ANTHELMINTIC PROPERTIES OF SANTONIN

By Jacob E. Shillinger

Associate Veterinarian, Zoological Division, Bureau of Animal Industry, United States Department of Agriculture

INTRODUCTION

In the world of therapeutics certain drugs or preparations have been used for so many years that the statements in the literature, especially in the textbooks and also in articles in professional journals, as to the action of these drugs have a tendency to reiterate impressionistic ideas or traditions. Printed statements are ordinarily copied and passed on with little or no attempt to substantiate the claims made. With a widespread impression once established it is difficult to revise opinions with regard to drugs and a writer is placed in a precarious position if his results conflict with the generally accepted views.

WIDE VARIATIONS IN METHODS OF ADMINISTRATION

Santonin is one of the drugs having an extensive traditional reputation as an anthelmintic. Its use and results have been varied in the hands of the users as reported by them. After many years of use the method of administration and the dose rate of the drug still show wide variations. It is recommended by some persons who have used it as valuable in single-dose treatments and by others as valuable only in divided doses continued over a considerable period. By some it is administered alone as a pure drug and by others combined with one or more substances said to have synergistic value. Some administer santonin simultaneously with a purgative; others regard this as bad practice and prefer to follow it with a purgative several hours after administration, while still others give a purgative both preceding and following the drug. The type of purgative advised is not a matter of uniform opinion, and various substances, such as salines, oils, calomel, and arecoline, have been advocated. Some believe that feed should be withheld from the subject preceding the treatment, while others make no such provision; some administer the preparation mixed in the feed, while others claim that this procedure gives very poor results. Certain workers insist on the necessity of individual treatments, while another group advises its use in flock treatments.

The great safety of santonin has repeatedly been referred to as one of the outstanding qualities of the drug. This is a factor of considerable importance when it is necessary to treat very young or weak animals for intestinal parasitism. However, to be useful, an anthelmintic must combine a fair degree of efficacy and cheapness with reasonable safety.

1 Received for publication Mar. 19, 1927; issued June, 1927.

Journal of Agricultural Research, Washington, D. C.

Vol. 34, No. 9
May 1, 1927
Key No. A–118

(839)
SOURCES OF SANTONIN

The differences in results obtained are sometimes attributed to differences in the sources or nature of the santonin used. Recently certain commercial concerns have published the information that "that plant grows only in the wildest part of the Russian steppes, far from any seaport or commercial center, the most important area being the northeastern district of the Province of Turkestan." In this connection it may be noted that the plant from which santonin is obtained has been introduced into the United States and that it appears to thrive well in several semiarid sections of this country. While Turkestan is probably the native home of this plant, the Bureau of Plant Industry has grown it in an experimental way in several sections of the western slope of the United States. This fact, together with the reported increased foreign production, will probably operate to keep the cost of santonin at a reasonable figure in the future. The precise value of the domestic santonin has not been investigated by the writer, and in order to test the drug the Turkestan product was used.

EXPERIMENTAL WORK

A consideration of the writings of various workers shows a considerable divergence of opinion as to the value of santonin. The differences of opinion arise in large part from the fact that no uniform method of testing the drug has been used by investigators and that in only a few cases have accurate counts been made of the worms passed and a critical evaluation made of the results as ascertained by post-mortem examination of the animals treated.

In the present instance an effort has been made to get additional and definite information regarding the efficacy of santonin when used for anthelmintic purposes. A sample of the product with a guaranty of purity was procured from a representative of a firm interested in promoting its use. This was tested for purity in the Biochemic Division, Bureau of Animal Industry, and found to be free from adulteration. In order to get the most complete data possible it was used with and without purgation in varying doses, the drug being placed in hard gelatin capsules for administration. The dogs used in the experiment were confined in separate iron cages, were allowed their customary rations, and were given attention after treatment.

TESTS ON DOGS

First Series

In the first set of experiments with dogs the animals were made to fast for 24 hours and santonin was given in the doses and with the results indicated below:

Dog 1060, weight 28 pounds; 1 grain santonin; worms passed, none; post-mortem, fifth day, hookworms 49, tapeworms 4, whipworms 7.

Dog 1059, weight 38 pounds; 2 grains santonin; worms passed, none; post-mortem, fifth day, hookworms 20, tapeworms 2, whipworms 7.

Dog 1057, weight 40 pounds; 3 grains santonin; worms passed, whipworms 6; post-mortem, fifth day, hookworms 31, ascarids 11, tapeworms 9, whipworms 38.
May 1, 1927

**Anthelmintic Properties of Santonin**

Dog 1065, weight 35 pounds; 4 grains santonin; worms passed, none; post-mortem, fifth day, hookworms 46.

Dog 1055, weight 33 pounds; 5 grains santonin; worms passed, none; post-mortem, fifth day, hookworms 16, tapeworms 17, whipworms 5.

Dog 1067, weight 39 pounds; 6 grains santonin; worms passed, none; post-mortem, fifth day, hookworms 2, tapeworms 8, whipworms 27.

From a review of these results it is evident that santonin used alone on dogs which have fasted for 24 hours and not followed by a purgative is not effective in the doses given. In only one instance did it show any anthelmintic action and in that case, dog 1057, 6 whipworms were passed and 38 remained. There was therefore an efficacy of 14 per cent against whipworms. Santonin gave no evidence of anthelmintic action in doses of from 1 to 6 grains in dogs harboring hookworms, ascarids, and tapeworms, and failed to remove any whipworms from 4 of the 5 dogs infested. The failure of 3-grain doses to remove ascarids is especially significant.

**SECOND SERIES**

In the following tests the animals were kept without food for 24 hours, and were given santonin and calomel simultaneously in the doses and with the results as shown below:

Dog 1063, weight 10 pounds; 6 grains santonin and 5 grains calomel; worms passed, whipworms 1; post-mortem, seventh day, tapeworms 7, whipworms 1.

Dog 1064, weight 18 pounds; 7 grains santonin and 5 grains calomel; worms passed, whipworms 4; post-mortem, seventh day, hookworms 10, tapeworms 8, whipworms 4.

Dog 1061, weight 35 pounds; 8 grains santonin and 5 grains calomel; worms passed, whipworms 1; post-mortem, seventh day, negative.

Dog 1066, weight 35 pounds; 9 grains santonin and 5 grains calomel; dog vomited first day; worms passed, none; dog died sixth day; post-mortem, no worms; post-mortem changes so extensive at necropsy that ante-mortem pathology could not be ascertained.

Dog 1058, weight 14 pounds; 10 grains santonin and 5 grains calomel; worms passed, whipworms 11; post-mortem, seventh day, hookworms 4, ascarids 1, tapeworms 1. (*Dirofilaria immitis* in heart.)

Dog 1060, weight 41 pounds; 11 grains santonin and 10 grains calomel; worms passed, hookworms 2; post-mortem, seventh day, hookworms 10, ascarids 1 (young), whipworms 5.

Dog 1056, weight 42 pounds; 12 grains santonin and 10 grains calomel; worms passed, whipworms 120; post-mortem, seventh day, hookworms 23, whipworms 8.

In this series of dogs, six of which had worms, santonin with a purgative showed an efficacy, against whipworms, of 100 per cent in two cases, 95 per cent in one case, and 50 per cent in two cases, for the five dogs infested with these worms. In only one instance did it remove any hookworms from the four dogs infested and in this case it expelled 2 of the 12 present, or 17 per cent. No efficacy was indicated in its action against ascarids or tapeworms, in spite of the fact that the doses used, from 6 to 12 grains, are much higher than those usually recommended. The death of one animal, dog 1066,
6 days after dosing can not be ascribed definitely to the treatment, as other dogs receiving the larger quantities were not affected. No symptoms other than a subnormal appetite and apathy were observed in this dog.

**Third Series**

In the next series of tests an ounce of castor oil was given in the morning 15 hours after a dose of santonin administered the previous evening. The dogs had fasted 24 hours. The results of this test follow:

Dog 1099, weight 6 pounds; 1 grain santonin; worms passed, none; post-mortem, fifth day, hookworms 4, ascarids 3, tapeworms 23, whipworms 6.

Dog 1098, weight 6 pounds; 2 grains santonin; worms passed, ascarids 7; post-mortem, fifth day, hookworms 2, ascarids 2, tapeworms 12, whipworms 3.

Dog 1085, weight 6 pounds; 3 grains santonin; worms passed, ascarids, 1; post-mortem, fifth day, hookworms 7, ascarids 22, whipworms 87.

Dog 1087, weight 15 pounds; 4 grains santonin; worms passed, none; post-mortem, fifth day, hookworms 31, ascarids 1, tapeworms 5, whipworms 7.

Dog 1070, weight 19 pounds; 5 grains santonin; worms passed, ascarids, 1; post-mortem, fifth day, hookworms 1, tapeworms 16, whipworms 2.

Dog 1103, weight 24 pounds; 6 grains santonin; worms passed, ascarids, 1; post-mortem, fifth day, hookworms 19, ascarids 2, tapeworms 18, whipworms 19.

The result of this test shows that santonin in the doses given followed by castor oil in 15 hours failed to remove any hookworms, tapeworms, or whipworms, and that its action against ascarids was not dependable. In two of the six infested animals it failed to remove any ascarids and in the other four it was 100 per cent, 77 per cent, 33 per cent, and 4 per cent effective, respectively. These findings can not be correlated with the quantities given.

**Fourth Series**

The same dose of santonin was given to the dogs in this test in addition to an increased amount of castor oil (2 ounces) at a shorter interval, 8 hours, the dogs having fasted 24 hours, with results as noted below:

Dog 1083, weight 6 pounds; 1 grain santonin; worms passed, hookworms 5, ascarids 8; post-mortem, fifth day, hookworms 112, ascarids 43, whipworms 8.

Dog 1100, weight 8 pounds; 3 grains santonin; no worms passed; post-mortem, fifth day, hookworms 8, tapeworms 4, whipworms 9.

Dog 1102, weight 13 pounds; 4 grains santonin; no worms passed; post-mortem, fifth day, hookworms, 4.

Dog 1086, weight 23 pounds; 5 grains santonin; worms passed, ascarids, 1; post-mortem, fifth day, tapeworms 3, whipworms 4.

Dog 1104, weight 32 pounds; 6 grains santonin; no worms passed; post-mortem, fifth day, hookworms 41, ascarids 15, tapeworms 5, whipworms 5.
In this group of animals there was no indication that the increased and earlier purgation gave better results. In one out of five animals infested with hookworms it removed 5 of the 117 worms present, or about 4 per cent. In two of the four animals infested with ascarids it was 100 per cent effective, in one case it was 16 per cent effective, and in one it failed completely. It likewise failed to remove any tapeworms from three infested dogs or whipworms from five infested dogs. A consideration of the effect of the treatment in the case of one dog, No. 1084, illustrates the manner in which anthelmintics may be misjudged in the absence of post-mortem examination of test animals. The passage of eight ascarids and five hookworms would be sufficient to convince some observers of a high efficacy of the drug. However, a comparison of the number passed with the total number of parasites present shows an efficacy of only 16 per cent against ascarids, 4 per cent against hookworms, and 0 per cent against whipworms.

**SUMMARY OF TESTS ON DOGS**

Santonin, without purgation and in doses varying from 1 to 6 grains administered to dogs weighing from 28 to 40 pounds, removed 6 of the 90 whipworms present, or about 7 per cent, but had no effect on the hookworms, ascarids, or tapeworms.

In doses of from 6 to 12 grains administered simultaneously with 5 to 10 grains of calomel to dogs weighing from 10 to 42 pounds, santonin removed 2 of the 49 hookworms, or about 4 per cent, 136 of the 154 whipworms, or 88 per cent, but none of the ascarids or tapeworms.

In doses of 1 to 6 grains, followed by 1 ounce of castor oil administered 15 hours later to dogs weighing from 6 to 24 pounds, santonin removed 10 of the 40 ascarids, or 25 per cent, but had no effect on the hookworms, tapeworms, or whipworms.

In doses of from 1 to 6 grains with 2 ounces of castor oil administered 8 hours later to dogs weighing from 6 to 32 pounds, santonin removed 5 of the 179 hookworms, or 3 per cent, and 14 of the 72 ascarids, or 19 per cent, but none of the tapeworms or whipworms.

**TESTS ON SWINE**

Two pigs weighing 78 and 81 pounds, respectively, were given 5 grains of santonin each in a light feed after having fasted for 12 hours. Six days later this treatment was repeated. It was not feasible to examine the feces of these animals, but on post-mortem examination 15 ascarids were found in one and 68 ascarids in the other. The dosing of animals by mixing the medicinal agent with the feed has never been regarded as an economical or scientific method of treatment by the skilled veterinarian. Certainly in most cases the efficacy of the drug is lowered by the process.

Following this test three pigs, each weighing between 30 and 40 pounds, were given capsules containing 5 grains of santonin after they had fasted for 24 hours. This was administered in the evening and on the following morning, about 15 hours later, and two hours before the regular mash feed was given, a small quantity of mill feed saturated with water in which 5 ounces of Epsom salt had been dissolved was given them. Purgation resulted and 4 ascarids were
passed during the next two days. Post-mortem examination of the animals one week later showed 59, 8, and 37 ascarids, respectively.

One animal weighing 45 pounds, which had fasted 24 hours, was then given 6 grains of santonin in a capsule, followed in 12 hours with a purge of Epsom salt. Two ascarids were passed following the treatment. Post-mortem examination of the animal on the sixth day showed 45 ascarids present.

To another animal weighing 36 pounds which had fasted 24 hours a dose of 15 grains of santonin in capsule was administered, followed immediately by 10 grains of calomel. The animal passed 16 worms during the three succeeding days. Post-mortem examination on the seventh day showed four ascarids in the small intestine.

SUMMARY OF TESTS ON SWINE

Summarizing the santonin tests on swine it may be stated that the dosage of 5 grains in feed was of little or no value. While there is a possibility that some worms were passed, the retention of 15 and 68 worms after treatment is sufficient to condemn either the drug or the method of administration. Santonin administered in 5-grain doses to animals weighing 30 to 40 pounds after they had fasted 24 hours, followed by a purge in 15 hours, removed 4 worms from a lot of three pigs and left an aggregate of 104 in the lot. A dose of 6 grains administered after a fast of 24 hours and followed in 12 hours by a purge of Epsom salt, proved insufficient for a 45-pound animal, removing only 2 of the 48 worms present. A dose of 15 grains accompanied by 10 grains of calomel administered to a 36-pound pig which had fasted 24 hours, proved most effective, removing 16 of the 20 worms present in the animal.

TEST ON HORSES

Many writers have recommended santonin for freeing horses of worms. One writer states that an animal given the classical carbon bisulphide treatment for bots followed in two weeks with a dose of from ½ to 1½ drams of santonin and an aloetic purge 12 hours later, may safely be pronounced worm free. This procedure was followed, and the maximum dose of 1½ drams was given. Post-mortem examination 8 days later showed a great many Habronema of two species and some Trichostrongylus axei in the stomach. The intestine contained many cylicostomes of undetermined species and 132 large strongyles representing three species. Just what worms might have been removed is not known, but since so large a number of different varieties remained after the treatment it was not considered worth while to make further tests. No pinworms were found.

It should be mentioned in passing that the treatment suggested is not in line with what is known about the action of santonin and of carbon bisulphide. Santonin is rated generally as primarily valuable in removing ascarids, but carbon bisulphide has been shown by critical test to be approximately 100 per cent effective in removing ascarids from the horse, in addition to being equally effective in removing bots, which are not affected by santonin. There is, therefore, no point in following carbon bisulphide with santonin. It can be followed to advantage by chenopodium to remove the strongyles, cylicostomes, and pinworms from the large intestine.
CONCLUSIONS

The findings reported by Hall and Foster ² that santonin in single doses of from 1 to 3 grains gave about 24 per cent efficacy in removing ascarids from dogs, and those of Mote ³ to the effect that a value of 0 to 46 per cent appears to be within the actual range of utility for the drug in removing ascarids from swine, are in substantial agreement with the findings reported in this paper. All critical testing of which the writer is aware shows an anthelmintic value for santonin much below what has been and is now being claimed for it in advertisements and in papers based on impressions gathered solely from seeing worms passed. If accurate data were obtained on the value of santonin as an anthelmintic by systematic post-mortem examination of test animals, much of the misinformation concerning its value could be eliminated.

The ease of administration of santonin is an advantage and may tend to prejudice the minds of users against other drugs more difficult to use in favor of santonin, and while it has value, especially in repeated treatments, it is a very much overrated drug at present. In the opinion of the writer its value is principally that of a drug which does not cause irritation of the gastro intestinal tract and hence is of value for use in repeated doses in cases of gastroenteritis with ascariasis, or in repeated doses for removing whipworms.


51054—27——4