; and, I believe that a single grain of pure potash will, even in dilute solutions, destroy an equal quantity of the alkaloid.

A grain of caustic potash constitutes but a small medicinal dose of the drug, a twentieth of a grain of atropine,

on the other hand, is often found to act powerfully upon the human subject.

When belladonna preparations are employed in place of atropine, the power of the potash becomes weakened from the causes before alluded to, namely, the natural acidity of the drugs, and the necessity of first displacing the alkaloid from the acid with which it is combined, before the potash can act upon it as a destructive agent. Still, however, the table shows us that 15 minims of liquor potassæ will destroy a fluid drachm of the tincture, and that 25 minims are sufficient to produce the same change in 5 grains of the extract, at once demonstrating, that quantities very greatly beyond the medicinal doses of these drugs, nay, even poisonous doses, are rendered quite inert by a moderate amount of the alkaline solution.

The same remarks hold good with regard to daturine, and the preparations of stramonium.

When henbane preparations are examined, the amount of liquor potassæ required to neutralize the effect of a fluid drachm of the tincture, is ascertained to be about 10 minims, and the activity of 9 grains of the extract is destroyed by half a fluid drachm. Ten grains of the extract will frequently, when treated in this manner, produce distinct dilatation of the pupil.

This phenomenon, however, need not surprise us, as a single grain of the extract, when properly prepared, will produce the effect on the eye, when diluted with a fluid ounce of water. There are, however, many extracts of henbane found in commerce, which are neutralized when united in the proportion of ten grains to the half-drachm of liquor potassæ, and, in the table, experiments illustrating this fact are exhibited.

When the superior extracts are employed in the proportion of ten grains to the half drachm of the potash solution, although the local effect on the eye may be visible, still it is evident, that at least $\frac{9}{10}$ ths of the activity of the combination is rendered inert, and no caustic potash can possibly exist in any such mixtures until

the whole of the active principles have been broken up, or disintegrated.

The preservative power of ammonia salts.—Certain salts containing ammonia possess a peculiar power, when present in the solution of the active principles, of acting as preservative agents, and of preventing their destruction by the potash. To illustrate this, a solution of atropine was made, and a sufficiency of liquor potassæ added, it was then divided into two parts, to one of which a few grains of hydrochlorate of ammonia were added; after a few hours both portions of the solution were tested as to their power of dilating the pupil of the eye; the solution to which the ammonia salt had been added remained active, the other had lost all power. The explanation of this phenomenon is simple; in the presence of an ammonia salt, the potash unites with the acid, and liberates the ammonia, so that free ammonia, and not free potash, exists in the solution, and, consequently, the destructive change does not ensue.

If an alkaline bicarbonate were present, the same protective power would probably be exercised, as the effect of such a salt would be to convert the caustic alkali into a proto-carbonate, which possesses no power of disintegrating the active principle. When the potash solution is added in quantities more than sufficient to neutralize the acid of the ammonia salt, a destructive influence is immediately exerted.

3. The time required for complete decomposition of the active principles.

I mentioned in my first paper that about two or three hours appeared to be required, in order that liquor potassæ should neutralize the effects of henbane; recently I have determined by more accurate experiments, the time demanded in the case of atropine. A solution of the alkaloid was made by dissolving it in water, with the aid of

a few drops of spirit, in the proportion of a grain to the fluid ounce; liquor potassæ was afterwards added, in quantity known to be more than sufficient to destroy it, and a little put into different eyes every quarter of an hour.

After $\frac{1}{8}$ hour, full dilatation was produced.

„ $\frac{2}{8}$ hour, full dilatation was produced.

„ 1 hour, full dilatation was produced.

„ $1\frac{1}{8}$ hour, full dilatation was produced.

„ $1\frac{1}{2}$ hour, full dilatation was produced.

„ $1\frac{3}{4}$ hour, slight dilatation was produced.

„ 2 hours, slight dilatation was produced.

„ $2\frac{1}{4}$ hours, no effect was produced.

„ $2\frac{1}{2}$ hours, very slight dilatation was produced (?)

The same solution gave a negative result when tested the next day. The dilatation remained in proportion as the solution was applied, sooner or later after the addition of the potash. In another experiment no perceptible dilatation was observed after $2\frac{1}{2}$ hours, although the solution was tried upon several eyes. We may hence conclude, that, after two hours, solutions of atropine containing potash lose their power almost entirely, and, at $2\frac{1}{4}$ hours, the activity may be said to be extinct. Probably the *exact* time varies, being dependent on several minor circumstances, as temperature, the strength of the solutions, and the ratio between the potash and atropine, for such influences are found, in other decompositions, to have considerable effect.

4. *Clinical illustrations of the influence of liquor potassæ in rendering henbane and belladonna inert.*

Within the last few months it has occurred to me to see several cases in which patients have been very distinctly brought under the influence of these drugs, and in whom the symptoms have vanished by the addition of a few drops of liquor potassæ to their medicine, the full quantity of the original and active ingredient being persevered in. The first case was that of a man suffering from some stomach

and intestinal affection, for whom a draught containing nitrate of bismuth, suspended by tragacanth, and a drachm of tincture of henbane, was ordered to be taken three times a day; on the third day he complained of dryness of mouth and throat, the pupils of the eyes were very large, and scarcely acted upon by light. Ten minims of liquor potassæ were then added to each dose, and, at the next visit, the pupil was found to contract freely, and the distinctness of vision to be restored.

The second case was that of a young woman suffering from some painful inflammatory affection of the left ankle, and for whom iodide of potassium and bicarbonate of potash with a fluid drachm of tincture of henbane, were prescribed, three times a day. After continuing this medicine for seven days, with much relief to the ankle, she complained of imperfect vision as if a mist were before her eyes; on examination, the pupils were found enlarged, and contracted but slightly with light; she had also dryness of throat. Fifteen minims of liquor potassæ were ordered to be added to each draught, in lieu of the bicarbonate of potash. At the next visit, three days afterwards, the patient could see well, and the dryness of the throat had passed off.

On omitting the liquor potassæ, and increasing the henbane tincture to a drachm and a half, the eyes in two or three days became again much affected, but the symptoms rapidly vanished when only ten minims of liquor potassæ were added to the medicine.

The next case was that of a young woman, for whom, on account of very troublesome cough, was ordered tincture of belladonna, at first in ten-minim doses, but afterwards increased to fifteen. In a short time there was considerable dryness of the throat, imperfect vision, and dilated pupils, which were scarcely affected by light.

The tincture of belladonna was increased to twenty minims, and, at the same time, fifteen minims of liquor potassæ added: two days afterwards the pupils contracted freely, the vision was good, and there was no dryness of

the throat. I could relate two or three other cases illustrating the same fact.

Shortly after the abstract of my first paper appeared, an interesting occurrence took place, bearing strongly upon the present subject. A medical gentleman was prescribing for a lady the extract of belladonna, for the purpose of allaying a nervous or spasmodic cough; he commenced with $\frac{1}{8}$ grain doses, and gradually increased the quantity to $\frac{1}{2}$ grain, which was ordered to be taken several times in the day. The extract was rubbed up into a draught containing liquor potassæ. He was surprised to find that the belladonna neither allayed the cough, nor produced any other symptom; but, on seeing the abstract of my paper in one of the journals, found an explanation of the phenomenon. The next medicine was prescribed with the bicarbonate of potash, in place of the caustic solution; and the result was that he was soon called to see his patient, who was then suffering under the effects of a rather large medicinal dose of the drug, having dryness of the mouth and throat, dilated pupils, and indistinct vision.

These experiments and observations prove beyond doubt the accuracy of the results arrived at in my first communication, and demonstrate that the caustic fixed alkalies possess the peculiar power of destroying the active principles of henbane, stramonium, and belladonna, even when in dilute solution, and that such combinations are therefore both chemically and therapeutically incompatible, and should never be prescribed.