Evaluation of "Copacaps" in deer

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Introduction

The results of the survey of deer liver copper (Cu) concentrations conducted by us (Harrison et al., 1989b) justified the findings of Familton et al. (1985) and later those of Killorn and Wilson (1990) that Cu is the trace element of major concern to deer veterinarians and farmers. Investigations of effective methods of supplementation have therefore been warranted.

Earlier work by us (Harrison et al., 1989a) and Lawrence (1987) suggested that injectable Cu preparations were unable to maintain adequate liver Cu levels of deer, apparently due to their high rate of Cu excretion. Recent experiments by Booth et al. (1989) and Familton and Harrison (1992) have investigated the effectiveness of Cu oxide particles for long term supplementation of deer, demonstrating that a single dose will produce 4 to 6 months protection against deficiency.

"Copacaps" (Rhone Merieux) is a commercially available product of cupric oxide (CuO) rods contained within a gelatin capsule, registered for the treatment and prevention of Cu deficiency in cattle, sheep and more recently, deer. This report describes an investigation into the effectiveness and safety of "Copacaps" in red deer.

The objectives were to determine the extent of Cu uptake by the liver and the duration of protection against deficiency. Consecutive liver biopsy and blood samples were collected from all animals to provide an accurate profile of body Cu status. Animals of 3 different age groups (mature, yearling and weaner stags) provided a range in live weights and therefore dose rates (mg Cu/kg live weight). Possible toxic effects of high doses of CuO were monitored by measuring blood concentrations of the liver specific enzymes aspartate transaminase, gamma-glutamyl transferase and sorbitol dehydrogenase.

Materials and methods

Animals
These comprised: 36 mature red deer stags, ranging in age from 3 to 9 years, with a mean initial live weight of 175 ± 4.4 kg;
16 yearling red deer stags, with a mean initial live weight of 98 ± 1.4 kg and
24 weaner red deer stags, with a mean initial live weight of 48 ± 1.3 kg.

Treatments
Animals within each of the age groups were ranked serially according to initial liver Cu concentration and allocated at random (n=8) to the treatment groups.

Treatments consisted of 2 doses of "Copacaps", given at an approximately 6 month interval, at the following dose rates:
First dose - mature stags 0, 10, 20 and 60 g;
- yearling stags 0 and 10 g;
- weaner stags 0, 5 and 15 g.

Second dose - mature stags 0, 10, 20 and 80 g;
- yearling stags 0 and 10 g;
- weaner stags 0, 10 and 20 g.

The mature and yearling stags were initially dosed in mid-February, while the weaner stags were initially dosed in late March, allowing a period of recovery post-weaning before sampling and dosing. The second dose was given to animals of all age groups in early September. For the duration of the experiment, all animals were allowed to graze the same ryegrass-white clover sward. Between months 3 and 6 this was supplemented with a silage of similar botanical composition.

Liver biopsy and jugular blood samples were taken from all animals except weaner stags initially and then 1, 2, 4 and 6 months after the first dose. Samples were obtained from the weaner stags initially then 1, 2 and 4 months after the first dose. Samples were obtained from animals of all 3 age groups at 1.5, 3.5 and 6.5 months after the second dose. Animals were weighed on the day of biopsy sampling after an overnight fast. We have found it necessary to fast animals overnight, reducing gaseous build-up in the alimentary tract and subsequent obstruction of the liver by the caecum.

The liver biopsy sampling technique of Familton (1985) for deer was modified to a slightly different point of entry, i.e., the ninth intercostal space and dorsally towards the midline of the animal. The forward direction of the trocar and cannula at a slightly steeper insertion angle remained ventral to the midline of the animal, thus avoiding the liver hilus. It was found that this insertion site, with the liver directly beneath the ribs and diaphragm, was faster and more successful in obtaining samples.

Results

Liver Cu concentrations
Mature stags - mean liver Cu of control animals declined from an adequate concentration pre-treatment to sub-marginal concentrations (< 100 µmol Cu/kg) during autumn and winter (Figure 1c). There was a subsequent increase in the mean concentration during summer. Treatment with "Copacaps" (10, 20 or 60 g) maintained liver Cu concentrations above the threshold of deficient Cu status (100 µmol/kg) for at least the first 6 months. Subsequent retreatment of mature stags (10, 20 or 80 g) resulted in significant increases in liver Cu concentrations for a further 6 months. The dose rates at 60 and 80 g CuO resulted in liver Cu concentrations less than would be expected in animals suffering from Cu toxicity, indicating a safety factor of between 4 and 8 times the recommended dose.

Yearling stags - mean liver Cu concentrations are presented in Figure 1b. Apart from a transient increase at 2 months after the first dose, the mean

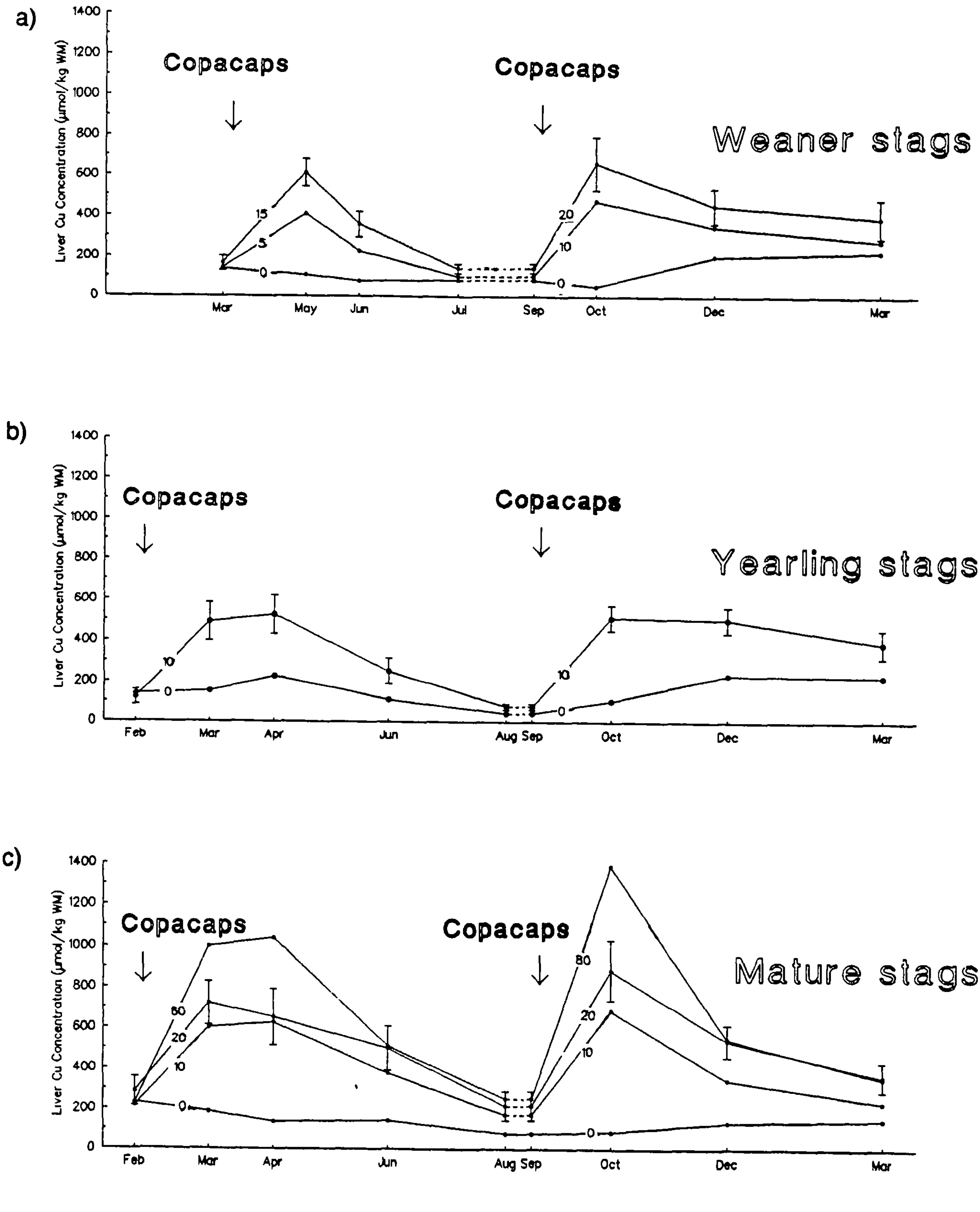

Figure 1. Mean liver Cu concentrations (µmol/kg WM) of a) weaner, b) yearling and c) mature stags after each of 2 doses of "Copacaps". Vertical error bars denote the standard error of the differences between means for all treatment groups within each age group.

concentrations of control animals decreased to sub-marginal levels during the period of autumn and winter, also increasing during summer. Mean concentration of treated stags (10 g) was significantly elevated above that of untreated controls up to 4 months after dosing, but this difference was non-significant at 6 months. Retreatment with 10 g CuO resulted in a significantly higher mean liver Cu concentration 6 months after dosing.

Weaner stags - mean liver Cu concentrations are presented in Figure 1a. Mean concentration of control animals declined to less than 100 µmol/kg during winter and also increased during summer. Mean liver concentrations of treated animals (5 or 15 g) increased significantly after the first dose. However, at 4 months after treatment, the mean concentration of animals receiving 5 g CuO was not significantly different to that of the control animals. Subsequent retreatment with 10 or 20 g CuO resulted in elevations in mean liver Cu concentrations which were significantly higher than those of control animals 6 months after dosing. A safety factor of at least 4 is in keeping with the results of the older animals.

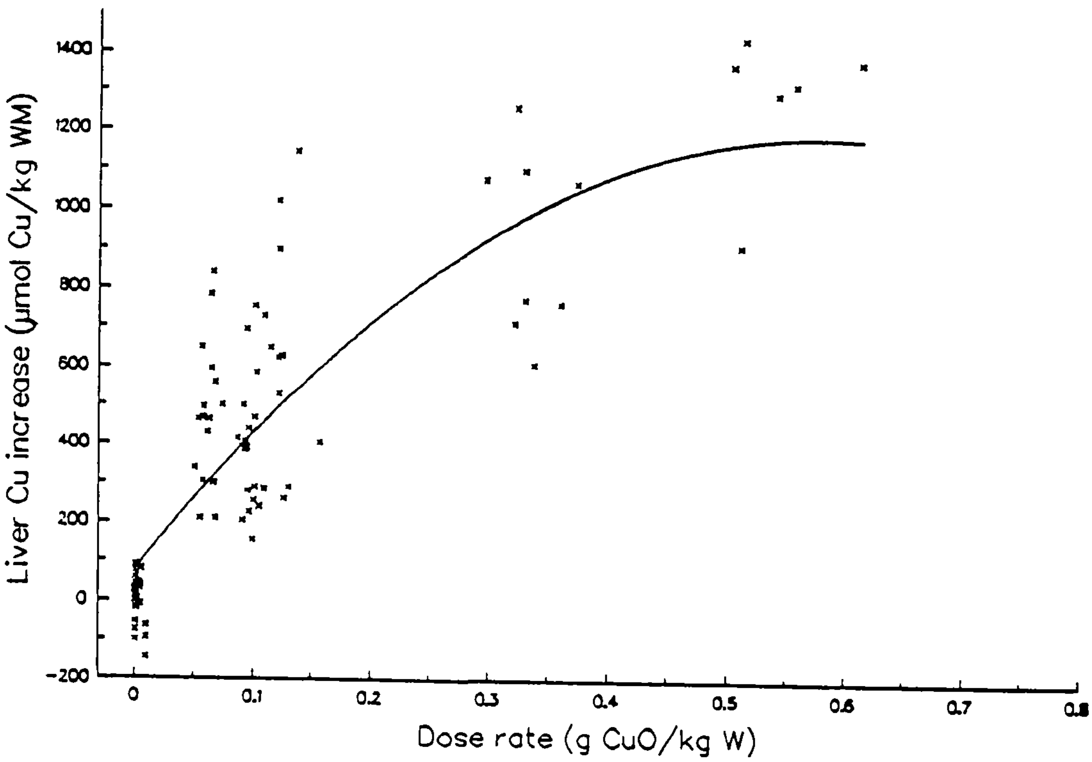

Figure 2. The response in liver Cu concentration (µmol/kg WM) of mature, yearling and weaner stags to increasing dose rate of "Copacaps" (g CuO/kg live weight) as measured 4 to 6 weeks after dosing.

Plasma concentrations of liver specific enzymes

Preliminary analysis indicates that there were no significant changes in the plasma concentrations of liver specific enzymes aspartate transaminase, gamma-glutamyl transferase or sorbitol dehydrogenase, confirming that even at 4 to 8 times the recommended dose rate, there was no risk of Cu toxicity.

Live weight changes

Mean live weight changes of treatment groups within age are presented in Table 2. Data of the yearling stags is in bold type; this age group displayed a significant response in growth rate to Cu supplementation, in particular subsequent to the second dose of CuO.

Table 2. Mean changes in live weight (kg) of each treatment group within age subsequent to the first dose (February to August - mature and yearling stags; March to July - weaner stags) and to the second dose (September to March - all age groups).

		live weight change (kg) after dose	
age	dose (g)	first dose	second dose
mature	0	-21±3.1	27±3.9
	10	-23±3.8	24±4.3
	20	-24±2.5	27±5.3
	60/80	-23±2.3	28±2.8
yearling	**0**	**6±0.3**	**30±1.2**
	10	**6±0.7**	**36±1.7**
weaner	0	5±2.5	39±0.9
	5/10	5±1.4	42±1.2
	15/20	4±1.8	41±2.6

Plasma Cu concentrations

Mean plasma Cu concentrations of all three age groups at the different sampling times are given in Table 3.

Table 3. Mean (±SEM) plasma Cu concentrations (μmol /l) of the treatment groups of each age group at each of the sampling times.

		Plasma Cu concentrations (μmol /l)							
		months after first dose					months after second dose		
age	dose (g)	0	1	2	4	6	1.5	3.5	6.5
mature	0	10±0.14	11±0.19	16±0.48	8±0.35	4±0.28	3±0.26	7±0.30	10±0 29
	10	11±0 09	13±0.19	18±0.28	12±0.21	8±0.24	11±0.21	12±0 29	13±0 45
	20	11±0 18	12±0 23	19±0.35	11±0 18	8±0.21	11±0.19	12±0 50	13±0 60
	60/80	11±0.13	14±0 12	18±0 39	11±0 23	8±0.22	11±0.25	12±0.51	15±0.37
yearling	0	12±0 22	13±0 26	12±0 18	8±0.34	5±0.24	8±0.25	9±0 38	12±0.33
	10	13±0.13	15±0.16	15±0 20	11±0 32	9±0.25	15±0.19	12±0.32	13±0 26
weaner	0	10±0.17	7±0 11	9±0 18	4±0 08		7±0.39	10±0.22	10±0 27
	5/10	11±0.16	10±0 24	12±0 13	7±0 29		11±0.32	12±0.14	11±0.19
	15/20	11±0.12	11±0.15	12±0.14	8±0 24		14±0.31	10±0.18	10±0.15

Discussion

The decrease in mean liver Cu concentrations of control groups of all 3 age groups to below 100 µmol/kg and the resultant decrease in mean plasma Cu concentrations to below 8 µmol/l (a relationship similar to that described by Mackintosh et al., 1986) have indicated the requirement for supplementation and justified the use of these animals on this property for an investigation of Cu supplementation. Pasture samples collected for mineral analysis were extremely contaminated from an unknown source, however indications are that Cu concentrations during autumn and winter were approximately 4 to 6 mg/kg DM, while molybdenum concentrations had increased from less than to greater than 1 mg/kg DM.

It is apparent that the availability of dietary Cu was insufficient to maintain either liver or blood Cu levels during autumn and winter. Such decreases in Cu status during autumn agree with our previous, unpublished results of investigations of animals on this property. Supplementation with Cu to protect deer on this property against deficiency would appear to be most critical during the autumn to spring period. That the decline in Cu status during autumn and winter was similar across all age groups indicates that the rut-induced inappetance of mature stags had little effect on their liver Cu concentrations and the availability of dietary Cu was probably of greater importance.

"Copacaps" CuO needles given to mature and yearling stags at appropriate dose rates (i.e., 10 - 20 g/head) effectively raised liver Cu concentrations of treated animals for 6 months. Such dose rates are approximately equivalent to 60 - 120 mg Cu/kg live weight. Although the dose rate to the weaner stags (100 mg CuO/kg live weight) was equivalent to that of the older stags, the period of prophylaxis was approximately 4 months.

Liver Cu concentrations of mature and yearling stags reached their maxima approximately 6 weeks after dosing, a period similar to that observed in cattle (Judson et al., 1982; Langlands et al., 1986). However, this maximum was attained earlier in treated weaner stags, estimated at 4 weeks. A similar difference between young and mature sheep or cattle has also been observed (Langlands et al., 1986). It is suggested that this may be due to the smaller stomachs of the weaner stags. This may result in a lower retention time of the particles in the rumen/reticulum and hence in the abomasum, where release of the Cu occurs. Frequent dosing of young animals may therefore be required to maintain adequate liver Cu reserves.

That there was no significant difference in live weight changes between treatment groups of mature stags was expected. The significantly higher (6 kg) mean growth rate of treated over control yearling stags occurred only after the second dose of CuO, even though the control animals were improving in Cu status during this period. That there was no significant difference in growth rate between treated and control weaner stags, even though the control animals were of a similar low Cu status to the untreated yearling stags serves to highlight the complexity of the relationship between supplementary Cu and animal response.

It is probable that maintenance of elevated liver Cu levels for up to 12 months following, a single CuO dose is unlikely. The curvilinear response in liver Cu concentrations to increasing dose rate (Figure 2), together with the reported high apparent excretion rate of Cu by deer (Harrison et al., 1989a) demonstrates the necessity of smaller, more frequent doses of CuO rather than single, large doses. However, it is possible that timing of dosing, to coincide with shortfalls in availability of dietary Cu in particular areas or on specific farms may be as effective at preventing the effects of Cu deficiency as the maintenance of elevated liver Cu levels for 12 months.

The slow release nature of the product has allowed dosing at high levels (up to 80 g - equivalent to 4 to 8 times the recommended dose) without apparent adverse effect on the health or integrity of the liver. In conclusion, "Copacaps" has proved to be an effective and safe product for Cu supplementation of deer.

References

Booth, D H , P R Wilson and A M Alexander, 1989. The effect of oral oxidised copper wire on liver copper in farmed deer N Z. Vet J. 37(3): 98-101.

Familton, A. S., 1985. A liver biopsy technique for use in red deer. Proc. deer vet course. Deer Branch N Z Vet. Assoc. 2: 60-63.

Familton, A. S., D. O. Freudenberger and A. R. Sykes, 1985. Trace elements in deer. Proc deer vet course. Deer Branch N.Z. Vet. Assoc. 2: 32-38.

Familton, A S. and T J. Harrison, 1992 Copper supplementation of sheep, goats and deer - effect, duration and toxicity. Proc Sheep and Beef Cattle Society of N.Z. Vet Assoc (in press).

Harrison, T. J , A. R. Sykes and A S Familton, 1989a Efficacy of Coprin in deer and sheep An evaluation and comparative study. Proc. N.Z. Soc. Anim. Prod. 49: 11-14

Harrison, T. J , A. R Sykes, A S Familton and R McLaren, 1989b Copper levels in livers of red deer in the South Island and their relationship with soil group Proc deer vet course. Deer Branch N.Z. Vet. Assoc. 6: 158-162.

Judson, G. J., D. W. Dewey, J. D. McFarlane and M J Riley, 1982 Oxidised copper wire for oral therapy in cattle. In Trace element metabolism in man and animals - 4. pp 187-189. Proc. 4th Int. Symp. on trace elements in man and animals Perth, Australia.

Killorn, K and P. R. Wilson, 1990. Copper: a review Proc. deer vet course Deer Branch N.Z. Vet. Assoc. 7: 183-194.

Langlands, J. P., J E. Bowles, G. E. Donald and A. J. Smith, 1986 Trace element nutrition of grazing ruminants 1. Degree of oxidation, diet, frequency of dosing and location in the gastro-intestinal tract as factors affecting the ability of oxidised copper wire to promote hepatic copper storage Aust. J. Agric. Res. 37: 179-188

Lawrence, D. W , 1987. Copper supplementation of deer: Trial work Proc deer vet course. Deer Branch N.Z Vet. Assoc. 4: 189-193.

Mackintosh, C. G., P. R. Wilson, N. S. Beatson, K Turner and P. Johnstone, 1986 Preliminary report of the liver.serum copper relationship in red deer. Proc. deer vet course Deer Branch N Z Vet Assoc 3 156-163