Onderstepoort Journal of Veterinary Science and Animal Industry, Volume 3, Number 1, July, 1934.

Plant Poisoning in Stock and the Development of Tolerance.

By

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(Continued from *Onderstepoort Jour. Vet. Sci. and Animal Ind.*, Vol I, 1933, pp. 149-156.)

GIFBLAAR [*Dichapetalum cymosum* (HOOK.) ENGL.]

In previous publications (Steyn, 1932 and 1933) it was mentioned that animals develop a tolerance to *Chrysocoma tenuifolia* Berg and *Centaurea picris* D. C., whilst this was not the case with *Asclepias physocarpa* Schltr.

Field observations seem to indicate that gifblaar does not belong to those plants which induce the development of tolerance when eaten in non-lethal quantities over prolonged periods.

In the tables given below the results of two experiments are recorded:—

Tolerance Experiment.—Gifblaar Leaves.

Rabbit No.	Wgt. in Kg.	Amount of Plant Given per Kg. Body-weight.	Result.
A	2·8	0·05 gm. dry leaves from 24/4/33–29/4/33 0·1 gm. dry leaves from 1/5/33– 5/5/33 0·2 gm. dry leaves from 11/5/33–12/5/33 Total amount of leaves received = 3·36 gm.	Died suddenly on 13/5/33 from gifblaar poisoning.
B	2·7	0·05 gm. dry leaves from 24/4/33–29/4/33 0·1 gm. dry leaves from 1/5/33– 5/5/33 0·2 gm. dry leaves from 11/5/33–12/5/33 Total amount of leaves received = 3·24 gm.	Tolerance test on 18/5/33: Received 1·0 gm. dry leaves per Kg. body-weight. Died from gifblaar poisoning 12 hours after having been drenched.
C	2·3	0·05 gm. dry leaves from 24/4/33–29/4/33 0·1 gm. dry leaves from 1/5/33– 3/5/33 Total amount of leaves received = 1·38 gm.	Died suddenly on 3/5/33 from gifblaar poisoning.
D	1·9	0·05 gm. dry leaves from 24/4/33–29/4/33 0·1 gm. dry leaves from 1/5/33– 5/5/33 0·2 gm. dry leaves from 11/5/33–12/5/33 Total amount of leaves received = 2·3 gm.	Tolerance test on 18/5/33: Received 1·0 gm. dry leaves per Kg. body-weight. Died from gifblaar poisoning 10 hours after having been drenched.
E	1·9	Treated as D..... Total amount of leaves received = 2·3 gm.	Tolerance test on 18/5/33: Received 1·0 gm. dry leaves per Kg. body-weight. Died from gifblaar poisoning 6 hours after having been drenched.

Rabbit No.	Wgt. in Kg.	Amount of Plant Given per Kg. Body-weight.	Result.
F	1·5	Treated as D..... Total amount of leaves received = 1·8 gm.	Tolerance test on 18/5/33: Received 1·0 gm. dry leaves per Kg. body-weight. Died from gifblaar poisoning 5 hours after having been drenched.
G	2·1	Treated as D..... Total amount of leaves received = 2·52 gm.	Tolerance test on 18/5/33: Received 1·0 gm. dry leaves per Kg. body-weight. Died from gifblaar poisoning 12 hours after having been drenched.
H	1·8	Treated as D..... Total amount of leaves received = 2·16 gm.	Tolerance test on 18/5/33: Received 1·0 gm. dry leaves per Kg. body-weight. Died from gifblaar poisoning 12 hours after having been drenched.
I	1·8	Treated as D..... Total amount of leaves received = 2·16 gm.	Tolerance test on 18/5/33: Received 1·0 gm. dry leaves per Kg. body-weight. Died from gifblaar poisoning 16 hours after having been drenched.
J	2·4	0·1 gm. dry leaves from 24/4/33–29/4/33 0·2 gm. dry leaves from 1/5/33– 5/5/33 0·4 gm. dry leaves from 11/5/33–12/5/33 Total amount of leaves received = 5·56 gm.	Tolerance test on 18/5/33: Received 1·0 gm. dry leaves per Kg. body-weight. Died from gifblaar poisoning 14 hours after having been drenched.
K	1·8	0·1 gm. dry leaves from 24/4/33–29/4/33 0·2 gm. dry leaves on 1/5/33 Total amount of leaves received = 1·44 gm.	Died suddenly on 1/5/33 from gifblaar poisoning.
L	2·1	0·1 gm. dry leaves from 24/4/33–29/4/33 0·2 gm. dry leaves from 1/5/33– 2/5/33 Total amount of leaves received = 2·1 gm.	Died suddenly on 2/5/33 from gifblaar poisoning.
M	1·7	Treated as J..... Total amount of leaves received = 4·08 gm.	Tolerance test on 18/5/33: Received 1·0 gm. dry leaves per Kg. body-weight. Died from gifblaar poisoning 8 hours after having been drenched.
N	1·9	0·1 gm. dry leaves from 24/4/33–29/4/33 0·2 gm. dry leaves on 1/5/33 Total amount of leaves received = 1·52 gm.	Died suddenly on 1/5/33 from gifblaar poisoning.
O	2·1	Treated as J..... Total amount of leaves received = 5·04 gm.	Tolerance test on 18/5/33: Received 1·0 gm. dry leaves per Kg. body-weight. Died from gifblaar poisoning 5 hours after having been drenched.
P	2·0	0·1 gm. dry leaves from 24/4/33–29/4/33 0·2 gm. dry leaves from 1/5/33– 3/5/33 Total amount of leaves received = 2·4 gm.	Died suddenly on 3/5/33 from gifblaar poisoning.
Q	2·2	0·1 gm. dry leaves from 24/4/33–29/4/33 0·2 gm. dry leaves on 1/5/33 Total amount of leaves received = 1·76 gm.	Died suddenly on 1/5/33 from gifblaar poisoning.
R	2·3	0·1 gm. dry leaves from 24/4/33–28/4/33 Total amount of leaves received = 1·15 gm.	Died suddenly on 28/4/33 from gifblaar poisoning.

The gifblaar leaves used in the above experiment were collected in a very young stage of development on the Magaliesberg, Pretoria North. The leaves were air-dried, and ground, and the powder thoroughly mixed before use. The M.L.D. per Kg. body-weight rabbit was found to be 0·75 gm.

It was intended to administer the dry leaves as follows:—

A. *Nine Rabbits (A to I).*

0·05 gm. (i.e. 1/15 M.L.D.) dry leaves per Kg. body-weight from 24.4.33 to 29.4.33 (inclusive).

0·1 gm. (i.e. 2/15 M.L.D.) dry leaves per Kg. body-weight from 1.5.33 tot 5.5.33 (inclusive).

0·2 gm. (i.e. 4/15 M.L.D.) dry leaves per Kg. body-weight from 11.5.33 to 12.5.33 (inclusive).

B. *Nine Rabbits (J to R).*

0·1 gm. (i.e. 2/15 M.L.D.) dry leaves per Kg. body-weight from 24.4.33 to 29.4.33 (inclusive).

0·2 gm. (i.e. 4/15 M.L.D.) dry leaves per Kg. body-weight from 1.5.33 to 5.5.33 (inclusive).

0·4 gm. (i.e. 8/15 M.L.D.) dry leaves per Kg. body-weight from 11.5.33 to 12.5.33 (inclusive).

This manner of dosing was adopted as previous experiments upon rabbits seemed to indicate that the plant has cumulative effects, i.e., that the active principle is inactivated or excreted very slowly.

Of the nine rabbits in group A and group B two and six died respectively before the tolerance test could be applied. The remaining ten rabbits received 1·0 gm. (i.e. $1\frac{1}{3}$ M.L.D.) dry gifblaar leaves per Kg. body-weight on the sixth day after the preliminary treatment with small quantities of dry leaves had been discontinued. Not a single animal survived the tolerance test, thus clearly indicating that no decrease in susceptibility to gifblaar had occurred in the course of the preliminary treatment. It is hardly possible that an increase in resistance had occurred but disappeared in the interval that elapsed between the time of discontinuation of the preliminary treatment and the application of the tolerance test.

The results recorded in the above table clearly indicate the difference in susceptibility of the different animals to gifblaar. They also bring out the fact that the active principle of gifblaar is inactivated in, or (and), excreted from the body at a very slow rate. The M.L.D. of the dry leaves per Kg. body-weight of rabbit was determined as 0·75 gm., and yet we find the following noteworthy cases in the above table: (*a*) *Rabbit C* (2·3 Kg.) died suddenly after having received only 1·38 gm. of dry leaves in the course of ten days. This amount of leaves is less than the M.L.D. given in one dose. This could be regarded as a case of sensitization, unless we

accept that the animal possessed an idiosyncrasy for gifblaar; (*b*) *Rabbit R* (2·3 Kg.) is a case similar to Rabbit C. The former died from gifblaar poisoning after having received 1·15 gm. of dry leaves in the course of five days. This amount of plant is much less than the M.L.D. of dry leaves administered in one dose; *Rabbits K, L, N, P,* and *Q* died after having received in the course of a number of days amounts of dry leaves slightly higher than the M.L.D. given in one dose.

An experiment similar to the above was conducted with the dried underground stems of gifblaar collected by Dr. A. C. Leemann (of the Division of Plant Industry, Pretoria) at Rietondale, Pretoria.

Material was collected at intervals of one week from the 17.7.33 when the plant was in the dormant state, to 1.9.33 when it had produced a large number of leaves. In all, seven collections were made. Each consignment of underground stems were dried and the M.L.D. per Kg. rabbit determined. Leemann considered it likely that in the dormant state the underground stems of the plant contained precursors of the active principle of the plant and that these precursors when brought into the animal body may induce the development of a tolerance to the plant.

The first consignment of plant material was given to two rabbits, and for each further consignment two rabbits were added, so that for the seven collections fourteen rabbits were employed. In order to explain the manner of dosing the collections are numbered 1, 2, 3, 4, 5, 6 and 7, and the rabbits A to N. Rabbits A and B received consignment 1 the first week, consignment 2 the second week, and so forth. Rabbits C and D did not receive consignment 1, but all consignments from the second collection onwards. Rabbits E and F did not receive consignments 1 and 2, but all from the third collection onwards, and so forth. Rabbits M and N therefore only received consignment 7. All the rabbits were drenched every alternate day from the time they were placed in the experiment. The initial dose, which was equivalent to one-tenth M.L.D. per Kg. body-weight, was slightly increased at weekly intervals until about ½ M.L.D. was reached. Each rabbit was drenched for about six weeks and the tolerance test applied five days after discontinuation of the preliminary drenching experiment. In the tolerance test the animals received 2 M.L.D. of gifblaar leaves.

The results of this experiment were identical with those described in the former experiment, namely (*a*) there was no evidence of decreased susceptibility to gifblaar after preliminary dosing with small quantities of the underground stem; and (*b*) there was evidence of increased sensitivity to the plant and very slow inactivation, or (and), excretion of the active principle.

The interesting observation was made that there was a continuous decrease in the M.L.D. of the dried underground stems per Kg. rabbit from 5·3 gm. on 1.7.33 to 50 gm. on 17.9.33. This phenomenon appears to indicate that the active principle is concentrated in the underground portions of the plant while in the dormant state and that a high percentage of the active principle is passed into the leaves as soon as these appear. A definite opinion in regard to this phenomenon can, however, only be expressed when experiments were conducted upon the same plant.

SUMMARY.

From the results of experiments conducted upon thirty-two rabbits it appears (*a*) that the continuous ingestion of leaves or underground stems of gifblaar does not induce the development of tolerance to this plant; and (*b*) that the active principle of gifblaar has cumulative effects, that is, it is inactivated in the body or excreted at a very slow rate. It is also possible that repeated small doses of the plant may cause progressive damage to organs of vital importance (heart) and that the sum total of these consecutive and progressive lesions is sufficient to cause death in spite of the fact that the active principle has been partly or completely excreted.

There also was a certain amount of evidence that some animals became sensitized to the effects of the plant, unless we accept that these animals possessed an idiosyncrasy to gifblaar.

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