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NOTES ON
"CHANGED ALOIN"
AND
THE RESIN OF ALOES.

BY
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"CHANGED ALOIN" AND THE RESIN OF ALOES.

PART I.—"CHANGED ALOIN."

ALOES, "the inspissated juice of the leaves of various species of aloe," has been used in medicine for upwards of 2000 years. It was not, however, till 1851 that the Messrs Smith of this city discovered in aloes a crystalline principle, to which they gave the name of aloin, because it was supposed by them to be the active principle of the drug. After this important discovery of aloin, much difference of opinion existed regarding its physiological action. So late as 1870, we find Dr Tilden of London maintaining that "the active constituent of aloes is still unknown," "that the purgative property is not due to aloin," and suggesting that the purgative power is due to the resin of aloes. Notwithstanding these statements, it has been clearly demonstrated by various experimenters, and confirmed by clinical observation, that aloin is an active aperient, and is sufficient to account for the purgative property of aloes.

It was no part of my purpose, in the following experiments, to investigate the properties of aloin, about whose action there ought to be no reasonable doubt, but to investigate the properties of "changed aloin," and to determine the action of the so-called resin of aloes.

In 1872, when preparing a specimen of aloin for the Vienna Exhibition, the Messrs Smith took four ounces of aloin and dissolved it, with a view to recrystallization, in order to obtain very pure crystals of aloin. From this solution two ounces of very beautiful crystals were obtained. The residue was set aside for eight months, when it was found that a substance had formed, easily reducible to a fine powder. This substance was uncrystallized, and in appearance not altogether unlike the resin of aloes. To this substance I have given the name *changed aloin*. There can be no doubt about its being aloin, which had undergone some chemical change by exposure to the air, probably a species of oxidation. They were naturally anxious to ascertain if this aloin which had undergone some chemical change still possessed its physiological action. They applied to me to investigate this subject, which I accordingly did, and found it possessed of all the activity of aloin itself. My experiments were performed on a healthy young rabbit. I had a

cage so constructed that I could easily weigh the fæces and measure the urine passed in twenty-four hours. For six days I fed the rabbit daily, at a fixed hour, on ten ounces of carrots, and each day ascertained carefully the amount of fæces and urine passed. During these six days no changed aloin was administered. The results are given in the following Table:—

TABLE I.

No Injection.

1st day, urine	56	fluid drachms,	fæces	0.
2d	74	"	"	0.
3d	68	"	"	0.
4th	53	"	"	0.
5th	60	"	"	traces.
6th	64	"	"	"
Average,	62·5	"	"	"

During the next six days, I injected daily, at a fixed hour, one grain of this changed aloin in solution. The injections were made subcutaneously on the sides of the animal. The animal was fed on the same diet, and at the same hour, as during the previous six days. The amount of urine and fæces was daily ascertained, and the results are given in the following Table:—

TABLE II.

One Grain of Changed Aloin Injected Daily.

1st day, urine	48	fluid drachms,	fæces	59	grains.
2d	60	"	"	121	"
3d	68	"	"	184	"
4th	60	"	"	38	"
5th	64	"	"	10	"
6th	64	"	"	8	"
Average,	60·7	"	"	70	"

On comparing carefully these two tables, it will be seen that the urine remained much the same during the whole twelve days. The average during the first six days was 62·5 fluid drachms, and during the second six days 60·7 fluid drachms. The urine was slightly diminished, but the difference was very small, and quite within the range of variability. It was very different with the fæces. During the first six days there were no fæces, or only traces on the fifth and sixth days. During the second six days the average amount of fæces was 70 grains daily. The first day after the injection of the changed aloin, there were 59 grains of fæces, the second day 121 grains, and the third day 184 grains. The amount gradually diminished during the next three days. For three days there was a gradual increase, and, afterwards, a gradual decrease for three days. This state of matters is easily accounted for. Having once

freely emptied the bowels by means of changed aloin, we could not expect the same amount of fæces to be continued whilst there was no increase of food. Nevertheless, the results were so marked and followed so soon after the injection, that there is no resisting the conclusion that this changed aloin acted as an aperient, and possessed all the activity of crystallized aloin.

Being anxious to ascertain the action of this "changed aloin" on man, I had it made into pills with the extract of gentian, each pill containing from one to two grains of changed aloin. These pills I administered to various individuals and in very different circumstances, and in all cases found them a mild but certain aperient. I administered these pills to several persons of sedentary habits, and succeeded in removing the constipation so common in such circumstances. I found that one or two grains daily of changed aloin were sufficient to accomplish that object. I also gave these pills to pregnant females shortly before confinement, and in several cases administered them to females a few days after they had been delivered, and in both cases found them to answer exceedingly well. In no case was there any griping, nor did any bad result follow. I thus found that clinical observation fully confirmed the conclusion drawn from experiments on the lower animals, that this aloin, which had undergone considerable change by exposure to the air, still possessed all the activity of the active principle of aloes. These experiments are interesting and of considerable value, as proving that aloin, which undoubtedly is the active principle of aloes, may undergo considerable chemical change without losing its physiological action.

PART II.—RESIN OF ALOES.

ALOIN is the most important constituent of aloes, inasmuch as it has been clearly shown to be the active principle of the drug. It occurs in beautiful crystals, which are supposed to be a hydrid of the amorphous aloin. It constitutes about 25 per cent. of aloes. It gives no ash when burned. In addition to aloin, the Messrs Smith of this city have recently succeeded in obtaining from aloes a volatile oil, which exists in very small quantity in the drug, only one ounce being obtained by them from 400 lbs. of aloes. This oil has a resemblance in taste and smell to oil of peppermint. To the presence of this oil is due the odour of aloes.

Another important constituent of aloes is the *resin of aloes*, the substance which is deposited when a decoction of aloes cools. This *resin* often contains a variable amount of aloin, on account of the extreme difficulty of entirely exhausting aloes of its aloin. The Messrs Smith were kind enough to prepare for me some of this

resin with very great care, so as to obtain the resin in a pure state, and as free from aloin as any resin can well be. They also furnished me with the following particulars regarding experiments made on this resin:—

They took 883 grains of resin, thoroughly dried, and found that of this quantity 753 grains were soluble in rectified spirit, and 130 grains were insoluble. The *soluble resin* yielded one per cent. of ash when burned. The *insoluble resin* gave 23 per cent. of ash.

Very peculiar views regarding this *resin* are held by Dr Tilden and others regarding its physiological action, and in most works on *materia medica* it is spoken of as *modified aloin*, as aloin oxidized or otherwise changed by exposure to the air. The experiments above related are sufficient to disprove the common opinion that this resin is modified aloin. Chemically, it is essentially different from aloin, and physiologically it bears no resemblance to it whatever. Were it *changed aloin*, it would produce no ash when burned, and, moreover, we would expect it to have the physiological action of aloin, which “changed aloin” undoubtedly has, as I have demonstrated in the first part of my paper.

I come now to consider the action of this *resin of aloes*, a substance regarding whose chemical composition there is much diversity of opinion, and whose physiological action has hitherto never been fully investigated. The fact that this resin often contains a variable amount of aloin, has led some observers to the conclusion that the resin of aloes possessed purgative properties. With the view of determining this important question, I made the following experiments. These were performed on healthy young rabbits.

For six days I gave a rabbit daily 14 ounces of carrot, feeding it always at the same hour. The urine and fæces were carefully collected, and their amount duly ascertained. The following Table represents the results:—

TABLE III.

No Injection.

1st day, urine	86	fluid drachms,	fæces	209	grains.
2d ”	82	”	”	167	”
3d ”	73	”	”	3	”
4th ”	78	”	”	341	”
5th ”	82	”	”	0	”
6th ”	64	”	”	70	”
Average, ”	77·5	”	”	136·6	”

During the following six days, I gave the rabbit daily, at the same hour, 14 ounces of carrot, and injected subcutaneously one grain of the “resin of aloes” in solution. The results are given in the following Table:—

TABLE IV.

One Grain of Resin of Aloes Injected Daily.

1st day, urine	96 fluid drachms,	fæces	6 grains.
2d	60	83	"
3d	76	213	"
4th	84	100	"
5th	60	290	"
6th	100	105	"
Average,	79.3	132.8	"

On comparing these two tables, we find that during the second six days the urine was slightly increased, but not to such an extent as to warrant the conclusion that the resin of aloes is possessed of diuretic properties. With regard to the fæces, it will be observed that the amount varied much on different days; from nothing to 341 grains during the first six days, when no injection was given, and from 6 grains to 290 grains during the time of the injection. The daily average was nearly the same in both cases, being 136.6 grains when no injection was used, and 132.8 grains when one grain of the resin of aloes was injected daily. In this case the fæces were slightly diminished during the time of the injection, clearly proving that one grain of the resin of aloes failed to produce any purgative action.

Being anxious to ascertain if larger doses of the resin of aloes would produce any different results, I accordingly injected subcutaneously two grains of the resin daily, and fed the animal as before with 14 ounces of carrot daily. The results are given in the following Table:—

TABLE V.

Two Grains of Resin of Aloes Injected Daily.

1st day, urine	72 fluid drachms,	fæces	202 grains.
2d	80	16	"
3d	76	200	"
4th	78	190	"
5th	72	771	"
6th	70	460	"
Average,	74.6	306.5	"

It will be seen at once that the urine remained much the same throughout the whole of these experiments, a result entirely at variance with the opinion of those who believe in the diuretic properties of the resin of aloes. It was very different, however, with the fæces. During the time that two grains of the resin were injected daily, the fæces varied from 16 grains to 771 grains—average 306.5 grains; whilst the average only amounted to 136.6 grains when no injection was used, and to 132.8 grains when one grain of resin was injected daily. On examining carefully the results of the last six days, it will be observed that the large daily average

is due entirely to the large amount of fæces obtained on the fifth and sixth days, but on five of the six days was the daily average above the average when no injection was used and when one grain of the resin was injected daily. There can be no doubt, then, but the resin of aloes which I used acted as a purgative in doses of two grains, though in doses of one grain it failed to produce any purgative action.

With the view of ascertaining the action of this resin on man, I had pills prepared with extract of gentian, each pill containing two grains of the resin of aloes, and found that four of these pills produced three or four watery stools, again confirming by clinical observation the conclusion to which I had come by experiments on the lower animals. On communicating the results of my experiments to the Messrs Smith, they suggested that it was possible that the resin of aloes which they gave me might have contained a small quantity of aloin, and the purgative effect might have been due to this aloin. The resin of aloes with which I was experimenting was very carefully prepared from a solution of aloes in boiling water, and had received four additional washings. The Messrs Smith informed me that resin prepared even with such care might contain a small amount of aloin, owing to the difficulty of thoroughly exhausting aloes of its active principle. They accordingly took a quantity of the resin of aloes prepared in the manner above described, and dissolved it in rectified spirit, which dissolves the aloin as well as the resin, and to this they added boiling water and then agitated the mixture so as to form an emulsion from which the resin of aloes afterwards separated in a very fine state. The resin so prepared may be regarded as pure resin and as free from aloin as any resin can well be.

The following experiments were performed with the resin prepared in the manner just described, and were conducted in much the same way as were my previous experiments.

A healthy young rabbit weighing 39 ounces, was fed daily at a fixed hour with 14 ounces of carrot for six days, and the urine was carefully measured and the fæces weighed every day. The results are given in the following Table :—

TABLE VI.

No Injection.

	1st day, urine	56 fluid drachms,	fæces	4 grains.
2d	"	76	"	30 "
3d	"	88	"	2 "
4th	"	80	"	203 "
5th	"	64	"	67 "
6th	"	64	"	57 "
Average,	"	71.3	"	60.5 "

During the next six days I fed the rabbit on the same diet and in the same manner, and injected subcutaneously two grains of

resin of aloes. The first two injections were with the resin I first used, the others with the new resin prepared with extra care.

The results are given in the following Table :—

TABLE VII.

Two Grains of Resin of Aloes Injected Daily.

1st day, urine	68 fluid drachms,	fæces	127 grains.
2d	56	192	„
3d	56	87	„
4th	64	30	„
5th	48	3	„
6th	66	232	„
Average,	59.6	111.8	„

On comparing these two sets of experiments it will be seen that during the second six days the urine was slightly diminished, but the fæces were considerably increased. The average when no injection was used was 60.5 grains daily, whereas the average rose to 111.8 grains when two grains of the resin of aloes were injected. It must be remembered that the first two injections were with the resin I had formerly used, and which was found in doses of two grains to be slightly aperient, as shown in Table V. The average for these two days was 159.5 grains, but only 88 grains for the other four days.

Having found that 14 ounces of carrot were more than the rabbit could consume, I fed it during other six days on 11 ounces of carrot daily. During the six days I used no injection, being anxious to learn if discontinuing the administration of the resin of aloes would in any way affect the amount of the fæces.

The results are continued in the following Table :—

TABLE VIII.

No Injection.

1st day, urine	36 fluid drachms,	fæces	2 grains.
2d	76	81	„
3d	64	198	„
4th	52	420	„
5th	56	0	„
6th	68	120	„
Average,	54.6	136.8	„

During the next six days I fed the rabbit also on 11 ounces of carrot daily, and injected each day two grains of the *new resin* of aloes which was so carefully prepared.

The results are given in the following Table :—

TABLE IX.

Two Grains of Resin of Aloes Injected Daily.

1st day, urine	44 fluid drachms,	fæces	154 grains.
2d	56	"	197 "
3d	64	"	94 "
4th	80	"	50 "
5th	52	"	272 "
6th	60	"	108 "
Average,	59.3	"	145.8 "

On comparing the last four tables, it will be seen that the daily average quantity of urine was greatest during the time when no injection was used, a fact totally at variance with the opinion of those who hold that the resin of aloes is diuretic. With regard to the fæces it will be observed, that the average amount of fæces during the last six days exceeded that of the previous six days by 9 grains, an increase so small that we cannot draw from it any conclusion in regard to the purgative property of the resin of aloes. The largest amount of fæces obtained during one day, when the injection was used, was 272 grains; whereas, on the other hand, 420 grains were obtained one day when no injection was given. The daily average increased during each successive period of six days, without reference to the injection of the resin of aloes. During those twenty-four days the rabbit increased in weight from 39 to 43½ ounces. On a careful comparison of these experiments with the resin of aloes, it will be observed that no appreciable effect was produced, even by the subcutaneous injection of two grains of this resin.

During the first six days, when no injection was used, the daily average amount of fæces was 60.5 grains; during the second six days it was 111.8 grains, with two grains of resin of aloes injected daily; during the third six days, with no injection, the daily average was 136.8 grains; and during the last six days, with two grains of resin of aloes injected daily, the average was 145.8 grains. There is but one conclusion to be drawn from these experiments, namely, that the resin of aloes is not purgative, and cannot be the active principle of the drug.

I had some of this resin made into pills, with extract of gentian, each pill containing two grains of resin, and found that six such pills failed to produce any effect whatever. I thus found that my clinical experience fully confirmed the conclusion arrived at from my experiments on the lower animals. Dr Farre, of London, gave to patients doses of three grains of resin of aloes, and said he found it almost inert, and that it seldom produced any evacuation. He, however, holds the rather doubtful conclusion, that though it is inert when separated, it is probably active when combined. In those cases where three grains produced evacuation, the activity was most likely due to the resin containing a small quantity of aloin.

As previously stated, it is exceedingly difficult to exhaust the aloes entirely of its aloin; and in proportion as it contains any of this substance, so will it prove more or less active. This fact has been illustrated in Table V. When the resin is prepared with the care that the last sample was, with which I experimented, I believe it will prove altogether inert. Similar results were obtained by Dr Garrod, although it is evident from his experiments that the resin was not always free from aloin. He says the *extract* is far more active as a purgative than the resin, and admits that the resin often proved almost inert. Had the resin with which he experimented been entirely exhausted of aloin, it would, I believe, have proved always inert. Nevertheless, the experiments of Dr Farre and Dr Garrod are exceedingly valuable and very interesting, and tend very much to prove that the resin is an inert substance.

I have thus far established the point, that the opinion of Dr Tilden, regarding the activity of the resin of aloes, is altogether untenable. It is contradicted by the experience of the observers just named, and my experiments both on man and on the lower animals are conclusive on the point.

In speaking of the action of the resin of aloes, I must not omit to mention, that to this resin is generally ascribed the griping property of aloes. I believe that aloes does not gripe nearly so much as writers on materia medica would lead us to believe. When it does gripe it is probably on account of some impurity in the drug, and certainly it cannot by any possibility be due to the resin. It was with the view of determining this question that the experiments of Dr Farre and Dr Garrod were performed, and they both came to the same conclusion, that the resin was not the cause of the griping. My experience fully coincides with theirs. I gave it to a large number of patients, and in very different circumstances, in doses varying from 4 to 12 grains, and in no single instance did it produce griping. It thus appears that the resin is not only inert, but is also a very harmless substance.

These experiments are also interesting as bearing on the chemical constitution of the resin of aloes. The results are entirely at variance with the generally received opinion, that the *resin* is "modified aloin." I have clearly demonstrated that "changed aloin," which very much resembles *resin* in appearance, is an active aperient, possessing all the activity of aloin itself, whereas the *true resin* is altogether inert.

The following may be regarded as conclusions fairly deducible from the foregoing experiments:—

1. That aloin may, by exposure to the air, undergo considerable chemical change, without losing its physiological action as an active aperient.
2. That the *resin* of aloes, when thoroughly exhausted of aloin, possesses no purgative properties, and therefore cannot be the active principle of aloes.

3. That the resin of aloes is not the cause of the griping which sometimes follows the administration of the drug.

4. That aloin is an active aperient, and is in all likelihood *the active principle* of aloes.

When these experiments are viewed in connexion with the researches of numerous experimenters in regard to the activity of aloin, we are forced to the conclusion, that *aloin is the only active principle contained in aloes*, and is sufficient to account for all the purgative properties of that medicine. And that being the case, I cannot conclude this paper without expressing a regret, that in the "Addendum to the British Pharmacopœia of 1867," published in 1874, no mention is made of aloin. It ought to find a place amongst the medicines recognised in the British Pharmacopœia. It possesses the following advantages over the crude drug:—

1. Being uniform in strength, its dose can be more accurately determined.

2. Its dose being half a grain to one grain, it can easily be introduced into tonic pills without making such pills too large.

3. By using the active principle, we get rid of all impurities which are so apt to cause griping.

Its uniformity in strength, the smallness of its dose, and the certainty of its action, should commend it to the favourable consideration of all medical practitioners.

I have found the following an excellent pill for the constipation so common in females of a sedentary habit. I believe it possesses some advantages over the pil. aloes et ferri of the B. P.:—

R Aloin., gr. ss.

Ferri sulph. exsic., gr. jss.

Extract. nucis vomicæ, gr. ss.

Extract. belladonnæ, gr. ss.

Fiat pil.—One or two pills daily.



