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# A PHARMACOLOGICAL APPRECIATION OF SHAKESPEARE'S HAMLET: ON INSTILLATION OF POISONS INTO THE EAR

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Shakespeare's works abound in references to drugs and [165] poisons; some of these pertain to the mystic vagaries and superstitions of kakopharmacy or dirt medicine, alchemy and witchcraft; others, on the other hand, are borrowed from the more scientific, even though empirical, data furnished by the materia medica and poison-lore of antiquity and the Middle Ages. In the present paper I have attempted to analyze and discuss in the light of modern science a passage in Hamlet which is of extreme interest to the student of medical history from the pharmacological and toxicological points of view. I am referring to the manner of Hamlet's father's death as described by [166] his ghost in Act I, Scene 5, lines 59 to 73. The passage in full reads as follows:

> "Sleeping within mine orchard,
> My custom always in the afternoon,
> Upon my secure hour thy uncle stole,
> With juice of cursed hebenon in a vial,
> And in the porches of mine ears did pour
> The leperous distilment; whose effect
> Holds such an enmity with blood of man
> That swift as quicksilver it courses through
> The natural gates and alleys of the body;
> And with a sudden vigour it doth posset
> And curd, like eager droppings into milk,
> The thin and wholesome blood: so did it mine;
> And a most instant tetter bark'd about,
> Most lazar-like, with vile and loathsome crust
> All my smooth body."

The points of interest to us as medical men in connection with these lines are: Firstly, what is meant by the poisonous

[166] hebenon, or hebona as it appears in some editions? Secondly, what were the properties of that poison as known to Shakespeare? Thirdly, what do we know of the poison in the light of modern toxicology? Fourthly, how common was the method of instillation of poisons into the ear in ancient and medieval times? And lastly, what does modern pharmacology teach us as to the possibility of absorption of drugs and poisons through the intact ear? I may say at once that all of the above points with the exception of the last have been more or less discussed by Shakespearean scholars. I have, however, not been able, even after a most laborious search through the literature, to find any information as to the possibility of absorption of poisons through the intact ear. This fact has led me, in connection with this historical research, to undertake an experimental investigation on the subject, especially as I have during the past year been engaged in the study of absorption of pharmacological reagents through devious and unexpected channels, the results of which have partly already been published.

## Variations in Readings

Two different readings for the poisonous plant employed by Hamlet's uncle in the murder are found in different editions of the play. In the first edition of Hamlet, the Quarto of 1603 ($Q_1$), we find:

**"With juyce of Hebona**
**In a viall."**

In the Quarto of 1604 ($Q_2$) and in all the subsequent quartos ($Q_3$, $Q_4$, $Q_5$ and $Q_6$) the reading is also Hebona, as follows:

**"With juyce of cursed Hebona in a viall."**

In the Folio of 1623 ($F_1$) and in subsequent folios, on the other hand, the reading is hebenon, as quoted above, and this reading is followed by all subsequent editions of Hamlet. It is thus seen that two different words, *hebona* and *hebenon* are employed for the poisonous plant used by the murderer. What these words mean, whether the two words are but different terms for the same plant or whether the two refer to two different kinds of poisons and what these poisons were, has been a bone of contention among Shakespearean students for many years.

Various explanations of these words are given by different [166] scholars. I have found altogether five interpretations: some holding that hebona or hebenon means the yew-tree; others that it refers to henbane or *hyoscyamus niger;* still others explain it as *ebony;* a few suggest that the word may refer to hemlock; and a few others think that the deadly nightshade or belladonna is here meant.

Thus Grey[1] says, "Hebenon stands by metathesis, for henebon, that is, henbane, of which the most common kind, *hyoscyamus niger* is certainly narcotic, and perhaps, if taken in considerable quantity, might prove poisonous." Singer[2] says: "The French word *hébénin* applied to anything made from ebony comes indeed very close to the hebenon of Shakespeare." Elze[3] suggests: "Perhaps should we not conjecture that hemlock was intended here?" Beisley[4] states, on what grounds it is not clear, that "Hebenon might have been originally written *eneron,* one of the names common at that time for *solanum maniacum,* called also the deadly nightshade." Tschischwitz[5] says: "Hebona can be only a mistaken substitution of the Spanish and Italian *ebano,* the French *ébène* and the Latin *ebenus* and *hebenus,* all of which mean ebony. Nicholson[6] and Harrison,[7] on the other hand, both of whom are profound Shakespearean scholars, adduce some very good evidence that hebona is the original reading and that it refers to the yew-tree, well known to the ancients for its poisonous properties. A review of all the evidence on the subject leaves only two explanations of the word worthy of consideration: that of hebona, meaning the yew-tree, and that of hebenon as a corruption of the word henbane.

## CONCERNING HEBEN, THE YEW-TREE

There is a great deal of evidence in favor of the hebona of the quarto texts of Hamlet as having reference to the English yew-tree or *taxus baccata.* Though the form hebona is somewhat unusual, the word *hebon* is not uncommon among other Elizabethan writers. Thus in Marlowe's Jew of Malta, Act III, Scene 4, we find:

> . . . . "The blood of Hydra, Lerna's bane
> The Juice of Hebon, and Cocytus' breath."

[166] where hebon is generally taken for *heben,* the yew-tree, branches of which were much used by archers in old England for making their bows. In Spenser's Faerie Queene, we find the following verses:

"Lay now thy deadly Heben bow apart" (I, Pr. 3, 5).
"His speare of heben wood behind him bare" (I, vii, 37, 2).
"Trees of bitter gall and Heben sad" (II, vii, 52, 2).
"Heben lance and covered shield" (II, viii, 19, 6).

The yew-tree, *taxus baccata,* has borne the reputation of being poisonous from remote antiquity. Dioscorides, speaking of the juice of green yew leaves, writes that it speedily produces death.[8] Pliny speaks of it as "taxus tristis et dira,"[9] and adds that drinking-cups made from this tree were found
[167] to impart a deadly property to the wines drunk out of them. Statius,[10] Lucretius[11] and Plutarch,[12] all describe the taxus or yew-tree as being poisonous. "Metuendaque succo taxus," says the first of these; "the juice of the yew is to be feared." Nicholson indeed points out that Shakespeare's expression, "cursed hebona" and "holds such enmity with blood of man," may have been suggested by Pliny's description of the plant. Spenser's epithet of "deadly" applied to the heben bow must also refer to the poisonous properties of the yew. Shakespeare himself mentions the yew-tree four times in his plays and in every case connects it with death or some sad event. Thus in Twelfth Night, Act II, Scene 4, line 55, we read:

"My shroud of white, stuck all with yew,
O prepare it."

In Titus Andronicus, Act II, Scene 3, line 107, we read:

"But straight they told me they would bind me here,
Unto the body of a dismal yew."

In Macbeth, Act IV, Scene 1, line 27, the witches howl:

"Slippes of yew
Silvered in the moon's eclipse."

And in Richard II, Act III, Scene 2, line 113, we find:

"Learn to bend their bows
Of double fatal yew."

The expression "double fatal" in the last quotation refers evidently to the poisonous properties of the yew in addition to its being a weapon of warfare. All the citations given above

certainly point to the prevalence of the belief in Shakespeare's [167] times that the yew-tree was poisonous and may have well suggested to him its use in the play. Let us now inquire into what modern toxicology can tell us concerning the properties of *taxus baccata.*

## On the Toxicology of Taxus Baccata

If we examine scientifically the literature on the subject of yew poisoning we shall be surprised to find abundant evidence as to the poisonous nature of the plant. Not only the berries but also, and to a greater degree, the leaves and the bark of *taxus baccata* have proved poisonous. The ancient authorities on the subject have already been cited; a considerable number of cases of poisoning are described by modern writers. Thus Falk [13] has collected 32 cases of poisoning by *taxus baccata,* nine of which resulted from eating of the red berries and 23 from the swallowing of infusions of the leaves. Twenty of the patients died, making the percentage of fatal cases 62½ per cent. Hurt [14] reported the death of a child of three and a half years who swallowed a quantity of yew berries. New [15] reported a case of poisoning in an insane patient who swallowed a large quantity of them. Taylor [16] reports two cases of severe yew poisoning. Heffter [17] describes a fatal case of poisoning in an adult; and other cases may be found cited in the toxicological reference works by Kobert,[18] Kunkel [19] and Blyth.[20]

The leaves of the yew were not infrequently employed to induce abortion.

The chemistry of *taxus baccata* has been studied by the French toxicologist Marmé,[21] who isolated an active principle with alkaloidal properties which he named *taxin.* This is an amorphous white powder having the empirical formula $C_{37}H_{52}NO_{10}$, soluble in alcohol, ether and chloroform, insoluble in benzene and slightly soluble in water. The substance melts at 82°C. and gives an intense purple-red color with $H_2SO_4$ and a reddish-violet color with Froehde's reagent. The salts of taxin are freely soluble in water. Lewin [22] gives the lethal dose of taxin for frogs as being from 50 to 70 mgms., and for cats as being from 30 to 50 mgms. The lethal dose for man is not given, but death has been reported to occur rapidly

[167] after swallowing large quantities of the infusion from leaves in from one and a half to twenty-four hours. The chief experimental work on yew poisoning has been done by Borchers,[23] who found that death was produced primarily through respiratory paralysis. Taxin, however, was found by him also to be poisonous to the heart and to the central nervous system. Concerning the pathological findings in fatal cases, there is nothing characteristic reported by reliable pathologists, the only constant lesion being an intense inflammation of the intestines.

### On the Relation of the Word Heben to Ebony

Mention has already been made of the hypothesis advanced by some Shakespearean students that hebona might really refer to the ebony tree. It therefore behooves us to inquire whether the ebony tree or *diospyros ebenus* of India is poisonous or not. There is no evidence in the literature ascribing to the ebony tree any poisonous properties. Among modern authorities the most complete account of the medicinal properties of the ebony tree is by W. Ainslie.[24] This writer states that the juice of the ebony is perfectly innocuous, and that it is used by the natives as a remedy for certain complaints of the liver and in cases of dysentery. Shakespeare, therefore, could hardly have used the word *hebona* to mean the ebony tree.

The confusion of hebona with ebony, however, is interesting from the etymological point of view. The English word heben, yew-tree, is really the same word as ebony applied to the *Diospyros ebenus*. The Greek ἔβενος, the Latin ebenus, the Italian and Spanish ebano and the French ébène, all names for ebony, all come from the original Hebrew root *eben,* which means a stone, and refer to the hardness of ebony wood and not, as may be at first glance supposed, to its color. Nicholson and Harrison call attention to the fact that in the Middle Ages the word ebenus or ebony was applied to any hard wood, and thus it came to pass that the same term was used to mean also the yew-tree, the wood of which is remarkable for its hardness. Thus arose the Scandinavian and high and low German words *Eben,* the Dutch Iben, the Swedish Eben, the modern German Eibe(n) and the Danish Heben, a form which is also found in Elizabethan literature.

Whereas the advocates of the yew-tree theory regard the [167]
reading *hebenon* of the Folios as a misprint for the earlier
hebona, another set of critics hold the view that *hebenon* is the
correct reading and that it is a synonym of the well-known
henbane. There is a good deal of sound evidence that can be [168]
adduced in favor of this view. In the first place, metathesis of
consonants is not at all an unusual phonetic phenomenon.
Secondly, the argument advanced by some that hebenon is
spelled with an "o" while henbane has an "a," is not a valid
one because, according to Hanbury and Flückiger,[25] the writ-
ing *hennibone* for henbane is found in a vocabulary of the
thirteenth century. Thirdly, the poisonous properties of
hyoscyamus or henbane were known from the remotest an-
tiquity and, furthermore, henbane was a common drug in
Shakespeare's time. Fourthly, the poisonous properties of
henbane are not infrequently mentioned in old English litera-
ture. Thus, Drayton in his Barons' Wars, p. 51, speaks of

> **"The poisoning henbane and the mandrake dread."**

And again

> **"Here Henbane, Poppy, Hemlock here**
> **Procuring deadly sleeping."**

Again in The Philosopher's Fourth Satire of Mars by Anton (1616), we find the following verse:

> **"The poison'd henbane whose cold juice doth kill."**

Fifthly, henbane is an official drug mentioned in old English pharmacopeias and dispensatories such as those by Dale and Salmon and others, and has been used from ancient times in the form of *ear drops*. Lastly, but not least in importance, and indeed of great significance, is the fact that Pliny describes toxic symptoms following instillation of henbane oil into the ear.

> **"Oleum fit ex semine quod ipsum auribus infusum temptat mentem."** [1]

Which means that the oil of hyoscyamus seeds instilled into the ears produces madness. It is to be noted that the very popular

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[1] **Natural History, XXV, 17.**

[168] English translation of Pliny by Holland appeared in 1600. Inasmuch as the first quarto edition of Hamlet was probably written in 1600, though not published until 1603, Shakespeare undoubtedly must have been familiar with Holland's work and very probably might have had it in mind in issuing the later editions, and for that reason might have changed the reading of hebona to hebenon.

### On the Toxicology of Hyoscyamus

The poisonous properties of hyoscyamus or henbane are too well known to be given here in detail. Henbane is certainly just as poisonous and in fact more poisonous than the yew-tree. Cases of poisoning with hyoscyamus are not at all uncommon and are described in the literature, ancient, medieval and modern. Detailed descriptions of such cases may be found in Blyth, Kobert, Kunkel, Peterson and Haines [20] and other text-books on toxicology. It is well to bear in mind, furthermore, that while *hyoscyamin,* the lethal dose of which is a little over one grain, is the principal constituent of hyoscyamus niger, the crude plant also contains variable quantities of the even more powerful alkaloids, *atropin* and *hyoscin* or scopolamin. The minimal lethal doses of hyoscin are even less than that of hyoscyamin. A strong extract of hyoscyamus would therefore be a very powerful poison.

### Discussion

Whether hebona or yew-tree, or whether hebenon or henbane, is the correct reading in the passage before us will probably be never settled, nor will we venture to assert an opinion as to which drug or poison Shakespeare meant. Indeed, for the appreciation of Hamlet either reading may be chosen. As a pharmacologist, however, I cannot help surmising that both hebona and hebenon might have been written by Shakespeare himself. It would not be too far-fetched to suppose that the idea of a powerful poison was suggested to the author by the yew-tree on the one hand, while the unusual administration of it through the ears was suggested by henbane, on the other. Certainly the practice of instilling hyoscyamus into the ear was not unknown in Shakespeare's times, and the appearance

of Holland's translation of Pliny just about the date of the first [168]
quarto edition of Hamlet lends further support to this view.

Much has been made of, by older writers, of Shakespeare's description of the effects of the poison as an argument for and against the yew or the henbane theory by the respective critics on the one side or the other. These arguments are amusing to the modern toxicologist, as we cannot say that the symptoms pictured in the passage before us are more applicable to the one poison than the other. Nor have we a right to expect the author to have known the detailed symptomatology produced by either. Three features are mentioned in connection with the hebona or hebenon poisoning which we are discussing. Firstly, Shakespeare speaks of the rapidity of the toxic effect:

> **"Swift as quicksilver it courses through**
> **The natural gates and alleys of the body."**

Secondly, reference is made to peculiar leprosy-like cutaneous manifestations of the poisonous effect:

> **"A most instant tetter barck'd about**
> **Most lazar-like, with vile and loathsome crust**
> **All my smooth body."**

Thirdly, mention is made as to the circulatory effect:

> **"With a sudden vigour it doth posset**
> **And curd, like eager droppings into milk,**
> **The thin and wholesome blood."**

It cannot be said that the yew-poisoning runs a more rapid course than that following hyoscyamus. Both are rapid in their action. Harrison quotes an old French writer as stating that the yew-tree gives rise to a characteristic cutaneous eruption and uses this point as a strong argument in favor of hebona, the yew. None of the modern authorities, however, describe any specific cutaneous lesions in connection with poisoning by *taxus baccata*. In fact, skin eruptions result perhaps more commonly after the giving of hyoscyamus and belladonna even in non-lethal doses. Lewin [27] describes erythema, urticaria, pustules, and even purpura occurring in sensitive persons after therapeutic doses of hyoscyamus preparations. Nor does modern toxicology and pharmacology show any specific effect of toxin or hyoscyamin on the blood corpuscles or the [169]
plasma, so that Shakespeare's simile must be taken merely as

[169] a forcible poetic description of the rapid paralysis of respiration and circulation produced by the poison used.

### On the Instillation of Poisons Into the Ear

The method of poisoning described in connection with the murder of Hamlet's father is unique and unusual. Although drugs were used in treatment of ear affections in ancient times, no reference is found of their instillation into the ears for homicidal purposes. The doubtful credit for such *finesse* in the administration of poisons must be ascribed to medieval experts and more particularly to the Italians and French. A character in one of the old plays says "Poison speaks Italian." It is well known that poisoning rose to the distinction of an art at that time in Italy and France. A perusal of fascinating books dealing with professional poisoning in the Middle Ages, such as those by Legué [28] or by Thompson [29] and others, will furnish astounding corroboration of this fact. One of the famous older works dealing with the art of poisoning is the *Magia Naturalis* or Natural Magie of the Italian de la Porta. This writer discusses various subjects, and in a chapter on cookery gives some delicious recipes for demoniacal concoctions calculated to produce unfailing results. The following example from de la Porta, quoted by Thompson, will serve as a good illustration of some of the poisonous concoctions used in his times.

#### Venenum Lupinum

**"Take of powdered leaves of aconitum lycoctonum, taxus baccata, with powdered glass, caustic lime, sulphide of arsenic and bitter almonds; mix them with honey and make into pills the size of a hazelnut."**

That such experts in the art of poisoning should have thought of instilling poisons into the ear is therefore not surprising. We find several references to such a procedure in old English literature. The following is a quotation from Marlowe's Edward II, Act V, Scene 4:

**"I learned in Naples how to poison flowers:**
**To strangle with a lawn thrust down the throat;**
**To pierce the windpipe with a needle's point;**

Or whilst one is asleep, to take a quill
And blow a little powder in his ears:
Or ope his mouth and pour quicksilver down."

Another reference to poisoning through the ears is found in a later passage in Hamlet, Act III, Scene 2, in connection with the re-enactment of the murder by the players under the direction of Hamlet. Here we read:

"His name's Gonzago; the story is extant, and writ in choice Italian."

A note in the Arden edition of Hamlet in connection with this passage says:

"In 1538 the Duke of Urbino married to a Gonzaga, was murdered by Luigi Gonzago, who dropped poison into his ear."

One other case of poisoning through the ears, of especial interest to us as medical men, is mentioned by Robert[20] in his thesis on the Poisonings of the Middle Ages. It is well known that King Francis II of France died very suddenly; his death was supposed to have been due to poisoning, and the celebrated French surgeon, Ambroise Paré, was deliberately accused, of course without foundation, of having murdered the king by blowing a poisonous powder in his ear.

It is very interesting to note that the original Hamlet story has no mention of instillation of poison into the ear.[21] In the Hamlet story by Saxo Grammaticus, Hamlet's father is killed by his brother with a steel weapon. The instillation idea is original with Shakespeare and was probably suggested by the prevalence of the horrible form of homicide by poisons so common at the time and the toxic properties of the yew-tree and henbane which we have already discussed in detail.

## On the Absorption of Drugs and Poisons Through the Intact Ear

In connection with Shakespeare's passage which we have just discussed in detail, an interesting scientific question arises as to whether drugs or poisons can be absorbed through the intact external ear canal and drum into the general circulation and produce constitutional symptoms. During the past year the author has been engaged in the study of absorption of drugs

[169] and poisons through unusual and unexpected channels, such as the eye,[32] the bladder, the urethra, the ureters, pelvis of the kidneys,[33] vagina,[34] etc. It was interesting, therefore, to inquire into and investigate experimentally the possibility of absorption of drugs through the ear. The results of these experiments will be published in detail in the *Journal of Pharmacology and Experimental Therapeutics*. It may be here stated that the author has found that a number of poisons can be and are absorbed through the intact ear.

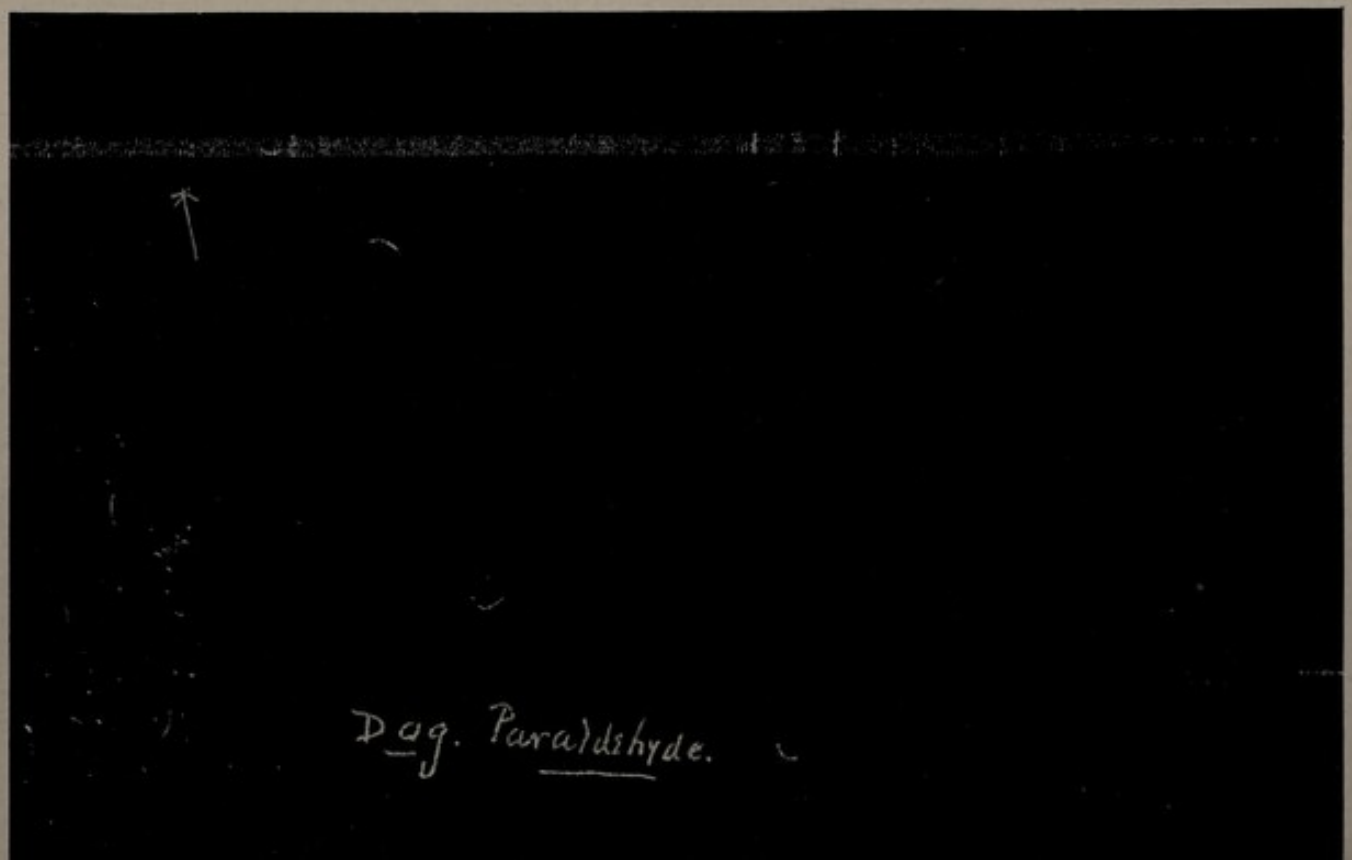
The powerful alkaloid, aconitin, in the form of the hydrochloride, was found to be absorbed through the intact ears of animals even when introduced in an aqueous solution. Fig. 1 shows the characteristic effects of aconitin poisoning in a cat.

Equally rapidly and easily is absorbed through the ear the powerful volatile alkaloid nicotine. Fig. 2 illustrates the toxic action of this drug.

The question of absorption of belladonna and atropin was undertaken with especial interest in connection with Shakespeare's reference to henbane. It was found that atropin in an aqueous solution is not absorbed through the ear, but an alcoholic solution of the belladonna alkaloids in the form of a weak tincture gave positive experimental proof of the absorption of that drug as shown by the paralysis of the vagus terminals in the heart.

It is well known that a large number of drugs are introduced by physicians into the ears for medicinal purposes. Hyoscyamus in the form of an oil or a tincture has been long employed for the relief of earache; a compound tincture of hyoscyamus under the name of Balsamum tranquillans is official in several European pharmacopeias. In the light of
[170] the experimental investigations just reported, such a use of hyoscyamus as an anodyne would certainly seem to be rational.

Another drug used in the treatment of ear affections with an intact drum is phenol or carbolic acid. A specialist tells me that he prescribes often in cases of middle-ear inflammation a few drops of a 5 per cent solution of carbolic acid in glycerin. I have found in experimenting on animals that such a solution of phenol in glycerin is absorbed through the ear, as evidenced


Dog. Paraldehyde.

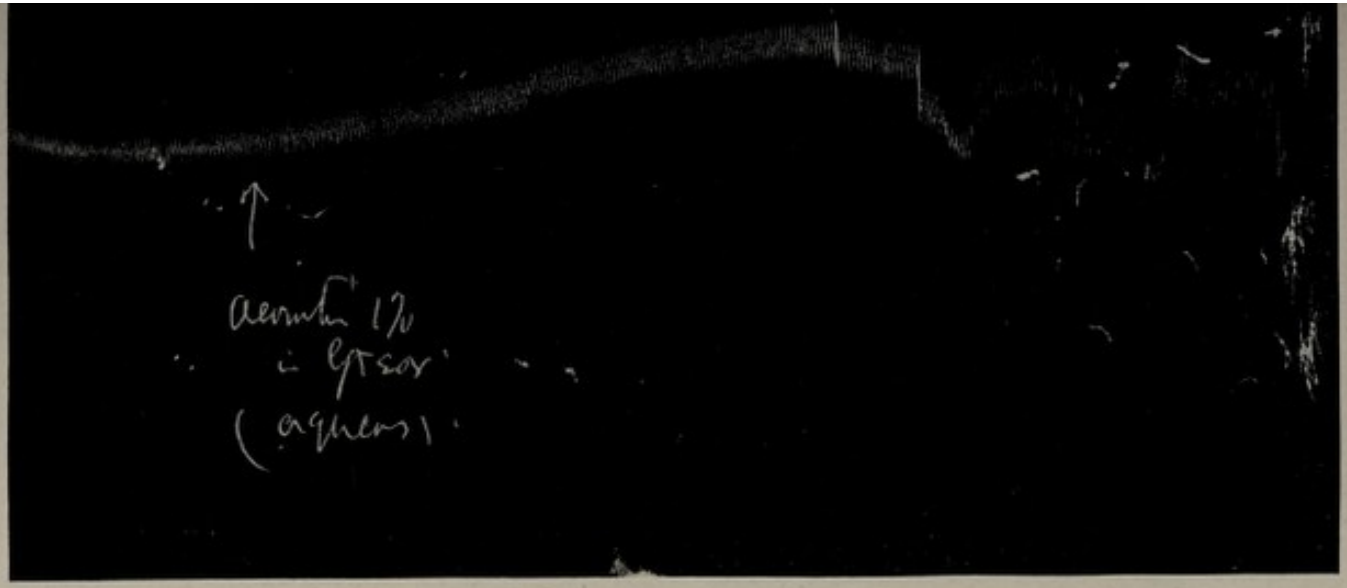
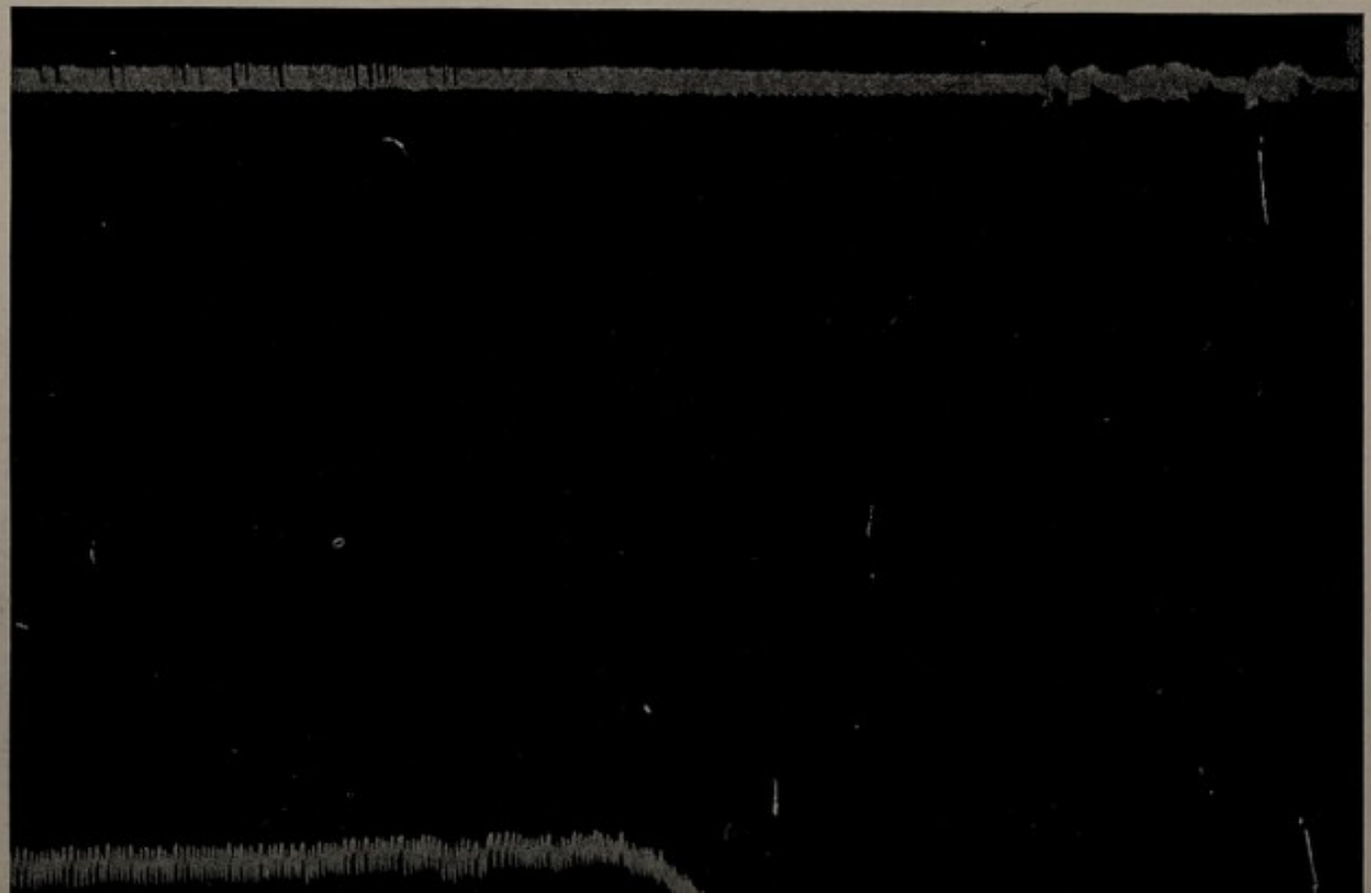


FIG. 1.—Dog. Paraldehyde Anesthesia. 1 per cent of Aqueous Solution of Aconitin HCl. in left ear. Showing effect on heart and respiration.



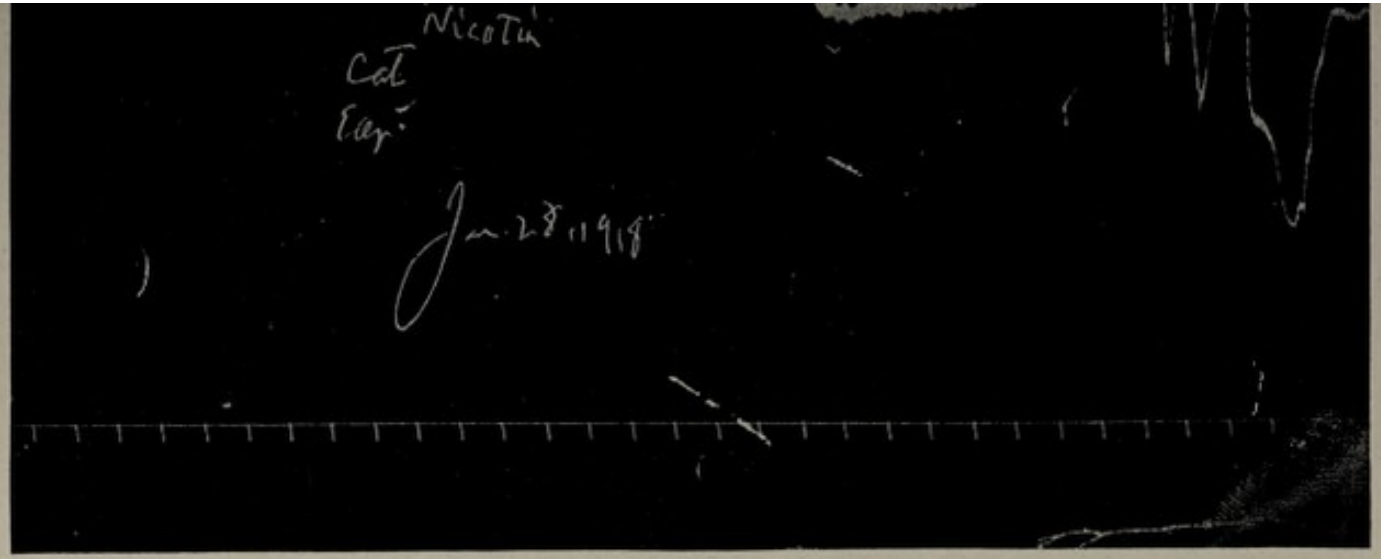



FIG. 2.—Cat. Urethane Anesthesia. A few drops of Nicotin instilled into the ear produce death in 15 minutes.

by its effects on blood pressure. The use of carbolic acid in the [170] treatment of ear affections, therefore, is on the one hand a rational one but on the other hand somewhat dangerous.

We cannot in this historical paper enter into a detailed account of the above experiments; they will be published in their proper place. Suffice it, however, to say that a number of drugs, and among them hyoscyamus or henbane, can be and are absorbed through the intact ear, and we may therefore conclude our appreciation of Shakespeare's passage from Hamlet which we have just been discussing, with saying that after all "Shakespeare was certainly right."

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