weight of caffeine computed by difference. Results obtained by the method are listed in Table II.

Table II.—Results of Analysis of Aspirin, Caffein and Cinnamylephedrine in Admixture

Aspirin		Caffeine		Cinnamylephedrine HCl	
Recovery, Gm.	Recovery, %	Recovery, Gm.	Recovery, %	Recovery, Gm.	Recovery, %
1.494	99.6	0.100	100	0.0498	99.6
1.491	99.4	0.101	101	0.0497	99.4
1.493	99.5	0.101	101	0.0488	97.6
1.492	99.4	0.101	101	0.0486	97.2
1.490	99.3	0.100	100	0.0493	98.6
1.487	99.1	0.100	100	0.0495	99.0
1.487	99.1	0.100	100	0.0496	99.2
1.487	99.1	0.100	100	0.0495	99.0
Av.	99.3		100		98.7

The direct titration of the cinnamylephedrine-caffeine residues may be carried out in 50% alcohol, but the indicator is so affected by the medium that results are reliable only when one is thoroughly familiar with the end-point under such conditions.

When applied to tablets containing lubricants, the method must be modified to obtain correct recoveries of caffeine. The residue of caffeine, cinnamylephedrine and lubricant may be taken up with acid, the grease or wax removed by shaking with petroleum ether or a little benzene, and the cinnamylephedrine and caffeine recovered by extraction from the aqueous layer after rendering it ammoniacal.

For qualitative purposes, cinnamylephedrine base may be separated from caffeine by leaching the mixture with carbon tetrachloride or ether, in which caffeine is but slightly soluble, filtering, evaporating the solvent and recrystallizing the residue from alcohol-water mixture.

SUMMARY

(1) The preparation of the *N*-cinnamylephedrines by the action of cinnamyl chloride on the corresponding ephedrines has been described, and some properties of the bases and their hydrochlorides have been observed and recorded.

(2) A method for the separation and estimation of aspirin, caffeine and cinnamylephedrine in admixture has been described.

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Toxicity of Red Squill Powder and Extract for Chickens, Rabbits and Guinea Pigs*

By J. A. Lubitz and C. R. Fellers

INTRODUCTION

It is believed that red squill powder is non-toxic to some animals (hogs, dogs, cats, chickens) due to an emetic principle present in the red squill powder. This principle causes emesis when red squill is taken in toxic quantities, thereby preventing poisoning. The belief behind the specific raticide action of red squill is that rats have no vomiting mechanism and so cannot rid their systems of squill. Therefore, they become poisoned when squill is ingested in considerable quantity. It is interesting to note that according to Dukes (1) the act of vomiting is not common to all species of animals. Rodents, ruminants and solipeds seldom or never vomit, whereas carnivores and omnivores (except such as are rodents) vomit readily.

This work was conducted to determine the effect of a red squill extract on guinea pigs, rabbits and chickens, for there was doubt expressed as to the supposed harmless character of red squill extract baits to animals other than rats.

REVIEW OF LITERATURE

References in the literature (2, 3, 4) indicate that red squill is not readily taken by animals other than rats, and if consumed the emetic principle in the

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squill causes vomiting, which usually saves the animal.

Munch, Silver and Horn (2) report the following: "Squill powders were mixed with whole-milk powder, and various proportions were added to 100 Gm. of lean, hashed meat, which was then fed to cats. In food containing 10 to 25 parts of squill powder per million the unusual flavor was detected, and the food was eaten slowly but completely.

"Dogs refused ground meat containing 1000, 2500 and 5000 parts of squill powder per million of meat. When squill powder suspended in water was injected into the stomach by stomach tube, emesis and diarrhea followed in several instances after doses of 100 mg. per Kg. of body weight. As dogs refused food containing a small concentration of squill powder, such as 1000 parts per million, it does not seem that they would be hurt by squill. Two separate instances have been noted where dogs gulped down squill rat baits containing 10 per cent of squill mixed with sausage. Emesis was the only effect noted.

"No effect was observed following the injection into chickens' crops of quantities less than 2000 mg. of squill powder per Kg. of body weight. Diarrhea followed the injection of 2000 and 3000 mg. per Kg. Squill powder was mixed with cracked corn and with laying mash in 10 per cent concentrations. Chickens refused to eat such food. Two chickens were placed on a diet containing 10 per cent of squill powder in growing mash. After refusing to eat for several days, they consumed the mash without much hesitation. This food was continued for two weeks, during which time the chickens apparently grew as well as controls fed on untreated mash.

"Pigeons refused to eat mash containing 10 per cent of squill powder. Injection of 2000 mg. of squill powder per Kg. of body weight into the crop failed to produce any noticeable effect. The injection of 3000 and 4000 mg. per Kg. resulted in emesis, but no other untoward effect could be noted.

"'A dose of 250 mg. of squill powder per Kg. was given in a gelatin capsule to a 4-month-old pig weighing about 16 Kg. The pig became ill but recovered in about two days after the feeding.

"Injected in aqueous suspension into the stomach of woodchucks, the minimum lethal dose of a sample of squill was found to be 500 mg./Kg. (the same as for rats). Vomiting, however, frequently followed even smaller doses. Baits containing squill were refused.

"Prairie dogs and pocket gophers refused to eat freshly exposed squill baits."

Koller (5) in his book reports that the toxic doses of a fresh squill sample given by Hubner are as follows: cats 200 mg./Kg., dogs 1500 mg./Kg., rabbits 3500 mg./Kg., guinea pigs 6000 mg./Kg., and hens 35,000 mg./Kg.

Ward, Barber, Garlough and Munch (4) report that red squill powder and red squill extract are toxic to hogs when given by stomach. They also state that most hogs will not eat enough red squill rat poison voluntarily to cause death, and that red squill powder causes emesis in hogs which tends to protect the animals when baits are consumed normally.

According to Mills (6) (unpublished data in his files) Read's laboratory in London ran a series of tests with squill powder having a lethal dose of 800 mg./Kg. on rats, and gives the following as toxic doses: cattle 300 to 500, pig below 300, fowl about 1000, rabbit above 1000 and guinea pig between 400 and 500 mg./Kg.

Silver and Munch (7) report that a human subject swallowed 15 gr. of a toxic red squill powder with no apparent harm, and later took 40 gr., which caused nausea and vomiting within 15 minutes, but no other effect.

EXPERIMENTAL

SQUILL SAMPLES

The red squill extract used in this work had a toxicity of 900 mg./Kg. when fed to male albino rats. The red squill powder used had a toxicity of 800 mg./Kg. when fed in the same way. For this work the red squill samples were diluted with water so that they could be conveniently pipetted. The diluted samples were fed orally by pipette to guinea pigs, rabbits and chickens at various dosage levels.

Toxicity to Guinea Pigs.—Guinea pigs were fed at 6300 mg./Kg., 1800, 900, 450 and 200 mg./Kg. levels with the diluted red squill extract. This red squill extract was fatally toxic to guinea pigs on all of the feeding levels.

The guinea pigs underwent the same type of rolling convulsion as do rats suffering from red squill poisoning. No vomiting was observed. The results of this feeding test indicate that guinea pigs are much more susceptible to poisoning by red squill extracts than are rats.

In like manner, guinea pigs were fed red squill powder on 100 mg./Kg., 200 and 300 mg./Kg. levels. Diarrhea was observed in most of the guinea pigs after the squill feeding. At the 100 mg./Kg. level 2/4 guinea pigs died, at the 200 mg./Kg. 0/2 died and at the 300 mg./Kg. level 3/3 died. We can conclude that guinea pigs are more susceptible to red squill powder than are rats.

Toxicity to Rabbits.—Rabbits were fed the red squill extract using the same technique as with guinea pigs. Three feeding levels were used: 450 mg./Kg., 900 mg./Kg. and 1800 mg./Kg. The rabbits evinced no untoward effects from the squill extract feeding. No vomiting was observed. We may, therefore, conclude that levels of red squill extract which are definitely toxic to rats seem to have no harmful effects on rabbits.

Red squill powder was fed to rabbits at levels of 1600 mg./Kg., 2400 mg./Kg. and 3200 mg./Kg. The rabbit on the 2400 mg./Kg. level succumbed and the rabbits on the other two levels were affected but survived. The indication is that rabbits are

very resistant to squill poisoning but very high feeding levels may be toxic. These rabbits underwent the same type of rolling convulsion as do rats preliminary to recovery or death from red squill poisoning. No vomiting was observed.

Toxicity to Chickens.—Chickens were also fed red squill extract in like manner. The feeding levels used ranged from 450 mg./Kg. to 4500 mg./Kg.

This experiment indicates that red squill extracts are non-toxic when fed to chickens, even in very large amounts.

Red squill powder was fed to chickens on the following levels: 2400 mg./Kg., 3200 mg./Kg., 4000 mg./Kg. and 4800 mg./Kg. No discomfort was observed following the squill powder feeding. This corroborates the findings of other investigators relative to the innocuous character of red squill powder when fed to chickens.

DISCUSSION

Rats, guinea pigs, rabbits and chickens are unable to vomit. However, rats and guinea pigs are susceptible to red squill poisoning while rabbits and chickens are not. It therefore seems that poisoning from red squill is due to a species susceptibility rather than any ability or inability to vomit. It should be noted, of course, that vomiting may protect susceptible animals from red squill poisoning by ridding the animal of the poison.

SUMMARY

1. Chickens and rabbits do not seem to be affected by levels of red squill extract and red squill powder which are definitely toxic to rats. However, rabbits may be susceptible to very high levels of red squill dosage.

2. Guinea pigs are less resistant to poisoning by red squill extract and powder than are rats.

3. It is believed that red squill poisoning is dependent on species susceptibility rather than on ability or inability to vomit.

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On the Preparation of an Extract Having "Marihuana-Like" Activity from the Fruits of Cannabis Sativa

By John R. Matchett and S. Loewe†*

Despite the considerable research carried on in recent years on the separation and characterization of the physiologically active principle or principles of the resin of *Cannabis sativa*, little has been reported concerning the fruits. Munch (1) prepared two physiologically active extracts and found one to be stimulating to mice and the other depressant. Reference to action similar to that of extracts prepared from the vegetative portions of the plant was not made.

Bouquet (2) has examined the fruits and concludes that they themselves are devoid of physiological activity. Any effects observed pursuant to their use he feels must be due to the presence of hulls which do contain resin.

This report records the unequivocal demonstration of the presence in cannabis fruits of a principle or principles having, in the dog, an action similar to that produced by the familiar cannabis resin. The substance or substances are to be found in the non-saponifiable portion of the solvent-extracted oil which is a major constituent of the fruits.

EXPERIMENTAL

The preparation of the active extract was carried out as follows:

Fruits of *Cannabis sativa* (675 Gm.), free from admixed vegetative material, were crushed and extracted to exhaustion with chloroform. Most of the solvent was evaporated at atmospheric pressure and the last traces removed *in vacuo*. The oily

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