THE USE OF Ro 5-2807 (ROCHE) AS A TRANQUILLISER IN WILD UNGULATES

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INTRODUCTION

One of the functions of the Nature Conservation Section of the Transvaal Provincial Administration is the translocation of various game species from unsuitable or threatened habitats to nature reserves or other suitable areas.

Relatively little use has been made of drug-capture techniques to obtain such game animals, and mechanical methods of capture are normally employed. Tranquillisers are thus of major importance to facilitate handling and transportation and to minimise injury to the animals.

The experimental drug, Ro 5-2807 (Roche), has been used for this purpose on giraffe *Giraffe camelopardis*, blue wildebeest *Connochaetes taurinus*, oribi *Ourebia ourebi*, impala *Aepyceros melampus*, eland *Taurotragus oryx*, and red hartebeest *Alcelaphus buselaphus*.

Ro 5-2807 is 7-chloro-1-methyl-5-phenyl-3H-1, 4 benzodiazepine-2-(1H)-one. It is thus closely related to Chlordiazepoxide which has been used with good results on zoo animals (Heuschele 1961) and on Transvaal giraffe (Kettlitz unpublished).

Clinically, Ro 5-2807 produces muscular relaxation and a degree of anxiolysis. It has been successfully employed as a tranquilliser on oribi *Ourebia ourebi*, steenbok *Raphicerus campestriss* and vaal rhebok *Pelea capreolus* (Pienaar and Van Niekerk 1963). Its clinical and physiological effects on horses have been studied by Osman (1963).

Ro 5-2807 is not water-soluble and is employed in oily solution for intramuscular injection in strengths of 50 mg./ml. and 100 mg./ml.*

GIRAFFE

Giraffe are captured by horsemen and transported in crates by motor vehicle to quarantine pens, in which they are normally kept for three to five months. Because of their size and susceptibility to injury, tranquillisers are practically essential to ensure successful transportation. The results obtained with Ro 5-2807 are summarised in Table I, which shows the variation when it was used in doses ranging from 1·0 to 1·8 mg./kg. Five out of 12 animals were immobilised for periods of 5–7 hours. No constant pattern of effect was evident, although anxiolysis was a feature of the effect in all cases. In one case, an animal remained calm and permitted handling for 30 hours after receiving a dose of 1·1 mg./kg. A similar dose in another animal produced incomplete tranquillisation for only five hours.

* Experimental preparations

Of the five animals immobilised, three evinced relaxation of the neck as well, necessitating constant care until partial recovery. The remaining two kept the neck erect whilst lying down.

In one case a hypnotic effect was produced when a female weighing 225 Kg. was given 1·3 mg./kg. The animal stood with forelegs apart, staring fixedly ahead. A repeat dose of 1·3 mg./kg. followed by another 1·3 mg./kg. 9·5 hours later produced the same result.

Giraffe normally vary in their behaviour and reaction to capture and handling, and this materially affects their reaction to any drug used on them. However, a dose of 1·3 mg./kg. can be relied upon to produce anxiolysis and possibly immobilisation of the limbs.

No effects on the respiratory or circulatory systems have been observed.

BLUE WILDEBEEST

Blue wildebeest have been captured by various methods such as driving them into nets, capturing them from motor vehicles, or by means of immobilising drugs. Data are available from observations on four animals, three of which were treated on two occasions with Ro 5-2807. The results are summarised in Table 2. It was noted that the action of the drug was modified to an appreciable extent when the animals were transported in closed crates by motor vehicle. A lower dose of Ro 5-2807 was required to effect anxiolysis and immobilisation.

In the case of wildebeest No. 1, the animal succumbed to the effects of an immobilising drug, Phencyclidine, before the action of Ro 5-2807 could be evaluated. Another animal succumbed to the same dose of Phencyclidine without being given Ro 5-2807.

The drug was then used at a rate of 2·2 mg./kg. on an animal which had been caught in a net. This immobilised the wildebeest within five minutes. The muscle relaxation phase lasted for 40 minutes and the animal was tranquillised for a total period of approximately 30 hours. Marked ataxia was evident during this period. The dose was reduced to 1·8 mg./kg. some months later when the animal was transported. This dose produced incomplete tranquillisation for approximately 20 hours, but was effective in quietening the animal during the three-hour journey.

Anxiolysis without muscle relaxation or ataxia, was produced in the third wildebeest with a dose of 1·3 mg./kg. and the effect wore off within six hours. The same animal later received a dose of 1·1 mg./kg. and was then transported for a period of three hours. In this instance muscle relaxation as well as anxiolysis was evident after five to 10 minutes, and the drug effects only wore off after approximately 20 hours.

The effects of being transported on an animal treated with Ro 5-2807 were again evident in wildebeest No. 4. Whilst in the quarantine pens, a dose of 2·0 mg./kg. was administered which immobilised the animal for 20 hours, and tranquillisation was evident for a further 10 hours. Some months later the same wildebeest received a dose of 1·4 mg./kg. and was then transported. The effects were exactly the same as in the previous instance, despite the reduction in dosage.

Respiration and circulation remained essentially normal in treated wildebeest.

TABLE 1: THE EFFECT OF RO 5-2807 ON GIRAFFE

No.	Sex	Estimated weight (Kg.)	Dosage (mg./kg.)	Time before onset of effect	Immobilisation	Tranquillisation	Duration of effect	Remarks
1	♂	180	1·8	± ½ hour	—	+	±10 hours	Marked anxiolysis and ataxia
			1·0	±4½ hours	—	+	±10 hours	,,
			1·0	±4 hours	—	+	±10 hours	,,
2	♀	225	1·3	± ½ hour	+	+	Immobilisation: 5½ hours Sedation: ±10 hours	Legs only affected Ataxia after rising
3	♀	200	1·5	± ½ hour	+	+	Immobilisation: 5 hours Sedation: ±12 hours	Slight ataxia
			1·1	±3 hours	—	+	?	,,
			1·4	±3 hours	—	+	?	,,
4	♂	180	1·4 1·3	± ½ hour	—	+	± 9 hours	No symptoms other than anxiolysis
5	♀	225	1·3	± ½ hour	—	+	±10 hours	Hypnosis
			1·3 1·3	± ½ hour	—	+	±20 hours	Hypnosis. Second dose given 9½ hours after initial
6	♀	320	1·3	± ½ hour	+	+	Immobilisation: 7 hours Sedation: ±15 hours	Complete relaxation of neck and limbs
7	♂	320	1·3	± ½ hour	+	+	Immobilisation: ± 5 hours Sedation: ± 8 hours	Neck and limbs relaxed, Relatively rapid recovery.
8	♀	160	1·3	± ½ hour	+	+	Immobilisation: 6 hours Sedation: 40 hours	Neck and limbs relaxed. Ataxia noticeable for 30 hours after administration.
9	♂	270	1·3	± ½ hour	+	+	Relaxed limbs during transit. Stood up immediately after release into pen.	Calm when not disturbed. Slight ataxia.
10	♀	250	1·1	± ½ hour	—	+	± 5 hours	Incomplete tranquillisation.
11	♀	110	1·1	± ½ hour	—	+	±36 hours	Anxiolysis and ataxia evident for ± 30 hours.
12	♀	180	1·1 1·3	1 hour	—	+	±30 hours	Second dose given 8 hours after first. Initial dose caused slight sedation.

ORIBI

Ro 5-2807 has been used with success on 62 oribi, four of which were immobilised, the remainder being caught in nets. Each animal was weighed before administration of the drug.

In an initial batch of 16 animals a dosage of 1·4–2·6 mg./kg. was employed which in most cases produced muscular relaxation and tranqillisation within 20 minutes. In one case a dose of 1·9 mg./kg. failed to produce complete tranquillisation after 30 minutes and an additional dose of 0·6 mg./kg. was given. The animal relaxed within seven minutes after the second dose. In a second case 2.3 mg./kg. failed to immobilise a ram after 50 minutes; an additional 0·3 mg./kg. produced muscular relaxation within 10 minutes. In a third case 1·4 mg./kg. produced incomplete tranquillisation after 15 minutes and was supplemented with 0·9 mg./kg. which ensured the full effect within five minutes.

In all cases, muscle relaxation was evident for at least six to seven hours. The limbs only were affected, the head and neck remaining erect. In these cases muscle relaxation was a desirable feature of the drug's action, as the animals had to be transported for periods of up to five hours.

Observation on the duration of the drug's effects were rendered difficult by the fact that the animals were released during the late afternoon. Full recovery was effected during the night, i.e. 10 to 18 hours after administration of the drug.

The results obtained with the first 16 oribi are summarised in Table 3.

A further 41 oribi, which were in relatively poor condition, were caught later in the year. A dosage of 2·2 mg./kg. was used and this produced similar effects, with muscle relaxation for six to seven hours. However, the duration of the drug's action was greatly extended due to the

TABLE 2: THE EFFECT OF RO 5-2807 ON BLUE WILDEBEEST

No.	Sex	Estimated Weight Kg.	Dosage	Time before onset of effect	Immobilisation	Tranquillisation	Duration of effect	Remarke
1	♀	115	0·65	Given while animal immobilised	—	—	—	Animal died from effect of immobilising drug
2	♀	135	2·2	5 minutes	+	+	Immobilisation—40 minutes Tranquillisation—30 hours	Marked ataxia until recovery.
			1·8	±20 minutes	—	+	±20 hours	Effectively tranquillised for 3-hour journey
3	♀	255	1·3	5–10 minutes	—	+	6 hours	No symptoms other than anxiolysis.
			1·1	5–10 minutes	+	+	±20 hours	Combined effects of drug and 3-hour journey.
4	♀	180	2·0	5–10 minutes	+	+	Immobilisation—20 hours Tranquillisation—at least 30 hours.	Drowsed when not disturbed otherwise alert with head erect.
			1·4	5–10 minutes	+	+	±30 hours	Limbs only affected. „

TABLE 3: THE EFFECT OF RO 5-2807 ON ORIBI

No.	Sex	Actual weight Kg.	Dosage mg./kg.	Time before onset of effect	Immobilisation	Tranquillisation	Remarks
1	♀	18·2	2·2	9 minutes	+	+	Limbs immobilised, head and neck erect
2	♀	15·9	2·2	—	+	+	Immobilised with Gallamine triethiodide
3	♂	9·1	2·2	—	+	+	Overdosed with Gallamine triethiodide
4	♂	15·9	2·2	15 minutes	+	+	Limbs immobilised, head and neck erect
5	♂	15·9	1·4 0·9	20 minutes	+	+	Second dose 15 minutes after initial dose
6	♀	15·9	1·4	15 minutes	+	+	Limbs immobilised, head and neck erect
7	♀	18·2	1·7	15 minutes	+	+	,,
8	♀	15·9	1·4	15 minutes	+	+	,,
9	♀	14·1	2·1	10 minutes	+	+	,,
10	♂	15·0	2·0	10 minutes	+	+	Limbs immobilised, head and neck erect
11	♀	15·9	1·9 0·6	37 minutes	+	+	Second dose given 30 minutes after first
12	♂	14·5	2·1	10 minutes	+	+	Limbs immobilised, head and neck erect
13	♂	13·6	1·6	5 minutes	+	+	Exhausted from chase. Head erect after 2½ hours
14	♀	9·1	2·2	10 minutes	+	+	Limbs immobilised, head and neck erect
15	♀	5·9	2·5	5 minutes	+	+	,,
16	♂	15·5	2·3 0·3	60 minutes	+	+	Second dose given 50 minutes after first

poor condition of the animals After the muscle relaxation phase had passed, the oribi remained lying on their briskets for 24–48 hours, rising and lying down again intermittently. The last five animals to be caught were given reduced doses of 1·1 mg./kg. The effects were exactly as described above.

When evaluating the effect of a tranquilliser on wild animals, note should be made of their physical condition and in this instance poor condition and physical exhaustion of the oribi materially affected the drug's action.

IMPALA

Impala are normally captured at night from vehicles equipped with strong spotlights. As the animals either have to be held by hand for long periods, or else kept in closed crates for a number of hours, tranquillisers are of great value in reducing stress and possible injury.

Ro 5-2807 was administered initially to seven impala lambs, each weighing approximately 18 kg. at a dosage rate of 5 mg./kg. Effects were noted after five minutes and muscle relaxation of the limbs and neck occurred. This effect lasted for approximately 12 hours. Anxiolysis was evident for a further 10 hours.

The dosage was subsequently reduced, and a further eight lambs were given 2·2 mg./kg. Muscle relaxation of the limbs and neck was again evident within five minutes, and after one to two hours, the animals lay on their briskets with head and neck erect. The recovery from the muscle relaxation phase took a further two to four and a half hours. Anxiolysis was again evident for a further 10 hours.

Following these initial trials, approximately 50 impala lambs, ages varying from five to seven months, were caught and Ro 5-2807 was administered at a rate of 1·0 to 1·3 mg./kg. with an average dose of 1·1 mg./kg. The effect was observed to occur within five to fifteen minutes and anxiolysis was the main feature. Slight ataxia and a tendency to lie down for the first three to four hours after drug administration were common features in most cases.

No side effects on heart-beat or respiration have been noted.

Immobilisation is not normally required when capturing impala and keeping them in quarantine pens, hence doses of Ro 5-2807 higher than 1·3 mg./kg. are not indicated at present.

ELAND

Ro 5-2807 has been used on 11 eland, of which six were young mature females, the remainder being calves. All the animals were captured from motor vehicles.

Because the animals were to be transported in crates for considerable distances, it was deemed inadvisable to give high doses of the drug, which would have resulted in the animals remaining recumbent for long periods. In all cases, the dose of Ro 5-2807 given varied from 0·8 to 1·1 mg./kg. All the calves received 1·1 mg./kg.

The latent period varied considerably: one animal became calm 20 minutes after drug administration, two others became tranquil 30 minutes and 40 minutes after the drug injection

respectively. The calves, all aged from two to three months, took as long as 60 minutes before they calmed down.

Three animals showed an incomplete response to the initial doses and received repeat doses, which in two cases ensured the desired effect within 20–30 minutes, the remaining animal appeared to offer resistance to the drug's action and was not treated again.

As the animals were kept in crates for periods varying from 18 to 24 hours, they tended to remain calm and tractable even after the drug's effects wore off. They were normal when unloaded.

RED HARTEBEEST

As in the case of eland, hartebeest were captured from motor vehicles, and placed in wooden crates as soon as possible. Nine antelope were captured of which two were males. Of the seven females, one was heavily pregnant, and the others may possibly have been pregnant.

Doses of Ro 5-2807 given ranged from 0·9 to 1·3 mg./kg., and at these dosage rates an anxiolytic effect only was noticeable. A period of 30–45 minutes elapsed before the full effect of the drug was noticeable.

Once the animals had calmed down, they showed remarkably little response to handling, although as soon as they were released from the crates, they behaved normally.

CONCLUSION

Ro 5-2807 has two important effects: it produces muscle-relaxation and an anxiolytic effect.

The use of the drug on six species of African ungulates suggests that a dosage of 1·1 to 1·3 mg./kg. given intra-muscularly will produce a satisfactory taming effect; doses higher than this will result in muscle relaxation.

In its present oil-based form, the drug has a relatively long latent period when doses up to 1·3 mg./kg. are employed. Doses higher than this tend to shorten the latent period.

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SUMMARY

The use of an experimental psychotherapeutic drug, Ro 5-2807 (Roche) on six species of wild game is described. The drug was used on giraffe *Giraffa camelopardalis* at dosages varying from

1·0 to 1·8 mg./kg.; on blue wildebeest *Connochaetes taurinus* at dosages ranging from 0·65 to 2·2 mg./kg.; on oribi *Ourebia ourebi* at dosages ranging from 1·4 to 2·6 mg./kg.; on impala *Aepyceros melampus* at dosage rates varying from 1·0 to 5·0 mg./kg.; on eland *Taurotragus oryx* at doses varying from 0·8 to 1·1 mg./kg.; and on red hartebeest *Alcelaphus buselaphus* at dosages which ranged from 0·9 to 1·3 mg./kg. Ro 5-2807 produced either an anxiolytic effect or anxiolysis plus muscular relaxation, depending on the dosage employed and the physical and mental state of the animal.

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