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TESTING A NEW FORMULATION OF IVERMECTIN (IVOMEC POUR-ON & BOLUS) AS BROAD SPECTRUM PARASITICIDE

By

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SUMMARY

Two new formulations of ivermectin (MSD AGVET), Ivomec pour-on used for cattle in a dose of 1ml/10kg.b.w. and Ivomec bolus used per mouth for sheep in a dose of 1/2 bolus for each 25kg.b.w. (10 mg/50 kg.b.w.), were tested for control of natural infestation by gastrointestinal nematode parasites (G.I.N.) in cattle and sheep as well as for treatment of mange infection in sheep

The two drugs showed promising results in the form of freeing the treated animals from the target parasites by a percentage varies from 60-100% (in a mean of 85%) and decrease in the mean egg/gram feces (EPGF) from 695 on day zero to 15 EPGF on 35th day post-treatment (d.p.t.) for the pour-on form and 80-100% in sheep G.I.N. with marked decrease in the mean total EPGF from 756 on day zero to 8.3 EPGF in 28th d.p.t.

The bolus form succeeded in eradication of mange from the treated sheep by an efficacy varying from 82.69-100%. The two drugs showed absolute protection for the treated animals till 21st d.p.t. and very marked decrease in EPGF even for the still positive animals till end of the observation period.

Cooperia, Nematodierus and *Trichuris* species appear slightly less susceptible to the used dose of the drugs than the other gastrointestinal nematode larvae.

Concerning the pour-on form, the drug was easily administered, safe for the administrator, rapidly absorbed and did not show any post administration reaction while the bolus form needs some precautions during adminstration.

It is worthy to mention that changing the mode of IVOMEC administration from injection to topical or swallowing way did not reflect the previous successful market known results of Ivomec injection, but it improved the drug application and use without decreasing its parasiticidal efficacy.

INTRODUCTION

Chemicals still as an important part in the efforts introduced to control different parasitic diseases and they remained as the easily available means of control during the last several years. Ability of the parasites to develop a resistance against the used drugs was reduced via the use of new modern synthetic Macrolactons as Ivermection (Campbell and Benz, 1984)

Ivermectin developed and manufactured by Merck Sharp and Dohme L. (MSD-AGVET) under a trade name Ivomec, which gave promising results against most of cattle parasites as Ivermectin 1% subcutaneous injection in a dose of 0.2mg/kg.B.W. (Cramer et al., 1988)

Improvement of the method of application to become an easily topical way for large ruminants and a bolus administered per mouth for small ruminants facilitates the application of the drug away from the injection problems of the previously available Ivermectin.

In the present study two new formulations of Ivomec (Ivomec pour-on for cattle and Ivomec bolus for sheep), were tested in their recommended doses for treatment of natural gastrointestinal nematode infestation in cattle and sheep as well as mange infection in sheep.

The drugs were tested in three separate experiments in naturally infested cattle and sheep to fulfill the requested rules of the Egytpian drug allowances authority to accept the drug registration for field use in Egypt.

MATERIAL AND METHODS

I-Drugs:-

a- Ivomec Pour-on solution containing Ivermectin 0.5%W/V. (MSD-AGVET) USA, (fore cattle).

b- Ivomedc Bolus each contain 10 mg of Ivermectin, (MSDAGVET) USA, (for sheep).

2- Dose and administration:-

a- For pour-on: 1ml per 10 kg. cattle body weight (500 mg/kg.b.w.), applied along the mid-line of the back in a narrow strip between the withers and tail-head through a "Squeeze-Measure-pour System" supplied with the product.

b- For bolus: 1/2 bolus for each 25kg sheep live weight, 2 bolus for sheep greater than 75kg. given orally by hand.

3- Animals:

a- Catlle for testing Ivomec pour-on:

Twenty three cattle (6 male and 17 female) of 3-4 years old, 300-350 kg live mass heavily infested with different gastrointestinal parasitic nematodes (G.I.N.) were selected in Messier governor farm in Kafr El-Shikh Governorate, Egypt.

Twenty animals were divided into 4 groups (5 each) according to the total G.I.N. eggs per gram of feces (EPGF) for testing the drug while three cattle-representative for the different level of infection- were kept as non-treated animals (control).

b- Sheep for testing Ivomec bolus:

A total of 200 local breed ewes were examine for natural infestation by different G.I.N. an also for different types of mange in a priva farm in El-Fayoum Govrorate, Egypt. Eight sheep having the highest level of nematoc EPGF were allocated into 8 groups (10 each

Five groups (50 sheep) were treated by the bolus to evaluate the efficacy of the drug against the different round worms previously detected in these aniamls, while the rest of the animals (3 gorups) were left as a control without treatment.

Fecal samples were collected from all animals (cattle and sheep) at days, -7, Zero, 7, 14,21, 28 and 35th days post-treatment (d.p.t.) Total number of different G.I.N. eggs/gm. of feces were calculated in each time using the Mc-Master technique according to Soulsby (1982), while a new technique using two sieve system "fluke finder" technique used for detection of *Fasciola* and *Paramphistomum* species eggs per gram of feces according to Malone et al. (1984).

Cultivation of the collected fecal samples were done using the modified Baermann technique and the detected larvae were identified according to Burger & Stoye (1968). The larvae were counted relatively for each individual animal where the mean number per animal in each group was calculated.

Efficacy of the drugs was calculated according to the disappearance of the target eggs from the feces of the treated animals as well as through the decrease in the man egg/gram of feces for all animals before and after treatment using the following equation:-

Clearance% = a-b/a X 100 where,

a= mean number (of aniaml, EPGF or mite) recorded at zero day.

b= mean number (of aniaml, EPGF or mite) recorded at day of observation.

Concerning the efficacy of Ivomec bolus against mange infection in sheep, another 22 infested sheep with different degrees of *Psoroptes* species mite were allocated into two groups, first of 17 animals exposed to treatment by the drug, while the other 5 animals representing the different levels of infection were kept as a control without treatment.

Diameter and site of the lesion in the affected areas were recorded for all of the affected aniamls.

Skin scrapings were collected from all animals at days, -7, zero, 7, 14, 21, 28 and 35uth d.p.t. The samples were treated using Sodium hydroxide 10% solution where the mite types were identified according to Soulsby (1982). The mean number of mite per microscopic field was calculated in each case.

The clearance rate was calculated mathematically according to the previous equation.

The animals in the three experiments remained under observation during the first 3 hours after medication where any abnormality in the site of application, or, in the general health condition of the animals was recorded.

RESULTS

1- Efficacy of Ivomec pour-on aganist gastrointestinal nematodes of cattle:-

The data displayed in Table (1) showed the mean number of EPGF for the different parasites detected in the examined cattle gorups at the begining of the experiment (day zero). The data showed that nematode eggs varied from 400-1200 EPGF with mean number of 695 EPGF per aniaml, while the three control cattle showed 600, 800 and 1000 EPGF with mean number reached to 800 EPGF per animal.

Other parasites as *Fasciola, Paramphistomum* and *Moneizia* species eggs were detected in different numbers in some aniamls in both groups as in Table (1).

Table (2) showed the percentage of different types of gastrointestinal larvae detected after cultivation of the collected fecal sampels for both treated and control animals. Five types of larvae were recorded including *Trichostrongylus* species (9.75% and 8%), *Ostertagia* species (35.5% and 29.0%), *Haemonchus* species (33.25% and 13.25%), *Cooperia* species (13.25% and 12.0%) and *Nematodirus* species larvae (8.25% and 15.0%) in both groups respectively.

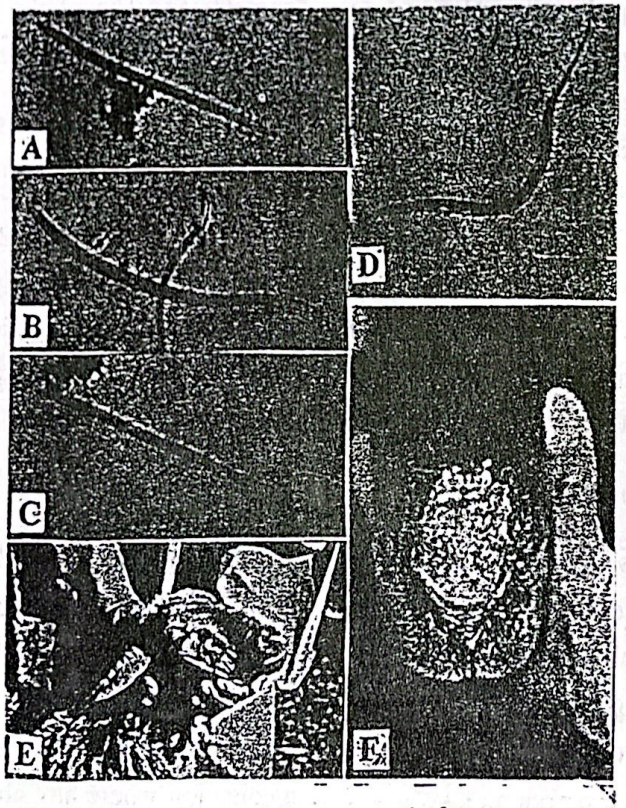

Fig. (1): Parasites detected from sheep before treatment
1-A) *Cooperia* species larva (X10)
1-B) *Ostertagia* species larva (X 10)
1-C) *Haemonchus* species larva (X 10)
1-D) *Nematodirus* species larva (X 10)
1-E) Mange infection in whole sheep face.
1-F) Mange infection in circular area in sheep nose.

Table (1) Mean number of eggs/gram feces for different parasites detected in the examined cattle groups on day "zero" of the experiment.

Group No.	Detected parasites							
	G.I.N. eggs		*Fasciola eggs*		*Moneizia eggs*		*Paramphistomum eggs.*	
	Low-high	Mean No.	Low-High.	Mean No.	Low-High	Mean No.	Low-High	Mean No.
Group I	1000-1200	1080	4-8	5.6	200-300	200 (3 animals)	3-6	4.5 (2 animals)
Group II	700-900	780	4-8	6.0	200	200 (one animal)	4-8	5.6 (3 animals)
Group III	500-600	520	2-6	3.6	100&200	150 (2 animals)		
Group IV	400	400	1-8	3.6 (3 animals)			1-5	2.8
Mean/treated animal	400-1200	695	1-10	4.7	100-300	183.33	1-8	4.3
Mean EPGF/control non treated animal	600-1000	800	3-6	4.3	200	200 (one animal)	2-4	3.33

Table (2): Different types of nematode larvae detected in the cultivated cattle fecal samples on day " Zero"of the experiment.

Group No.	Mean % of the different larvae in 100 counted larva						
	Total *G.I.P* eggs detected		*Trichostrongylus spp.*	*Ostertagia spp.*	*Haemonchus spp.*	*Cooperia spp.*	*Nematodirus spp.*
	Low-high	Mean No.	Mean %	Mean %	Mean %	Mean %	Mean %
Group I	1000-1200	1080	8	41	32	12	7
Group II	700-900	780	9	37	30	14	10
Group III	500-600	520	11	33	31	16	9
Group IV	400	400	12	30	40	11	7
Total			39	142	133	53	33
Mean/animal	400-1200	695	9.75	35.5	33.25	13.25	8.25
Mean EPGF/control non treated animal	600-1000	800	8	29	36	12	15

The results displayed in Table (3) revealed that application of Ivomec pour-on on the mid-dorsal line of G.I.N. infested cattle produced a marked decrease in the mean EPGF/treated aniaml reaching to zero in groups of low EPGF (group III & IV) while it decreased to 200 EPGF (3 animals) & 100 EPGF (2 animals) instead of 1080 & 780 EPGF in groups of high EPGF (I & II) respectively after 7 days post treatment.

At this time of observation (7th d.p.t.), 15 cattle from the treated 20 animals did not shed any nematode eggs in their feces giving a curability percentage of 75%. The percentage of egg free animals was increased to 85% from the third week post treatment till the days 35th of the observation. The mean G.I.N. eggs per gram for each treated aniaml decreased from 695 to 40 EPGF producing a drug efficacy of 94.25% at the end of the first week after treatment. The number of G.I.N. eggs/gram still in decreasing manner in the 5 previously recorded animals till the 21 st d.p.t. where only 3 treated cattle still shedding few numbers of eggs (100-200 EPGF) producing 15 EPGF as a mean egg per gram for each treated animal producing 97.30% efficacy in minimizing the mean total number of EPGF/treated animal.

It was worth to mention that no new infection was recorded in the treated animals till 35th d.p.t. (end of the observation period).

The mean EPGF for the control non treated cattle did not show marked difference during the observation period as in Table (3) .

Cultivation of fecal samples collected after treatment revealed that the eggs detected in the still positive five animals were mainly for *Cooperia* and *Nematodirus* species where they were the ony larvae still detected after cultivation of their fecal samples. The drug showing complete eradication of *Trichostrongylus*, *Ostertagia* and *Haemonchus* species larvae, where non of them could be recorded in the cultivated feces from the first week p.t. till end of the observation period (35th d.p.t.).

The drug succeeded also in decreasing the mean number of *Cooperia* and *Nematodirus* species by a percentage reached to 80% & 85% respectively in the treated cattle at 7th d.p.t. This percentage increased within the 21st d.p.t. where their larvae were detected in very few numbers only in two cattle of the treated animals showing an efficacy reached to 90% till the end of the experiment (35th d.p.t.).

The drug did not show any efficacy against the other parasites present randomly in the treated animals as *Fasciola, Paramphistomus* and *Moneizia* species as in Table (4).

Concerning the side effect of the drug, only one milking cow showed decrease in milk yield, a condition which did not appear in the othe milking cows. On the other hand, there is a clea improvement in the general health conditions o the treated animals with disappearance of diarrhe from animals previously showing high egg coun per gram before treatment. Also no abnormalitie could be detected in the treated animals in th general health conditions, in the site of dru administration or even in the hand and respirator functions of the administrator.

2- Efficacy of Ivomec Bolus agains gastrointestinal nematodes of sheep:-

Sheep were used for evaluation of the other for fo the drug; Ivomec bolus, as recommended t

Table (3): Effect of Ivomec pour-on (1ml/10kg.b.w.) on the mean egg per gram of feces collected from the treated cattle during the observation period:

	Mean number of Gastro-intestinal nematode eggs / gram/animal post treatment (P.T.)										
Observation periods	On day 'Zero'		On day 7 P.T.			On day 14 P.T.	On day 21 P.T.	On day 28 P.T.	On day 35 P.T.	Mean efficacy %in the whole period	
Treated groups	Low-high range	Mean No.	Mean egg/gram/ animal	Efficacy % /free animal	Efficac/ egg/gram/ animal	Mean egg/gram/ animal	Mean egg/gram/ animal	Mean egg/gram/ animal	Mean egg/gram/ animal	Per free animal	Per egg/gram/ animal
Group I (5 animals)	1000-1200	1080	200 (3 animals)	40.0	88.89	200 (2 animals)	200 (2 animals)	200 (2 animals)	200 (2 animals)	60	92.60
Group II (5 animals)	700-900	780	100 (2 animals)	60.0	94.88	100 (two animal)	100 (one animal)	100 (one animal)	100 (one animal)	80	96.80
Group III (5 animals)	500-600	520	0.0	100	100	0.0	0.0	0.0	0.0	100	100
Group IV (5 animals)	400	400	0.0	100	100	0.0	0.0	0.0	0.0	100	100
Mean/treated animal	400-1200	695	40.0	75.0	94.25	30.0	15.0	15.0	15.0	85.0	97.30
Mean/control non treated animal (3 animals)	600-1000	800	866.6			766.6	800	533.3	633.3		

P.T. = Post treatement.

Table (4): Efficacy of Ivomec pour-on against enteric parasites of cattle.

Target Parasite	Time of observation															
	On day 7 P.T.			On day 14 P.T.			On day 21 P.T.			On day 28 P.T.			On day 35 P.T.			Mean efficacy
	*No.A .Exam	No. +Ve	Effic-acy	No.A. Exam	No. +Ve	Effic-acy	No..A. Exam	No. +Ve	Effic-acy	No..A Exam	No. +Ve	Effic-acy	No..A Exam	No. +Ve	Effic-acy	
Trichostrongy lus Larvae	20	0	100	20	0	100 %	20	0	100 %	20	0	100 %	20	0	100 %	100%
Ostertagia spp larvae	20	0	100	20	0	100 %	20	0	100 %	20	0	100 %	20	0	100 %	100%
Haemonchus spp larvae	20	0	100	20	0	100 %	20	0	100 %	20	0	100 %	20	0	100 %	100%
Cooperia spp larvae	20	4	80%	20	3	85%	20	2	90%	20	2	90	20	2	90%	87.0%
Nematodirus spp larvae	20	3	85	20	2	90%	20	2	90%	20	2	90%	20	2	90%	89.0%
Fasciola eggs	18	18	0.0 %	18	18	0.0 %	18	18	0.0 %	18	18	0.0 %	18	18	0.0 %	0.0%
Moneizia egg.	6	6	0.0	6	6	0.0 %	6	6	0.0 %	6	6	0.0 %	6	6	0.0 %	0.0%
Paramphistom-um egg	10	10	0.0 %	10	10	0.0 %	10	10	0.0 %	10	10	0.0 %	10	10	0.0 %	0.0%

No. A. Exam. = Total number of examined animals. ** No. + Ve = Number of positive animals.

the producing company, for control of G.I.N. and mange infection.

Concerning the treatment of G.I.N. in sheep, table (5) showed the original condition of the selected flock before treatment. The mean numbers of nematode EPGF reached to 756 (360-1150) per animal. In addition, *Trichuris* species eggs were recorded in 14 sheep only in a mean number of 257.1 (200-300) EPGF per infected animal only. Infection by G.I.N. in the selected control sheep varied between 460 to 970 EPGF with mean number of 706.6 per each sheep. *Trichuris* species eggs were recorded in 8 sheep only with a mean number of 175 EPGF for each infected sheep.

Fasciola, Moneizia and *Paramphistomum* species eggs were recorded in some of the treated and control sheep as shown in Table (5).

Cultivation of the fecal samples collected before treatment revealed the presence of 5 types of G.I.N. larvae in mean percentages of 36.4% & 38.33% for *Haemochus* species, 23% & 24 for *Ostertagia* species, 15% & 11% for *Trichostrongylus* species, 14.2% & 11.66% for *Cooperia* apecies and 11.4% & 15% for *Nematodirus* species larvae in both treated and control sheep respectively as shown in Table (6-A & B) and plate (1- A-D).

The results displayed in Table 7 cleared the treatment of 50 sheep which were naturally infested with G.I.N. by Ivomec-bolus per mouth induced complete disappearance of G.I.N. eggs from feces of 45 animals giving an efficacy rate of 90% directly after one week PT. Two animals; one in group IV and the other in group V showed nearly the same EPGF as that recorded before treatment (these 2 animals appear as they lose the dose, they were excluded from the experiment and teated separately).

The other three non-cured animals (from group of high G.I.N.) showed a marked decrease in the mean EPGF. One sheep had 200 EPGF of G.I.N., second one of 300 EPGF for G.I.N. and *Trichuris* species while the third one of 200 EPG mainly of *Trichur* is species.

Treatment resulted in a marked decrease in the mean EPGF for each treated animal from 756 EPGF before treatment to 32 EPGF on day 7th p.t. with reduction efficacy of 95.2%.

Weekly examination of these animals revealed that the remaining 3 positive cases still shed nematode eggs but the number of EPGF decreased to 100, 100 & 200 EPGF, this led to decrease in the mean of EPGF for each animal in the flock from 14.6 to 8.3 EPGF durig 14th to 28th d.p.t. and therefore the efficacy rate increased to 94% per cured aniaml.

At 35th d.p.t. other 3 (new) animals (from the groups that previously showed high EPGF) shed nematode eggs and there was an increase in the total EPGF of the original 3 aniamls to give a mean of 200 EPGF for the 6 animals at this day of observation.

In respect of the total efficacy of the drug during the whol experiment, the treated animals showed feces free from nematode eggs by a percentage of 92.5% while the rate of decreasing in the mean EPGF reached to 99.28%.

Table (5): Mean number of eggs/gram feces for different parasites detected in the examined sheep groups at day "zero" of the experiment.

(5-A): Treated groups:

Group No.	Detected parasites									
	G.I.N. eggs		*Trichuris eggs*		*Fasciola eggs*		*Moneizia eggs*		*Paramphistomum eggs.*	
	Low-high range	Mean No.	Low-High range	Mean No.	Low-High range.	Mean No.	Low-High range	Mean No.	Low-High range	Mean No.
Group I	1200-1400	1150	200-300	225 (4)	6-8	6.8			4-6 (6)	4.75
Group II	900-1100	1000	300	300 (2)	6-8	7.0	200-300	150(6)		
Group III	700-800	730			4-12	7.5			6-8 (5)	6.6
Group IV	500-600	540	200-300	280 (5)	4-6	4.6	200 (one)	200 (one)		
Group V	300-400	360	200-300	233 (3)	8-10	9.1			4-6 (3)	5.0
Total		3780		3600		35		350		16.35
Mean/animal	300-1400	756	200-300	257.1	6-10	7.0	200-300	175	4-8	5.5

(5-B): Control non treated groups:

Group No.	Detected parasites									
	G.I.N. eggs		*Trichuris eggs*		*Fasciola eggs*		*Moneizia eggs*		*Paramphisto mum eggs.*	
	Low-high range	Mean No.	Low-High range	Mean No.	Low-High range.	Mean No.	Low-High range	Mean No.	Low-High range	Mean No.
Group VI	900-1100	970			4-8	5.6				
Group VII	600-800	690	100-300	175(8)	2-4	2.8	200&300	150(2)	6-8(4)	6.75
Group VIII	400-500	460			6-8	7.0				
Total		2120		175		15.4		150		6.75
Mean/animal	400-1100	706.6	100-300	175(8)	2-8	5.13	200-300	150(2)	6-8	6.75(4)

G.I.N. = Gastro-intestinal Nematode.

Table (6): Different types of nematode larvae detected in the cultivated sheep fecal samples.

(6-A): Treated sheep groups:

Group No.	Mean % of the defferent larvae in 100 counted larva						
	Total *G.I.P* eggs detected		*Trichostrongylus spp.*	*Ostertagia spp.*	*Haemonchus spp.*	*Cooperia spp.*	*Nematodirus spp.*
	Low-high	Mean No.	Mean %	Mean %	Mean %	Mean %	Mean %
Group I	1200-1400	1150	18	22	40	9	11
Group II	900-1100	1000	13	24	33	17	13
Group III	700-800	730	14	21	35	18	12
Group IV	500-600	540	16	26	38	14	6
Group V	300-400	360	14	22	36	13	15
Mean/animal	300-1400	756	15	23	36.4	14.2	11.4

(6-B): Control non treated sheep groups:

Group No.	Mean % of the defferent larvae in 100 counted larva						
	Total *G.I.P* eggs detected		*Trichostrongylus spp.*	*Ostertagia spp.*	*Haemonchus spp.*	*Cooperia spp.*	*Nematodirus spp.*
	Low-high	Mean No.	Mean %	Mean %	Mean %	Mean %	Mean %
Group VI	900-1100	970	11	23	40	9	17
Group VII	600-800	690	12	25	36	12	15
Group VIII	400-500	460	10	24	39	14	13
Mean/animal	400-1100	706.6	11	24	38.33	11.66	15

The EPGF shed by the control non treated group fluctuated around the mean level. without marked change during the observation period (Table 7).

Cultivation of feccal samples collected from different sheep post treatment as in Table (8) revealed that at 14th d.p.t. and away from the two sheep losing the dose, *Trichostrongylus, Ostertagia* and *Haemonchus* species larvae disappeared completely from the treated sheep giving 100% susceptibility for the drug.

(The two sheep that lost the dose were excluded from the experiment and treated separately and showed consistent results).

Fecal culture of the three animals still having eggs in their feces cleared that, one animal still having *Nematodirus* and *Cooperia* species larvae, another animal having *Nematodirus* larvae and *Trichuris* eggs, and the third one having *Trichuris* eggs only in few numbers (Table 7). This gave an efficacy reached to 97.9% against Cooperia species larvae, 95.8% against Nematodirus larvae and 84.6% against Trichuris eggs at 14 d. p. t. This level of efficacy against the target nematode species was still effective till 28th d. p. t.

At 35th d. p. t. new infection appeared in another 3 animals. The first one showed *Nematodirus. Cooperia* and *Haemonchus* species larvae. The second sheep had *Nematodirus* and *Haemonchus* species larvae while the third one showed *Cooperia* species larvae only. There was a decrease in the efficacy of the drug against these 3 species (*Nematodirus, Cooperia* and *Haemonchus*) into 91.7%, 93.8% and 95.8% respectively. The mean efficacy of the drug during the whole observation period was 94.77%, 93.8% and 98.95% for the last three parasite species, respectively.

Similar to cattle the drug did not show any efficacy against *Fasciola, Paramphistomum* and *Moneizia* species eggs that were present randomly in the treated sheep as shown in Table (8).

3- Efficacy of Ivomec bolus against sheep mange:

Concerning the evaluation of ivomec bolus against sheep mange, data in Table (9) showed the condition of Psoroptes mite infection in 17 tested sheep and 5 control animals. The number of mite per prepared microscopic field (MPF) varied between 1-6 with mean of 3.0 MPF for the treated group and 2-4 MPF with mean of 2.6 MPF for the control sheep.The lesions before treatment encroached over the whole face (Fig 1-E) or were in the form of circumscribed areas of variable diameter (2-7cm) as in fig (1-F).

Examination of the previously selected and treated 17 sheep at 7th d. p. t. (Table 9) revealed complete disappearance of the mites from the microscopic field in 13 animals and decrease in their number in the other 3 sheep which were heavily fected before treatment, while one sheep appeared still had the same number of MPF and the lesion condition recorded before treatment (it may have lost the dose).

From these results it appeared that the drug gave an efficacy reached to 82.69% on day 7th p. t. and

Table (7): Effect of Ivomec bolus (1/2bolus/25 Kg.b.w.)on the mean egg per gram of feces collected from the treated sheep during the observation period:

Group No.	Mean number of Gastro-intestinal nematode eggs / gram/animal post treatment (P.T.)													
Observation periods	On day 'Zero'		On day 7 P.T.		On day 14 P.T.	On day 21 P.T.		On day 28 P.T.		On day 35 P.T.		Mean efficacy %in the whole period	
Treated groups	egg range low - high	Mean No.	Mean egg/gram/ animal	Efficacy % /free animal	Efficacy/ egg/gram /animal	Mean egg/gram/ animal	Mean egg/gram/ animal	Mean egg/gram/ animal	Efficacy % /free animal	Efficacy/ egg/gram/ animal	Mean egg/gram/ animal	Per free animal	Per egg/gram/animal
Group I	1200-1400	1150	200 (**) (2 animals)	80%	98.3%	200 (2 animals)	100 (2 animals)	100 (2 animals)	80%	98.3%	200 (##) (4 animals)	75.0%	98.6%
Group II	900-1100	1000	300 (**) (one animal)	90%	97.0%	300 (one animal)	200 (one animal)	200 (one animal)	90%	98%	200 (##) (2 animal)	87.5%	97.8%
Group III	700-800	730	0.0	100%	100%	0.0	0.0	0.0	100%	100%	0.0	100%	100%
Group IV	500-600	540	500 (*) (one animal)	90%	90.8%	0.0	0.0	0.0	100%	100%	0.0	100%	100%
Group V	300-400	360	400 (*) (one animal)	90%	89.9%	0.0	0.0	0.0	100%	100%	0.0	100%	100%
Mean/treated animal	300-1400	756	32 EPG (#)	90%	95.2%	14.6 EPG	8.3 EPG	8.3 EPG	94%	98.9%	25 EPG	92.5	99.28%
Mean/ control non treated animal	400-1100	706.6	675			687.5	637.5	533.3			620		

(*) These two sheep have the same number of egg/gm feaces recorded befor treatement , they are excluded from the experiment after this time.
(**) These three sheep have some eggs in their feaces but very few than that recorded befor treatement.
(#) EPG = mean egg per gram by dividing the total recorded eggs over 50 and then over 48 (total numberof the treated sheep).
(##) Appearance of new infection.

Table (8): Efficacy of Ivomec bolus (1/2 bolus/25Kg.b.w.) against different gastro-intestinal nematode larvae after cultivation of the collected fecal samples of the treated sheep.

Target Parasite	Time of observation															
Detected stages	On day 7 P.T.			On day 14 P.T.			On day 21 P.T.			On day 28 P.T.			On day 35 P.T.			Mean efficacy from 14-35th day P.T.
	No.Exam	No+Ve	Efficacy	No.exam	No.+Ve	Efficacy	No.Exam	No.+Ve	Efficacy	No.Exam	No.+Ve	Efficacy	No.Exam	No.+Ve	Efficacy	
Trichostrongylus Larvae	50	2 (*)	96 %	48	0	100 %	48	0	100 %	48	0	100 %	48	0	100 %	100%
Ostertagia spp larvae	50	2 (*)	96 %	48	0	100 %	48	0	100 %	48	0	100 %	48	0	100 %	100%
Haemonchus spp larvae	50	2 (*)	96 %	48	0	100 %	48	0	100 %	48	0	100 %	48	2 (##)	95.8 %	98.95%
Cooperia spp larvae	50	3 (*)	94 %	48	1	97.9 %	48	1	97.9 %	48	1	97.9 %	48	3 (##)	93.8 %	96.87%
Nematodirus spp larvae	50	4 (*)	92 %	48	2	95.8 %	48	2	95.8 %	48	2	95.8 %	48	4 (##)	91.7 %	94.77%
Trichuris eggs	14	1(*)& 2	78.6 %	13	2	84.6 %	13	2	84.6 %	13	2	84.6 %	13	2	84.6 %	83.4%
Fasciola eggs	50	50	0.0 %	48	48	0.0 %	48	48	0.0 %	48	48	0.0 %	48	48	0.0 %	0.0%
Moneizia eggs.	7	7	0.0 %	7	7	0.0 %	7	7	0.0 %	7	7	0.0 %	7	7	0.0 %	0.0%
Paramphistomum eggs.	14	14	0.0 %	14	14	0.0 %	14	14	0.0 %	14	14	0.0 %	14	14	0.0 %	0.0%

(*) sheep May be lost the dose. (##) appearance of new infection.
No.Exam = Number of sheep examined. No +Ve = Number of sheep showing larvae.

Table (9) :Condition of mange infestation in the tested sheep before treatment (zero day)

(9-A) : Experimental group.

Animal No.	Site of the lesion	Lesion diameter	No.of mite/ microsc. field
1-	Whole face (figure 1-F)	Whole face	4 mite/field
2-	Face	most of the face	2.0
3-	Nostrils	3 cm	2.0
4-	Nostrils & ear	3 cm & 2 cm	2.0 & 2.0
5-	Ear	3 cm	2.0
6-	Nostrils & ear	3 cm & 4 cm	2.0 & 1.0
7-	Nostrils & ear	4 cm & 3 cm	4.0 & 2.0
8-	Frontal part of the head (fig.1-G))	4 cm	1.0
9-	Spots in the face	2 cm each	1.0
10-	Spots in the face	2 cm each	1.0
11-	Muzzle	4 cm	2.0
12-	Middle part of the tail	5 cm	4.0
13-	Root of the tail	4 cm	2.0
14-	Root of the tail	3 cm	2.0
15-	Tail fold	6 cm	5.0
16-	Tail fold	6 cm	6.0
17-	Tail fold	7 cm	5.0
Total mite number			52.0
Mean / animal			3.0

(9-B): Control non-treated group.

Animal No.	Site of the lesion	Lesion diameter	No.of mite/ microsc. field
1-	Nostrils	4 cm	2.0
2-	Tail fold	5 cm	4.0
3-	Tail fold	4 cm	3.0
4-	Ear	3 cm	2.0
5-	Ear	3 cm	2.0
Total mite number			13.0
Mean / animal			2.6

Table (10-A): Efficacy of Ivomec bolus against sheep mange.

Animal No.	Zero day	Noumber of detected mite / microscopic field during observation period									
		7th day p.t.		14th. day p.t.		21th. day p.t.		28th. day p.t.		35th.day p.t.	
	No.of mite/ microsc. field	No./F	Effic-acy%	No./F	Effic-acy%	No./F	Effic-acy%	No./F	Effic-acy%	No./F	Effic-acy%
1-	4 mite/field	1.0	75.0	0.0	100%	0.0	100%	0.0	100%	0.0	100%
2-	2.0	0.0	100%	0.0		0.0		0.0		0.0	
3-	2.0 & 2.0	0.0	100%	0.0		0.0		0.0		0.0	
4-	2.0	0.0		0.0		0.0		0.0		0.0	
5-	2.0 & 2.0	0.0		0.0		0.0		0.0		0.0	
6-	2.0& 1.0	0.0		0.0		0.0		0.0		0.0	
7-	4.0	0.0	100%	0.0	100%	0.0	100%	0.0	100%	1.0 (#)	0.0%
8-	1.0	0.0		0.0		0.0		0.0		1.0 (#)	0.0%
9-	1.0	0.0		0.0		0.0		0.0		0.0	
10-	1.0	0.0		0.0		0.0		0.0		0.0	
11-	2.0	0.0		0.0		0.0		0.0		0.0	
12-	4.0	0.0		0.0		0.0		0.0		0.0	
13-	2.0	0.0		0.0		0.0		0.0		0.0	100%
14-	2.0	0.0		0.0		0.0		0.0		0.0	
15-	5.0	5.0 (*)	0.0% (*)	0.0	100%	0.0	100%	0.0		0.0	
16-	6.0	2.0	66.6%	0.0	100%	0.0	100%	0.0	100%	0.0	
17-	5.0	1.0	80.0%	0.0	100%	0.0	100%	0.0		0.0	
Mean		3.0	0.50	82.69%	0.0	100%	0.0	100%	0.0	100%	0.11	88.2%

No./F = Number per microscopic field

(*) = Error in swallowing

(#) = Appearance of new infection.

it showed a decrease in the mean MPF from 3.0 MPF to 0.5 MPF. Complete disappearance of mites in all (16 sheep) of the examined field (100% efficact) was recorded at 14th d. p. t. and the animal remained clean till 28 d. p. t. with good improvement in the lesion site which became reddish in color with appearance of the new wool.

At 35 d. p. t. new infection appeared in two animals (1 MPF) decreasing efficacy to 88.2% as in table (10-A), a condition that needs a second dose of treatment.

Lesions were still present with nearly fixed mean number of mites per microscopic field in the control non-treated sheep as in table (10-B).

DISCUSSION

The new macrocyclic lactones as Ivermectin is considered as a new effective line for control of different cattle parasites having minimum residue and low toxicity problems (Benz et al. 1989). It can kill tick strains which have resistance to arsenic and organophosphate insecticide (Hamel and Amelsfoort 1985). Ivermectin paralyzes and kills the parasite through interrupting their nerve impulses by enhanceing binding of their neurotransmitter (GABA) to special receptors at nerve junctions (Campbell and Benz 1984).

The ability of Ivomec injection to provide outstanding internal and external parasite control in one low volume injection for cattle has been

Table (10 -B): Level of mite infestation among the control non treated sheep during the observation period.

Animal No.	Zero day No.of mite/ microsc. field	7th day p.t. No.of detected mite/field	14th. day p.t. No.of detected mite/field	21th. day p.t. No.of detected mite/field	28th. day p.t. No.of detected mite/field	35th.day p.t. No.of detected mite/field
1-	2.0	2.0	2.0	2.0	3.0	3.0
2-	4.0	3.0	3.0	2.0	2.0	2.0
3-	3.0	3.0	4.0	3.0	2.0	3.0
4-	2.0	3.0	3.0	2.0	2.0	2.0
5-	2.0	2.0	2.0	2.0	2.0	2.0
Mean / animal	2.6	2.6	2.8	2.2	2.2	2.4

No./F = Number per microscopic field

demonstrated in different animal markets allover the world and approved by many authors as Campbell & Benz (1984), Schroder et al. (1985) and Cramer et al. (1988).

Now MSD AGVET introduces Ivomec in two new formulations (pour-on for cattle and bolus for sheep) giving it more advantage as easily administered drug away from the effort needed for subcutaneous injection.

Ivomec pour-on causing complete disappearance of G.I.N. eggs from th feces of 75% of the treated cattle at 7th d.p.t. increased to 85% at 35th d.p.t. The sheep bolus form caused 90% of G.I.N. egg free feces at 7th d.p.t. increased to 94% at 28th d.p.t., while new infection appeared in theree sheep (6%) at 35th d.p.t.

Both drugs caused marked decrease in the mean EPGF for all of the treated animals and this effect remain active till the end of the observation period (35th d.p.t.). This came in agreement with Jacobs et al. (1987), who mentioned that Ivomec treatment was more effective than Fenbendazole in the reduction of egg counts, particularly in the first or second month following treatment. This undoubtedly had to be related to the persistent activity of Ivomec in preventing rapid re-infection following treatment.

Ivomec bolus as that of pour on caused complete eradication (100% efficacy) for *Trichostrongylus* and *Oestertagia* species larvae from the cultivated fecal samples collected at 7th d.p.t. and remained free till the 35th d.p.t. while new infection by *Haemonchus* species larvae was detected in cultivated fecal samples of two sheep at 35th d.p.t. This may be due to loss in the bolus fragments before swallowing specially with originally high EPGF in these two animals.

The bolus form as that of the pour on form did not completely eradicate *Cooperia*(efficacy was 96.87% and 87% respectively) and *Nematodirus* species larvae (94.77% and 89% efficacy respectively) also, the bolus form was efficient by 83.4% only against *Trichuris* apecies.

Deficiency in Ivomec efficacy against *Cooperia*, *Nematodirus* and *Trichuris* species by the pour-on or the bolus forms coincides with that proviously published by Armour et al. (1985), Cramer et al., (1988) and Williams et al. (1989), by using the subcutaneous route of administration. This means that the efficacy rate did not relate to the change in the route of application.

In the authors opinion, failure of Ivomec pour-on, bolus or injection to produce complete eradication of the last three types of parasites may be due to the level of Gamma Amino Buteric acid (GABA) at the nerve junction or due to the metabolism of the component after being taken by the parasites.

The two forms of the drug did not show any effiacy against other parasites as *Fasciola*, *Paramphistomum* and *Moneizia* species. This may be reterred to that these types of parasites did not depent on GABA as a neuro-transmitter.

Ivomec bolus appears more efficient in eradication of *Psroptes* mange in sheep giving 100% efficacy from the day 14th till 28th PT. New

infection appeared in 2 shep at 35th d.p.t. giving a mean curability percent during the whole period reached to 88.2%.

From the previous study and away from the producer recommendation of use on cattle or sheep, the pour-on form of the drug appears more efficient and practical than the bolus one in comparison with the injectable form. This may be due to the relation between the mode of administration and the amount of active principles in each form of the drug per dose where Ivomec injection and bolus given in a dose of 200 mcg/kg.b.w., while the pour-on is applied in a dose of 500 mcg/kg.b.w.

This indicates that the high dose of the pour-on form can overcome the difference in the way of absorption, (pour-on reach the general circulation through penetration of its molecules to the pores present in the skin surface as of sweat and sebacious glands and hair roots specially with the very low surface tension of the preparation which facilitates this way.).

Concerning the bolus form, some times sheep regurgitated the dose or even kept it in their cheek for a time then threw it away after fragmentation specially with hand application. This appearaed clear in the previous trial.

The bolus in the given form has only a shallow mark for site of dividing, which some time did not give an accurate bolus dose which may have an effect on the lethal dose and this can play a role in appearance of infection after the 28th d.p.t. specially in heavily infested animals, a condition which needs a second dose of the drug.

For conclusion, using of Ivomec in its new form added new advantage to the product where it facilitates its way of application in the field without disturbance to its efficacy against the previous target parasites.

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