PARADICHLOREMINE AS AN ANTHELMINTIC 1

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INTRODUCTION

Paradichlorobenzene has in recent years become well known as an insecticide. It has been found to be very effective as a moth exterminator (3), 2 and has been advocated as a valuable aid in controlling the peach tree borer. Some information is also available concerning its efficacy against external parasites of animals (1).

The chemical and physical properties of paradichlorobenzene are given by Duckett (3, p. 6), by Konantz (8), and by Sollmann (10). Concerning its physiological properties, Duckett (3, p. 7), quoting from Francis and Fortescue-Brickdale (4, p. 99), says that "the benzene halogen derivatives have a slight odor, are insoluble in water, volatilize without decomposition, and are very stable. * * * Corresponding to their stability it is found that the halogen is not split off in the organism, and that they do not show hypnotic properties. * * * Chlorobenzene acts on the spinal cord to a greater extent than benzene."

According to Sollmann (10) nothing is known of the pharmacology of paradichlorobenzene. Duckett (3, p. 1) quotes Curschman as saying that poisoning of human beings by paradichlorobenzene through contact with the skin is impossible and that inhalation of the vapors of this product is perfectly harmless; and, furthermore, that paradichlorobenzene is harmful to human beings only in cases of internal application of large quantities, say from 30 to 40 grains.

Sollmann (10) reports that dogs tolerated doses of paradichlorobenzene up to 15 gm. without showing any ill effects, but he does not consider the drug very effective as an anthelmintic.

Experiments at the Porto Rico Agricultural Experiment Station were undertaken to determine the anthelmintic value of paradichlorobenzene, especially against the hook-worm.

EXPERIMENTAL DATA

Paradichlorobenzene was administered to dogs (1) as crystals in gelatin capsules in doses of 0.1, 0.3, 0.5, and 1 gm. per kilo of body weight; (2) dissolved in liquid petrolatum or in olive oil, in doses of 1 gm. per kilo of body weight; (3) as crystals in gelatin capsules in doses of 0.5 and 1 gm. per kilo of body weight, followed an hour later by an ounce of liquid petrolatum or of castor oil; and (4) as crystals in gelatin capsules followed immediately by (a) a meal of fat, (b) a meal of whole milk, (c) a meal of lean meat, and (d) a meal of dry bread.

1 Received for publication Apr. 6, 1927; issued November, 1927.
2 Reference is made by number (italic) to "Literature cited," p. 649.
Liquid petrolatum and olive oil were selected as carriers because, the one being a hydrocarbon and the other a bland oil, any anthelmin-
tic action produced would be considered as due to the paradichloro-
benzene dissolved in them, since they of themselves are without any
such action (6).

The animals were fasted overnight previous to administering the
drug, and given no food for a period of two hours following dosing.
The feces were then collected for a period of from 48 to 72 hours and
examined. Table 1 shows the efficacy of paradichlorobenzene in
experiments 1, 2, and 3.

From the table it will be seen that in the case of dog No. 26, in
which the worms (Ancylostoma caninum) found in the large intestine
were considered impotent, paradichlorobenzene, administered in the
form of crystals at the rate of 0.1 gm. per kilo of body weight, was
inefficacious for roundworms, tapeworms, and whipworms, and 28.5
per cent efficacious against hookworms.

Administered at the rate of 0.3 gm. per kilo of body weight, the drug
was inefficacious for roundworms and whipworms, and averaged 2
per cent efficacious against hookworms, and 1.5 per cent against
tapeworms, in the case of dogs Nos. 19 and 20.

Administered at the rate of 0.5 gm. per kilo of body weight, the drug
was inefficacious for tapeworms, and averaged 25.45 per cent
efficacious against hookworms, in the case of dogs Nos. 1, 2, and 19.

Administered at the rate of 1 gm. per kilo of body weight, the drug
averaged 66.5 per cent efficacious against roundworms in two trials,
and 49.5 per cent against hookworms in the case of dogs Nos. 4, 5, 9,
10, 11, 12, 15, and 16.

Administered dissolved in liquid petrolatum at the rate of 1 gm.
per kilo of body weight, the drug was inefficacious for tapeworms and
4.5 per cent efficacious against hookworms, as shown in the
case of dog No. 13.

Administered in olive oil at the rate of 1 gm. per kilo of body weight,
the drug was 17 per cent efficacious against hookworms in the case
of dog No. 14.

Administered in crystal form in gelatin capsules at the rate of
0.5 gm. per kilo of body weight, and followed an hour later by an ounce
of liquid petrolatum, the drug was inefficacious for roundworms and
tapeworms, and averaged 60.5 per cent efficacious against hookworms
and 12.5 per cent efficacious against whipworms, in the case of dogs
Nos. 22 and 24.

Administered in crystal form in gelatin capsules at the rate of
1 gm. per kilo of body weight, and followed an hour later by an
ounce of liquid petrolatum, the drug was 4.5 per cent efficacious
against hookworms and 100 per cent efficacious against whipworms
in the case of dog No. 29.

Administered in the form of crystals in gelatin capsules at the rate
of 0.5 gm. per kilo of body weight, followed an hour later by an
ounce of castor oil, the drug was inefficacious for roundworms,
tapeworms, and whipworms, and averaged 15 per cent efficacious
against hookworms, as shown in the case of dogs Nos. 23, 25, and 27.

Administered in the form of the crystals in gelatin capsules at the
rate of 1 gm. per kilo of body weight, followed an hour later by an
ounce of castor oil, the drug was 62.5 per cent efficacious against
hookworms in the case of dog No. 28.
Table 1.—Efficacy of paradichlorobenzene, administered in several ways, as an anthelmintic for dogs

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<th>Percentage of efficacy</th>
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* Administered as crystals in gelatin capsules.  
* Dissolved in liquid petrolatum.  
* None found.  
* Dissolved in olive oil.  
* Gelatin capsules followed in an hour by liquid petrolatum.  
* Gelatin capsules followed in an hour by castor oil.
TOXICITY

Dogs Nos. 9 and 10 died showing pronounced symptoms of intoxication. The practice of the experiment station has been to fast the animals overnight before administering paradichlorobenzene, and to withhold feed for a period of two hours following dosing. In the case of dogs Nos. 9 and 10, however, the attendant inadvertently gave the animals fat meat immediately after dosing.

The dogs received the drug at about 9.30 a. m., and were down and trembling violently at 1 p. m. Dog No. 9 soon became unconscious and died about 36 hours later without having regained consciousness. Dog No. 10 was not so violently affected, but showed incoordination of movement after 24 hours, walking with an irregular gait or standing with its legs spread far apart.

To learn whether this result was due to the absorption of paradichlorobenzene, dogs Nos. 18 and 21 were given the drug at the rate of 0.5 gm. per kilo of body weight. Dog No. 18 received a piece of fat immediately following dosing, and dog No. 21 was given all the whole milk it would take.

Both dogs showed decided symptoms of intoxication at 1 p. m., but the symptoms were not nearly so pronounced as in the case of dogs Nos. 9 and 10. The symptoms were still evident at 4 p. m. but disappeared before the next morning.

Four days later the experiments were repeated with the same dogs. The same amount of paradichlorobenzene was given as before, but in addition dog No. 18 received lean meat and dog No. 21 dry bread and water. The drug was administered at 9 a. m., and the first symptoms of intoxication were visible at 1 p. m. These passed off rapidly, however, leaving the animals with no apparent permanent ill effect.

Dog No. 21 passed eight ascarids after receiving the first dose of paradichlorobenzene on October 13, and died a few days after receiving the second dose on October 17. No ascarids were found post-mortem, proving the drug to be 100 per cent efficacious against these intestinal worms in this instance. No percentage of efficacy against hookworms was determined in the case of dog No. 21.

EFFECT ON EDIBILITY OF MEAT ANIMALS

In connection with the experiments with paradichlorobenzene as an anthelmintic the drug was observed to render unfit for human consumption the meat of animals to which it was administered.

Previous to the arrival of the author at the Porto Rico Experiment Station paradichlorobenzene in crystal form had been administered to pigs. One pig, which had received a total of 14 gm. of the drug during a period of four months, was sold on the hoof, that is, before slaughter, as is the local custom. Those who purchased the meat could not eat it and were refunded their money. The meat smelled and tasted of paradichlorobenzene. The second pig, which had been kept as a check on the first experiment, was given 5 gm. of the drug in one dose and was not slaughtered until two weeks later. The meat of this animal also proved to be unfit for human consumption.

One authority reports tasting paradichlorobenzene in the eggs of hens which were fed corn that had been fumigated with the drug. To test the accuracy of the report the author, about December 27, 1925, fed to some of the hens at the station the ground liver of a dog.
to which paradichlorobenzene had been administered. Up to and including January 9, 1926, paradichlorobenzene could be tasted in the yolks of the eggs laid by these hens.

CONCLUSIONS

Administered in doses of 0.1, 0.3, 0.5, and 1 gm. per kilo of body weight in bland oils and in crystal form, followed by a bland oil in some instances, and by a purgative oil in others, paradichlorobenzene is somewhat efficacious against intestinal worms.

The results obtained were not sufficiently uniform to permit classifying paradichlorobenzene as an effective anthelmintic, and are in accordance with the findings of Sollmann (10).

The results from using paradichlorobenzene dissolved in olive oil and alone are in agreement with the opinion expressed in 1918 by Hall (5) that "olive oil seemed to be decidedly contraindicated in connection with anthelmintics."

Hall and Foster (6, p. 432) also point out the fact that liquid petrolatum seriously diminished the efficacy of chenopodium, which seems to be true also in the case of paradichlorobenzene.

The results apparently confirm also the hypotheses advanced by Caius and Mhaskar (2) and Hall and Shillinger (7) concerning the relationship of the chlorine content and the solubility of halogen compounds to their anthelmintic efficacies. Paradichlorobenzene contains only 2 atoms of Cl, is practically insoluble in water, and theoretically therefore should be inferior to such compounds as carbon tetrachloride and the new anthelmintic tetrachlorethylene, which contain a larger number of chlorine atoms and are more soluble in water.

LITERATURE CITED

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