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USE OF IVERMECTINE AS TOPICAL APPLICATION IN TREATMENT OF RABBIT MANGE

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ABSTRACT: Rabbit mange called rabbit plaque, it is a contagious disease affects all rabbits in the farm, spread rapidly and characterized by pruritus, alopecia, and crust formation on the legs, lips, ears or different parts of the body. This disease lead to severe economic losses include weight loss, reduced production, medication cost, misshaped rabbit, and mortality. In spite of many topical medications were used for treatment of rabbit mites, there were no satisfied results as well as the irritant effect of some of them, in addition to the long withdrawal time and drug residue of ivermectin injection so this study tried to apply a new approach to use an Ivermectin carried on glycerin as a topical treatment to overcome the side effect of other treatments. In this study fourty two rabbits naturally infested with mange were divided into seven groups (six rabbits/each), 1st group treated with Ivermectin 1% injection, 2nd group treated with topical Ivermectin 0.05%, and 3rd group treated with topical Ivermectin 0.1%, 4th group treated with topical Ivermectin 0.15%, 5th group treated with topical sulphur 15%, 6th group treated with topical cibermethrin 10%, and 7th group treated with topical cebacil gel (phoxim 50%). All rabbits were observed daily recording recovery and mortality rate, skin lesions sent for histopathology, and serum samples were taken at 0, 4, 8, 15, 22 days post treatment to measure Total protein, Albumin, Creatinine, Glucose, Cu, Zn, Fe, SOD and MDA. Our findings showed Cebacil gel caused 100% mortalities, so it should be excluded where it was toxic if used more than two days post treatment, Ivermectin 0.1% produced significant body weight changes when compared with control groups, Ivermectin 1% injection, and topical sulphur 15% while the remaining treatments produced non-significant body weight changes with an improvement of all biochemical blood parameters including SOD, MDA, Fe, Cu, Zn, Tp, Alb, Crea, and Glu.. Ivermectin 0.1% recorded 100% survival, no persistent skin scales, and the highest reduction rate of damaging indicator, SOD, while the other treatments revealed persistent skin scales and/or mortalities, so Ivermectin 0.1% was preferred as drug of choice for topical treatment of external mange in rabbits.

Keywords: Rabbit, Mange, Treatments, Sulfur, Ivermectin, Deltamethrin, Phoxiem

INTRODUCTION

Rabbit scabies (mange) is named rabbit plaque, identified as a highly contagious disease affecting rabbits of all breeds, ages, and sexes throughout the whole year (Elshahawy et al., 2016). It spread by direct and indirect contact and caused by an infestation of the skin by the rabbit itch mite (Sant, R., and Rowland, M. 2009).

Mite is an insect live on the skin in tunnels (graves) and feed on keratin of dead hair, tissue fluid, and lymph producing crusts, It usually presents in sandy area, on hay and other bedding and can carry the myxomatosis virus (Gould 2010; Arlian and Morgan 2017).

The commonly reported mites infesting rabbits include Psoroptes cuniculi (ear mange), Sarcoptes scabiei var cuniculi (body mange), cheyletiella parasitovorax (non-burrowing visible), and *Notoedres cati* which is very rare (Darzi et al.2007; Okumu et al., 2015).

The common symptoms include itching, pruritis, erythema, loss of hair, crusty, scaly and scabby lesions present in face, leg or ear when detached leaving a bloody area (Swarnakar et al., 2014; Nowland, and Rush 2015).

External mange has high economic losses in rabbit farms include mortality, medication costs, loss of body weights, and Sometimes, it has a zoonotic importance (Jenkins, 2001; Fischer, and Walton 2014).

This disease was commonly treated with topical insecticides, sulpher ointment, or ivermectin injection, (Ulutas et al 2005; Rock, 2007; Niaz, and Shoaib 2015) but the drug of choice is still controversial not only because of the side effect of traditional treatment, recurrence of infestation but also prolonged convalescent period leaving behind emaciated rabbit toward death, so this work aimed to compare the efficacy of topical ivermectin at different concentrations versus traditional treatment methods including ivermectin injection and other topical treatment of scabies and identify the clinical health reflex of these treatments.

MATERIALS AND METHODS

Experimental design

Fourty two rabbits of different breeds and genders naturally infested with external mange which characterized by alopecia, scales on different areas of the body, with or without pruritus. These rabbits were randomly divided into seven groups (six rabbits/each), three topical Ivermectin groups include, 1st group treated with topical Ivermectin 0.05% (5ml ivermectin 1% + 95ml glycerin), 2nd group treated with topical Ivermectin 0.1% (10ml ivermectin 1% + 90ml glycerin), and 3rd group treated with topical Ivermectin 0.15% (15ml ivermectin 1% + 85ml glycerin), as well as four traditional control groups include, 4th group treated with Ivermectin 1% injection, 5th group treated with topical sulphur 15%, 6th group treated with topical cibermethrin 10%, and 7th group treated with topical cebacil gel (phoxim 50%) (table. 1). Daily observation for all rabbits in all groups were done to record recovery and mortality rate. Weighing the body of all rabbits at 0, 8, and 22 days post treatment. Rabbits supplied from farm of Maryout Research Station, Ivermectin 1% was patent product produced by El-Nasr Co., Cibermethrin 10% EC was patent product produced by Arabic chemical industrial Co. with approval of Garda Chemicals limited-India, and Cebacil gel (Phoxim 50 mg/ml) was patent product produced by Agri Egypt chemical industrial Co. Sulpher, Vaslin, and Glycerine were raw materials purchased from Saif El-Nasr chemical Co.

Samples collection

Blood samples were collected at 0, 4, 8, 15, and 22 days post treatment then serum were separated and preserved in refrigerator to be sent to animal health institute laboratory, agriculture ministry, Egypt.

Biochemical tests

Biochemical analysis was applied on the collected sera by semi auto analyzer

(Merck) using commercial reagent kits as per manufacturer's instruction and compared with data obtained by Ozkan et al., 2012. All collected sera were tested for total protein (tp), albumin (Alb), creatinine (Crea), and glucose (Glu) according to Doumas, 1971; Domas, (1975, also SOD, and MDA activities were determined by commercial kits (Biodiagnostic Co., Cairo, Egypt), and was evaluated according to Sharma et al., 2017. Zinc (Zn), copper (Cu) and iron (Fe) concentrations were measured by spectrophotometer (X-ma, Model 6100/6300/6100S, Double beams, UV/VIS Spectrophotometer, Seoul, South Korea) according to Mert et al., 2008; Yatoo et al., 2013a; Yatoo et al., 2013b.

Macro and microscopic lesions

Skin lesions were photographed in mange affected rabbits of different groups and scissored from the affected sites (ears, limbs, face, or nose) of freshly dead infested rabbits within 3 day post treatment and preserved in formalin 10% for twenty four hours, washing was done in tap water then serial dilutions of alcohol (methyl, ethyl and absolute ethyl) were used for dehydration. Specimens were cleared in xylene and embedded in paraffin at 56 degree in hot air oven for twenty four hours. Paraffin bees wax tissue blocks were prepared for sectioning at 4 microns thickness by rotary Leitz microtome. The obtained tissue sections were collected on glass slides, deparaffinized, stained by hematoxylin & eosin stain for examination through the light electric microscope (Banchroft et al., 2013).

Statistical analysis

Data was analyzed by one-way analysis of variance (ANOVA), with Duncan's multiple range tests for significant between means ($P \leq 0.05$) by SPSS v16.0® (IBM Cooperation, Armonk, NY, USA).

RESULTS

Mortality and recovery rate

Table 2 showed 100% mortality in group 7 (phoxim gel 50%) within one week of treatment although disappearance of scales from 3rd day post treatment, followed by 50% mortality in group 6 (Cibermethrin 10%) with Dry hard scales not easly detached in two rabbits, 33.33% mortality in both groups 4, and 5 (Ivermectin 0.15%, and Sulphur 15%), 16.67% mortality in group 1 (Ivermectin 1% injection) with persistence of scales in all rabbits, and finally, there were zero mortality and complete recovery in both groups 2, and 3 (Ivermectin 0.05%, and Ivermectin 0.1%) with better general health improvement in rabbits treated with Ivermectin 0.1%.

Body weight at 0, 8, and 22 days post treatment

Table 3 exhibited rabbits treated with Ivermectin 0.1% (group 3) had significant changes in body weights at 8, and 22 days post treatment, 2.73 ± 0.39, and 2.73±0.42, respectively when compared with control groups, ivermectin 1% subcutaneous injection, and topical sulpher 15% oint., although at 22 days post treatment there were minor weight loss, 10 grams in rabbits treated with Ivermectin 0.1% (group 3), moderate weight loss, 100 grams in rabbits treated with Ivermectin 0.05% (group 2) and higher weight loss, 290 grams in rabbits treated with Sulpher 15% (group 5) while group 1, 4, and 6 recorded weight gain of 170, 250, and 100 grams respectively.

Macro and microscopic lesions recorded in rabbits naturally affected with mange

Figure 1, and 2 exhibited all rabbits were noticed with appearance of light or heavy skin scales in different affected areas of body, pruritus, alopecia, and sometimes inappetence before treatments, while post treatments the growth hairs occurred, pruritus disappeared, and returned their appetite. Figure 3, and 4 reported the freshly dead scabies affected rabbits were showed Focal superficial ulceration was detected in the epidermis associated with hyperkeratosis and acanthosis while the underlying dermis showed congestions and/or haemorrhages with lost or atrophied hair follicles and sebaceous glands, also, oedema with few inflammatory cells

infiltration were noticed in the underlying dermis and subcutaneous tissue in coincided with central embeded mite.

Biochemical blood parameters in treated rabbits naturally affected with mange (Table 4, and 5)

Topical Ivermectin of different cocentrations, 0.05, 0.1, 0.15% when used as new therapeutic approach in treatment of rabbit mange and compared with traditional treatments found the following, damaging indicator, MDA (Malano-Di-Aldhyde) has non-significant differences at 8, 15 dpt while ivermectin 0.05% has significant differences with ivermectin 1% injection, and 10% cibermethrin at 4, and 22 dpt, respectively. Antioxidant enzyme, SOD (Super-Oxid-Dismutase), has significant differences among groups at 4, 15, 22 dpt while ivermectin 0.05% has significant differences with 15% sulpher at 8 dpt. There were no significant differences in Zinc (Zn) among groups at 4 dpt but there were differences at 8, 15 dpt while at 22 dpt there was significant difference between ivermectin 0.1% and Sulpher 15%, also, Copper (Cu) was significantly different with other groups at 4, 8, and 22 dpt while at 15 dpt there was significant difference between ivermectin 0.05% and cibermethrin 10%. Both Creatinine (Crea) and Iron (Fe) were significantly different with other groups at 4, 8, 15, and 22 dpt while Glucose (Glu) has no significant differences with other groups at 4, and 15 dpt but there were differences among groups and between ivermectin 0.15% and ivermectin 1% injection at 8, and 22 dpt, respectively. Albumin (Alb) has significant differences with other groups at 4, and 15 dpt while at 8, and 22 dpt it was non significantly affected, also total protein (Tp) has significant differences with other groups at 4, 15 and 22 dpt while at 8 dpt it was non significantly affected. In general, Table 4, and 5 revealed Tp and Alb were significantly improved in all treated groups ranged from 5.8±0.08 to 7.84±0.04 g/dl and 2.59±0.57 to 4.3±1.9 g/dl, respectively with an improving rates of Tp, 1.2, 1.18, 1.24, 1.42, 1.84, and 0.9, and Alb, 1.2, 0.34, 0.52, 1.01, 0.47, and 0.44 in treated groups, 1, 2, 3, 4, 5, and 6 respectively. Crea showed a minor decrease (changes) from 1.25±0.075 to 0.78±0.12 mg/dl with an improving rates of 0.58, 0.41, 0.22, 0.29, 0.11, and 0.36 in treated groups, 1, 2, 3, 4, 5, and 6 respectively. Glu showed an increase from 77.2±1.1 to 104.3±1.3 mg/dl with an improving rates of 85.05, 30.8, 30.8, 17.7, 29.75, and 25.1 in treated groups, 1, 2, 3, 4, 5, and 6 respectively. Also, Zn and Cu were a significantly increased from 0.057±0.016 to 0.171±0.018 mg/100ml and 0.067±0.003 to 0.427±0.255 mg/100ml, respectively with an improving rates of Zn, 0.06, 0.049, 0.03, 0.069, 0.114, and 0.03, and Cu, 0.075, 0.108, 0.04, 0.029, 0.36, and 0.1 in treated groups, 1, 2, 3, 4, 5, and 6 respectively. Iron (Fe) showed a decrease toward normal with treatment from 293.9±20.3 to 66.2±7.6 Ug/100ml with an improving rates of 168.9, 220.25, 140.75, 147.5, 107.85, and 86.2 in treated groups, 1, 2, 3, 4, 5, and 6 respectively. MDA and SOD were also decreased from 1.8±0.12 to 0.89±0.095 U/ml and 51.74±1.71 to 28.81±2.38 U/ml, respectively with an improving rates of MDA, 0.65, 0.88, 0.2, 0.41, 0.45, and 0.5, and SOD, 27.22, 28.45, 32.67, 29.08, 13.04, and 27.33 in treated groups, 1, 2, 3, 4, 5, and 6 respectively.

DISCUSSION

External mange is a major problem in rabbit sector called rabbit plaque due to its rapid spread, difficult treatment, reduced productivity, and mortalities particularly in desert, and semi-desert areas of Egypt. So that, this study was applied on rabbits naturally affected with external mange and treated by different concentrations of topical ivermectin 0.05%, 0.1%, and 0.15% then compared with traditional treatments (ivermectin 1% subcutaneous injection, topical sulpher 15% oint., cibermethrin 10% dipping, and topical cebcil gel). Our results revealed the followings, on the level of body weights, mortalities, and clinical

signs, all groups showed there were a significant weight changes in group treated with 0.1% topical ivermectin when compared with ivermectin 1% subcutaneous injection, and topical sulpher 15% oint., while the other treatments have non-significant changes. Also, Cebacil gel caused 100% mortalities, so it should be excluded where it was toxic if used more than two days post treatment. Ivermectin 0.1% recorded no mortalities, 100% survival, and no persistent skin scales, while the other treatments revealed persistent skin scales and/or mortalities, so Ivermectin 0.1% was preferred as topical treatment. On the level of blood biochemical parameters, all treatments improved all parameters including SOD, MDA, Fe, Cu, Zn, Tp, Alb, Crea, and Glu but ivermectin 0.1% was recorded the highest reduction rate of SOD as antioxidant enzyme, 32.67 U/ml, while the highest reduction rate of MDA as damaging indicator, and Iron (Fe), 0.88 U/ml, and 220.25 Ug/100ml, respectively was recorded in ivermectin 0.05%. Copper, Zinc, and total protein were recorded the highest enhancement in sulpher treatead group, 0.36 mg/100ml, 0.114 mg/100ml, and 1.84 g/dl, respectively, while Albumen, Creatinine, and Glucose were recorded the highest enhancement in Ivermectin 1% injection, 1.2 g/dl, 0.58 mg/dl, and 85.05 mg/dl, respectively. Our results were matched with those of Nazir et al., 2016 stated Both Ivermectin and eprinomectin are highly effective in managing Sarcoptic mange infestation when used topically, Wilkins et al., 1980 has been found ivermectin diluted in mineral oil, and applied directly on the ear lesions was effective in rabbits with psoroptic mange, and McTier et al., 2003 found that selamectin topical treatment led to complete clinical and parasitological recovery in rabbits naturally infested with P.cuniculi. On the contrary, Ulutas et al., 2005 indicated eprinomectin (0.5 mg/kg) was partially effective in the treatment of rabbits naturally infested with P. cuniculi when given topically twice at 14 days interval on the skin at the base of the neck which might be attributed to the dose, and route of administration. On the other hand, Panigrahi et al., 2014 stated Subcutaneous injection of ivermectin 400 µg/kg body weight at weekly intervals for four weeks resulted in remission of clinical signs (disappeared pruritus, hair growth) and improvement of health condition in rabbits where Tp was improved from 68.4 to 69.2 g/L and Crea. from 1.2 to 0.9 mmol/L, also, Abdelaziz et al., 2020 mentioned the clinical signs disappeared at 28^{th} day post treatment for all treatments, Sulfur ointment was significantly improved both SOD, and serum Zn, 0.49± 0.02 U/mg Hb, and 0.69 ±0.08 ppm, respectively, while serum Fe, and Cu were not significantly affected. Jana et al., 2004 recorded after 14 days of treatment with ivermectin injection (200 mg/kg body weight) twice a week there was a significant increase of Tp, and Albu. to 5.72 ± 1.37 g/dl, and 2.92 ± 0.89 g/dl, respectively, also there were marked reduction in the severity of scratching and itching as Kurade et al., 1996 which reported similar observations regarding efficacy of ivermectin against psoroptic mange in rabbits. Several studies (Bowman et al., 1992; Bansod et al., 2004) showed that subcutaneous administration of ivermectin and doramectin led to complete clinical and parasitological recovery in psoroptic rabbits. On histopathological examination, our results showed focal superficial ulceration, hyperkeratosis, and acanthosis of the epidermis, while the dermis and subcutaneous tissue noticed with congestions, oedema, and haemorrhages accompanied with few inflammatory cells infiltration, atrophied or loss of hair follicles and sebaceous glands, and central embeded mite, these results were in accordance with that of Lossen et al., 1999; Chandey et al., 2000; Oraon et al., 2000, and Rania et al., 2017 who reported hyperkeratosis, acanthosis,

subepidermal dermatitis, and leukocytic infiltrations.

CONCLUSION

Use of ivermectin as topical treatment has multiple advantages including rapid mangecide, safe, less stress, less irritant, no drug residue, no withdrawal period, with low cost and improve rabbits health condition. Topical treatment of ivermectin 0.1% was the drug of choice for rabbits mange since it achieved no mortalities, 100% survival, no skin scales, and improved all biochemical blood parameters indicating the enhancement of rabbits health condition.

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Competing interests

In this study there was no any conflicts of interest.

Table (1): History of rabbits naturally affected with mange

Group Number/ treatment	Breed	Gender	Affected site	Bodyweight /kg (Zero dpt)
1/Ivermectin 1% injection	California	Male	Face, leg	1.535
	Rex	Female	ear wax	1.170
	California	Female	Nose	2.170
	Rex	Male	Face, leg	2.060
	Rex	Female	Leg, ear	2.200
	Newziland	Male	ear wax	1.180
2/Ivermectin 0.05%	Newziland	Male	Leg, nose	1.890
	Newziland	Female	Face	1.920
	Newziland	Male	Ear, nose	1.900
	Newziland	Female	Leg	1.550
	Newziland	Female	Leg	3.700
	California	Male	Ear	3.220
3/Ivermectin 0.1%	Gabaly	Male	Face, leg	2.350
	Newziland	Female	Nose, leg	2.355
	Newziland	Male	Leg, ear	3.265
	California	Female	Leg	3.020
	Newziland	Male	Leg	2.870
	Newziland	Female	Nose, ear wax	2.595
4/Ivermectin 0.15%	Rex	Male	Face, ear wax	2.345
	Rex	Female	ear wax	2.265
	Newziland	Male	Nose	1.750
	Rex	Female	Face, leg	1.105
	Newziland	Male	ear wax	2.050
	Newziland	Female	Face, leg	2.705

dpt: day post treatment

Table (1) continuous: History of rabbits naturally affected with mange

Group Number/ treatment	Breed	Gender	Affected site	Bodyweight /kg (Zero dpt)
5/Sulphur 15%	Newziland	Male	Face, leg	2.755
	California	Female	Ear, leg	2.430
	Newziland	Male	Leg	2.250
	Newziland	Female	Leg	1.930
	Newziland	Male	Nose	2.120
	Newziland	Female	Face	1.760
6/Cibermethrin 10%	Newziland	Female	Ear	2.200
	Newziland	Male	Leg	2.680
	Newziland	Male	Face	2.525
	Gabaly	Female	Face, leg	2.350
	Rex	Male	Face, leg	2.240
	Newziland	Female	Ear, leg	2.195
7/Cebacil gel (Phoxim 50%)	Newziland	Male	Ear	2.705
	Newziland	Female	Ear	2.410
	Rex	Male	Face, leg	1.980
	Newziland	Female	Ear, leg	2.185
	Newziland	Male	Face, leg	2.045
	Rex	Female	Face, leg	1.190

dpt: day post treatment

Table (2): Mortality and recovery rate in treated rabbits naturally affected with mange

Group Number/ treatment	Total affected number	Mortality		Recovery		Clinical signs one week post treatment
		Number	%	Number	%	
1/Ivermectin 1% injection	6	1	16.67%	5	83.33%	Dry hard scales not easly detached in all rabbits
2/Ivermectin 0.05%	6	0	0%	6	100%	Dry hard scales not easly detached in one rabbit
3/Ivermectin 0.1%	6	0	0%	6	100%	There is no scales, just inflamed leg with better improvement than Ivermectin 0.05%
4/Ivermectin 0.15%	6	2	33.33%	4	66.67%	No scales, better than Ivermectin 0.1%
5/Sulphur 15%	6	2	33.33%	4	66.67%	Dry hard scales not easly detached in one rabbit
6/Cibermethrin 10%	6	3	50%	3	50%	Dry hard scales not easly detached in two rabbits
7/Cebacil gel (Phoxim 50%)	6	6	100%	0	0%	Toxic if used more than two days post treatment

Table (3): Effect of treatments on body weight in rabbits naturally affected with mange

Group Number/ treatment	Mean body weight 0 dpt	Mean body weight 8 dpt	Mean body weight 22 dpt	Weight gain / gram	Weight loss / gram
1/Ivermectin 1% injection	1.72 ± 0.49	1.68 ± 0.41*	1.89 ± 0.30*	170	-
2/Ivermectin 0.05%	2.36 ± 0.87	2.31 ± 0.86	2.26 ± 0.86	-	100
3/Ivermectin 0.1%	2.74 ± 0.37	2.73 ± 0.39*	2.73 ± 0.42*	-	10
4/Ivermectin 0.15%	2.04 ± 0.56	2.15 ± 0.39**	2.29 ± 0.29**	250	-
5/Sulphur 15%	2.21 ± 0.36	1.92 ± 0.20**	1.92 ± 0.41**	-	290
6/Cibermethrin 10%	2.37 ± 0.20	2.35 ± 0.32	2.47 ± 0.27	100	-
7/Cebacil gel (Phoxim 50%)	2.09 ± 0.51	D	D	-	-

*: The mean difference is significant at the 0.05 level D: Dead dpt: day post treatment

Table (4): Effect of treatments on biochemical blood parameters in rabbits naturally affected with mange

Day of collection	Blood Parameters	Treatments					
		Ivermectin 1% inj.	Ivermectin 0.05%	Ivermectin 0.1%	Ivermectin 0.15%	Sulphur 15%	Cibermethrin 10%
Zero day (pretreatment)	TP (g/dl)	6.25±0.42	5.98±0.095	6.6±0.125 *	5.92±0.47	5.8±0.08 *	6.28±0.035
	Alb. (g/dl)	3.1±0.08 *	3.2±0.11	3.19±0.23	2.59±0.57 *	3.22±0.04 *	3.4±0.08 *
	Crea.(mg/dl)	1.25±0.075 ≠ *	1.12±0.035 *	1.13±0.04 *	0.89±0.03 ≠	0.88±0.075 *	1.06±0.11 ≠
	Glu. (mg/dl)	58.95±2.25 *	73.5±4.1 *	72.05±5.25 *	72.6±8.9 *	70.2±2.2	72.5±4.2
	Iron(Ug/100ml)	255.9±27.4	293.9±20.3	206.95±23.75 *	227.8±5.9	239.6±26.8	266.85±56.65 *
	Copper(mg/100ml)	0.068±0.005 *	0.079±0.014	0.08±0.003	0.08±0.01 *	0.067±0.003 *	0.07±0.009
	Zinc (mg/100ml)	0.063±0.006 *	0.09±0.02 *	0.101±0.02 *	0.068±0.007	0.057±0.016 *	0.09±0.009
	SOD (U/ml)	63.11±0.57 ≠	60.86±1.69 *	61.85±2.15 *	57.89±1.61 ≠	51.74±1.71 *≠	58.75±3.6
	MDA (U/ml)	1.54±0.13 *	1.8±0.12 ≠	1.23±0.24 *	1.4±0.075	1.51±0.13 *≠	1.63±0.19 *
4 dpt	TP1	6.3±0.085 *	6.26±0.23	6.84±0.06 *	6.7±0.265 *	6.4±0.14 *	6.4±0.115 *
	Alb.1	3.2±0.035	3.2±0.045 *	3.35±0.145	3.21±0.04 a *	3.22±0.135	3.45±0.075 *
	Crea.1	0.98±0.05 ≠	0.99±0.07 *	0.99±0.065 *	0.85±0.025 ≠	0.84±0.025 *	0.84±0.03 *
	Glu.1	79.9±4.7	74.35±2.15	77.2±1.1	80.75±11.25	75.6±3.6	78±3.3
	Iron1	237.25±11.55 *®	254.7±27.7 ≠	178.7±24.4 *	122.45±28.55 ®	205.5±17.9 ≠ ®	260.3±23.2 *®
	Copper1	0.078±0.006 ≠	0.086±0.006 *	0.08±0.011	0.094±0.003 ≠	0.09±0.001	0.074±0.005 *≠
	Zinc1	0.07±0.01	0.091±0.003	0.104±0.029	0.1±0.002	0.12±0.04	0.097±0.012
	SOD1	52.52±7.19	54.57±2.3 ≠	51.72±2.58 *	49.38±1.68	44.81±2.01 *≠	46.54±1.65 ≠
	MDA1	1.15±0.01 *	1.68±0.04 *	1.18±0.44	1.24±0.01	1.48±0.045	1.48±0.06

* , ≠, ®: The mean difference is significant at the 0.05 level dpt: day post treatment TP: Total protein Alb: Albumin
Crea: Creatinine SOD: Super oxide dismutase MDA: Malanodialdihyde Glu: Glucose

Table (4) continuous: Effect of treatments on biochemical blood parameters in rabbits naturally affected with mange

Day of collection	Blood Parameters	Treatments					
		Ivermectin 1% inj.	Ivermectin 0.05%	Ivermectin 0.1%	Ivermectin 0.15%	Sulphur 15%	Cibermethrin 10%
8 dpt	**TP2**	6.6±0.085	6.75±0.12	7.05±0.47	6.94±0.105	6.67±0.62	6.5±0.06
	Alb.2	3.41±0.045	3.42±0.175	3.37±0.04	3.32±0.255	3.36±0.06	3.51±0.04
	Crea.2	0.84±0.006*	0.87±0.01	0.99±0.035*	0.84±0.035	0. 8±0.11*	0.83±0.1b*
	Glu.2	83.25±1.35	78.85±1.85*	81.8±1.3a*	81.85±1.25*	76.8±8.2	89.1±3.3a*
	Iron2	225.2±49.8*≠	138.4±13.6*	133.45±49.85*	107.05±8.35≠	170.9±6.9≠	233.95±15.35*≠
	Copper2	0.11±0.01≠*	0.098±0.007®	0.091±0.01*	0.096±0.01≠	0.11±0.01 *	0.081±0.01≠ ®
	Zinc2	0.084±0.025*	0.091±0.004≠	0.108±0.006*	0.102±0.012≠	0.15±0.009≠*	0.106±0.009
	SOD2	47.14±4.81	49.7±9.3b*	44.25±2.57	40.7±0.9	39.49±5.52*	42.94±4.84
	MDA2	1.11±0.025	1.29±0.34	1.13±0.095	1.06±0.16	1.1±0.08	1.17±0.04
15 dpt	**TP3**	6.62±0.12*	6.9±0.065*	7.08±0.105*	6.98±0.22*	6.9±0.13	6.99±0.166
	Alb.3	3.6±0.205≠	3.45±0.03®	3.64±0.11*	3.39±0.09≠	3.39±0.13*	3.75±0.03≠®
	Crea.3	0.78±0.01*	0.79±0.02	0.96±0.11*	0.78±0.02	0.78±0.12*	0.8±0.03c*
	Glu.3	86.8±6.4	83.05±1.55	98.95±5.35	89.6±2.25	90.05±6.65	90.45±6.75
	Iron3	125.35±30.1	87.55±3.45*	88.4±14.3*	102.45±3.15*	155.35±22.95*	191.75±34.15*
	Copper3	0.126±0.011	0.13±0.01*	0.108±0.002	0.105±0.003	0.12±0.045	0.08±0.004*
	Zinc3	0.092±0.018*	0.12±0.018≠	0.13±0.01*	0.111±0.004≠	0.16±0.003≠	0.108±0.039
	SOD3	46.22±1.88*	44.15±0.78≠	31.62±0.45*	29.82±2.25*	39.12±2.16*≠	38.48±1.93* ≠
	MDA3	0.91±0.065	1.05±0.055	1.11±0.1	1.03±0.04	1.097±0.245	1.15±0.18

* , ≠, ®: The mean difference is significant at the 0.05 level dpt: day post treatment TP: Total protein Alb: Albumin
Crea: Creatinine SOD: Super oxide dismutase MDA: Malanodialdihyde Glu: Glucose

Table (4) continuous: Effect of treatments on biochemical blood parameters in rabbits naturally affected with mange

Day of collection	Blood Parameters	Treatments					
		Ivermectin 1% inj.	Ivermectin 0.05%	Ivermectin 0.1%	Ivermectin 0.15%	Sulphur 15%	Cibermethrin 10%
22 dpt	**TP2**	7.45±0.135*	7.16±0.12≠	7.84±0.04*	7.34±0.215	7.64±0.075≠	7.18±0.295*
	Alb.2	4.3±1.9	3.54±0.03	3.71±0.075	3.6±0.125	3.69±0.045	3.84±0.12
	Crea.2	0.67±0.07*	0.71±0.09	0.91±0.02*	0.6±0.03≠	0.77±0.06 *≠	0.7±0.04*
	Glu.2	144±51.6*	104.3±1.3	102.85±6.65	90.3±13.6*	99.95±20.75	97.6±0.6
	Iron2	87±9.8	73.65±5.65*	66.2±7.6*	80.3±7.7*	131.75±57.95*	180.65±28.95*
	Copper2	0.143±0.015	0.187±0.056*	0.12±0.017*	0.109±0.037*	0.427±0.255*	0.17±0.01
	Zinc2	0.123±0.028	0.139±0.033	0.131±0.006*	0.137±0.02	0.171±0.018*	0.12±0.007
	SOD2	35.91±2.57*	32.41±0.99≠	29.18±0.32*	28.81±2.38*	38.7±3.64*≠	31.42±1.28
	MDA2	0.89±0.095	0.92±0.14*	1.03±0.11	0.99±0.15	1.06±0.015	1.13±0.02*

*, ≠, ®: The mean difference is significant at the 0.05 level dpt: day post treatment TP: Total protein Alb: Albumin
Crea: Creatinine SOD: Super oxide dismutase MDA: Malanodialdihyde Glu: Glucose

Table (5): Improvement rates in blood biochemical parameters of different treated rabbits naturally affected with mange

	Ivermectin 1% inj. (group1)	Ivermectin 0.05% (group2)	Ivermectin 0.1% (group3)	Ivermectin 0.15% (group4)	Sulphur 15% (group5)	Cibermethrin 10% (group6)
TP (g/dl)	1.2	1.18	1.24	1.42	1.84	0.9
Alb. (g/dl)	1.2	0.34	0.52	1.01	0.47	0.44
Crea.(mg/dl)	0.58	0.41	0.22	0.29	0.11	0.36
Glu. (mg/dl)	85.05	30.8	30.8	17.7	29.75	25.1
Iron(Ug/100ml)	168.9	220.25	140.75	147.5	107.85	86.2
Copper(mg/100ml)	0.075	0.108	0.04	0.029	0.36	0.1
Zinc (mg/100ml)	0.06	0.049	0.03	0.069	0.114	0.03
SOD (U/ml)	27.2	28.45	32.67	29.08	13.04	27.33
MDA (U/ml)	0.65	0.88	0.2	0.41	0.45	0.5

TP: Total protein Alb: Albumin Crea: Creatinine SOD: Super oxide dismutase MDA: Malanodialdihyde Glu: Glucose

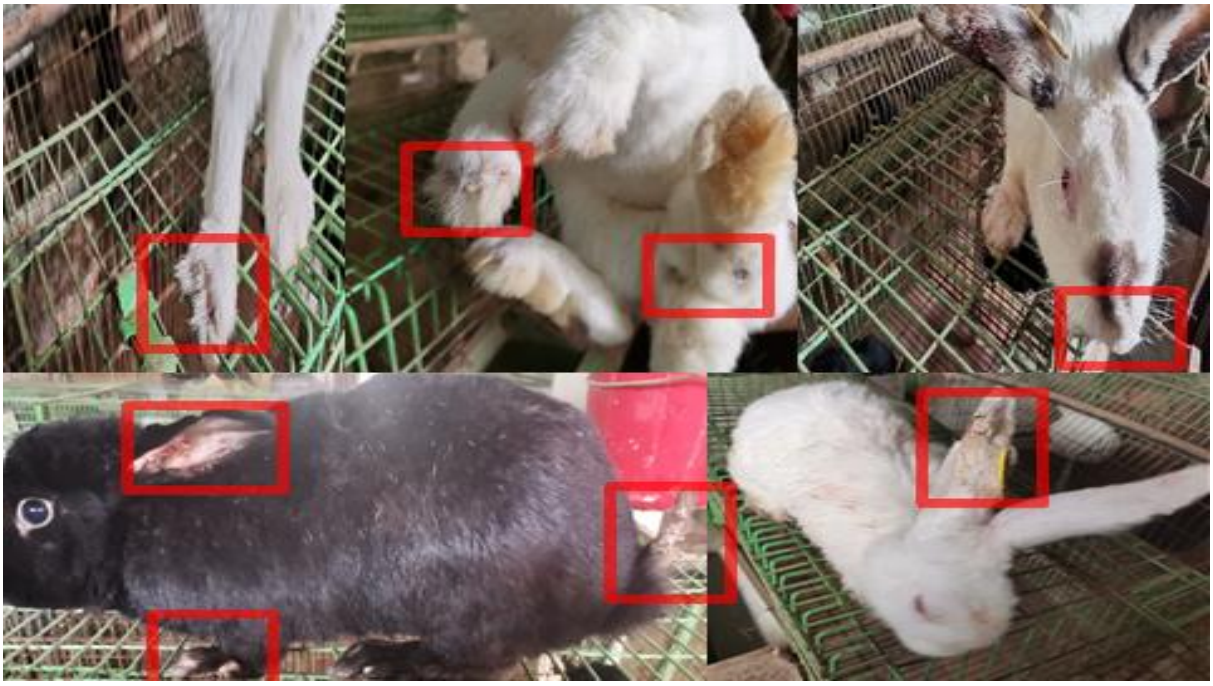

Fig. (1): Hair loss and skin scales in different parts of the body before treatment

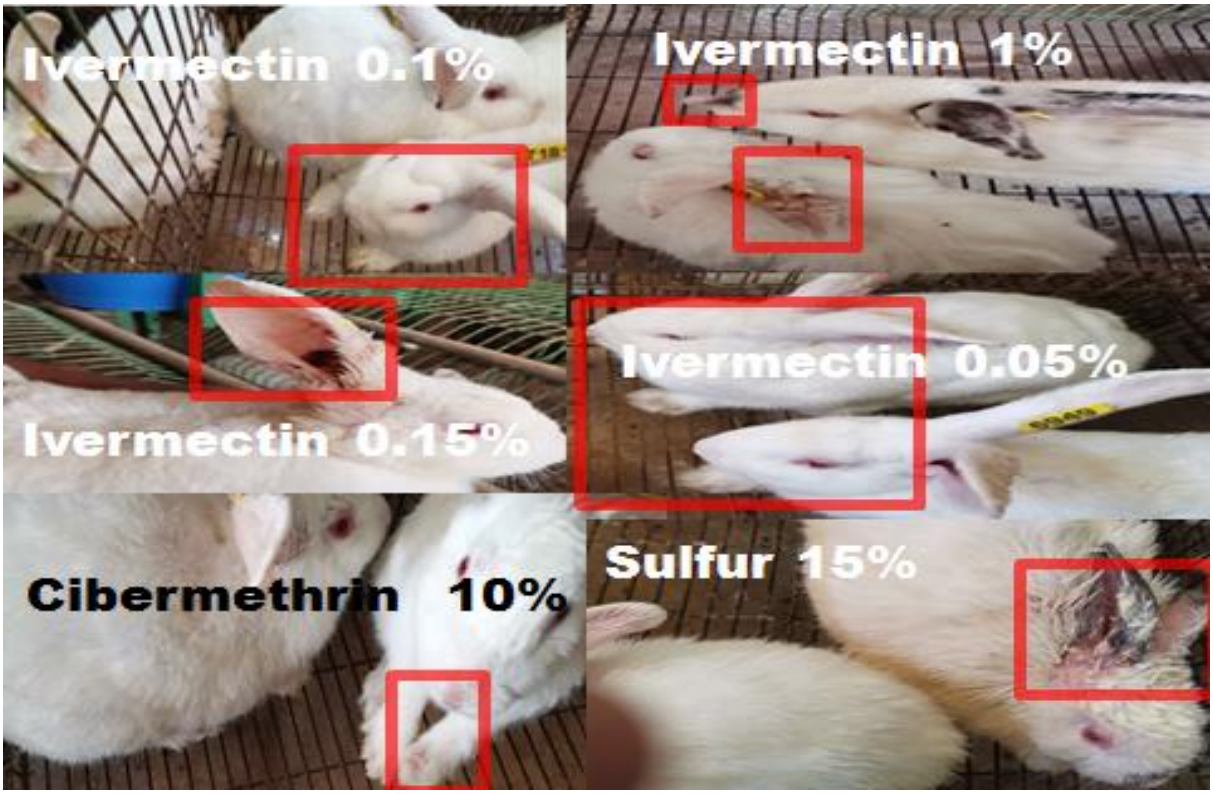

Fig. (2): Hair growth and disappearance of skin scales in most mange affected rabbits of all treatments at 7 days post treatment except ivermectin 1%

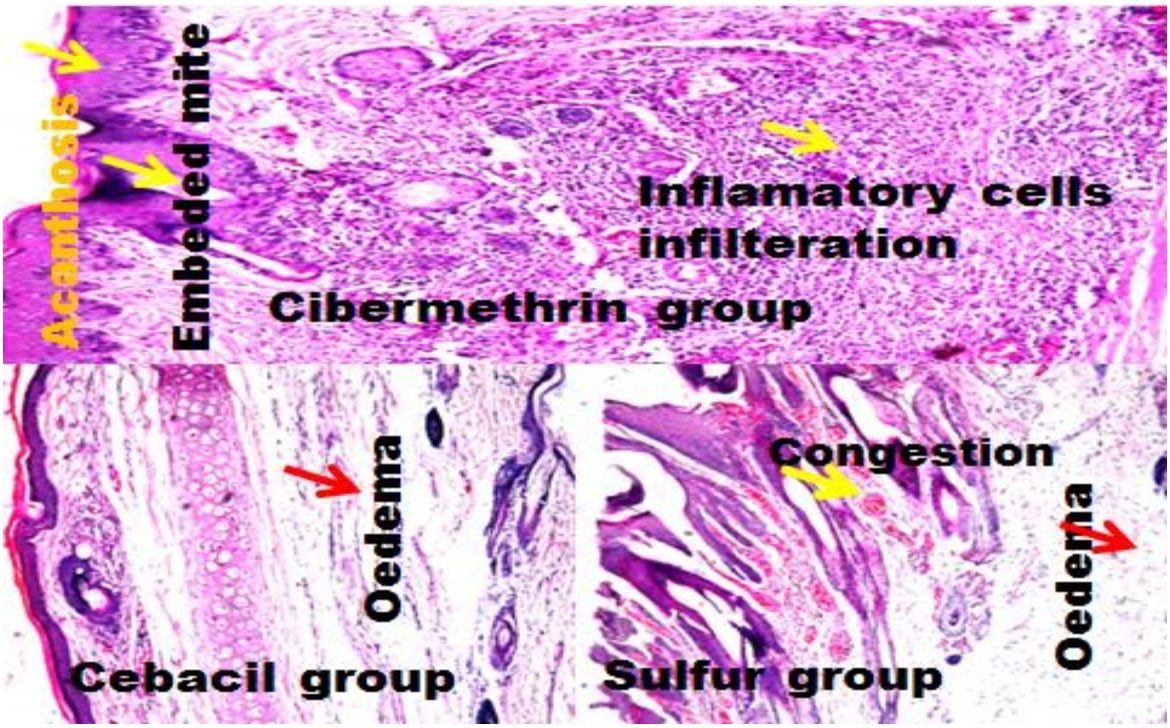

Fig. (3): Ear showed acanthosis in the epidermis and congestion, oedema, inflammatory cells infilteration with embedded mites in the dermis and subcutaneous layer

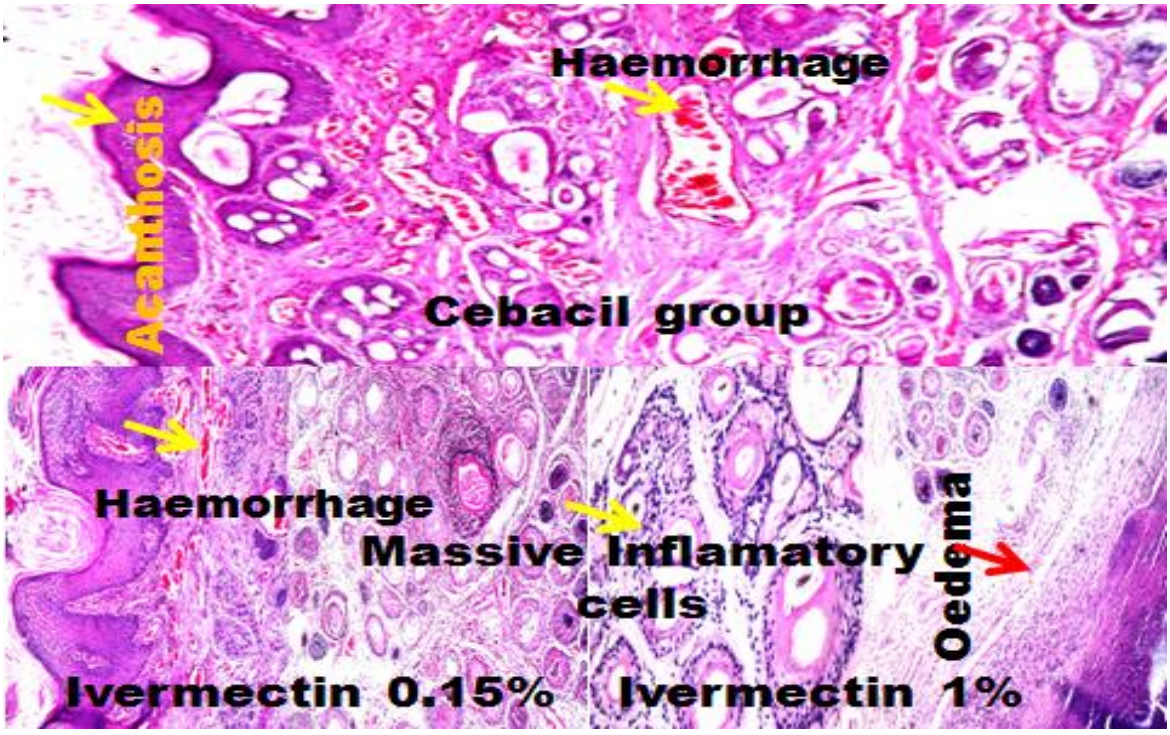

Fig. (4): the epidermis was intact or affected with acanthosis, hyperkeratosis, and Focal superficial ulceration while the dermis and subcutaneous layer showed oedema, haemorrhage, massive inflammatory cells and atrophied or lost hair follicles and sebaceous glands

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الملخص العربي
استخدام الايفرمكتين كدهان موضعي في علاج جرب الارانب

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يعد جرب الأرانب من الأمراض الجلدية التي تنتشر سريعا داخل عنابر الأرانب ويصيب جميع الأنواع والأعمار خلال جميع فصول السنة لذا يطلق عليه طاعون الأرانب وتكمن خطورته في صعوبة علاجه وتكاليف العلاج العالية وانتقال العدوي للإنسان كما أنه يتسبب في ارتفاع معدل الوفيات ونقصان الأوزان مما يؤدي الي زيادة الخسائر الاقتصادية في مزارع الأرانب. المسبب المرضي هو حشرة الحلم وتتميز أعراض المرض بسقوط الشعر ورغبة الحيوان في الهرش ثم ظهور قشور جلدية بالأماكن المصابة (الأرجل – الفم – الأذن – الوجه – الأنف) مع فقدان الشهية ونقص الأوزان ثم الموت في النهاية اذا لم يتم التدخل بالعلاج المناسب في الوقت المناسب حيث أن كثيرا من العلاجات تم استخدامها في الفترة الماضية مثل حقن الايفرمكتين 1% أو دهان مرهم الكبريت موضعيا أو استخدام المبيدات الحشرية الأمنة بالتغطيس ولكن هناك بعض المشاكل التي تواجه تلك الطرق التقليدية منها طول مدة فترة السحب لحقن الايفرمكتين 1% والتي لا تقل عن 28 يوم بعد الحقن بالإضافة للمتبقيات الدوائية والأثر المجهد والمتعب للحيوان نتيجة استخدام مواد موضعية تتسبب في هياج وحساسية جلد الحيوان لذا خلال تلك الدراسة تم استخدام الايفرمكتين موضعيا بتركيزات مختلفة لمقارنته وتقليل الأثار الضارة الناتجة عن الطرق التقليدية الأخرى بالإضافة الي قلة التكلفة وعدم حساسية جلد الحيوان منه. في تلك الدراسة اثنان وأربعون أرنب من مختلف الأنواع مصابون طبيعيا بالجرب في مناطق مختلفة من الجسم تم تقسيمهم الي سبعة مجموعات (ستة أرانب بكل مجموعة) - المجموعة الأولي تم علاجها يحقن الايفرمكتين 1% تحت جلد الرقبة و المجموعة الثانية تم علاجها موضعيا بالايفرمكتين 0.05% و المجموعة الثالثة تم علاجها موضعيا بالايفرمكتين 0.1% والمجموعة الرابعة تم علاجها موضعيا بالايفرمكتين 0.15% و المجموعة الخامسة تم علاجها موضعيا بدهان الكبريت 15% و المجموعة السادسة تم علاجها موضعيا بالتغطيس في محلول السايبرمثرين المخفف 10% و المجموعة السابعة تم علاجها موضعيا بدهان السيباسيل جل (فوكسيم 50%) وتم متابعة الأرانب يوميا لتسجيل الأعراض والوفيات وتم أخذ عينات من الجلد المصاب للهستوباثولوجي وسحب عينات دم لإجراء التحاليل الكيميائية الحيوية الدالة علي الصحة وجاءت النتائج كالتالي حدوث وفيات 100% في مجموعة السيباسيل جل لذا يعد ساما خاصة بعد يومين من استخدامه وأما في باقي المجموعات حدثت تغييرات غير معنوية في الأوزان مع تحسن تحاليل الدم الكيميائية الحيوية وتشمل SOD MDA, Fe, Cu, Zn, Tp, Alb, Crea, Glu. ولكن مجموعة الايفرمكتين 0.1% كانت الأفضل حيث أنها لم تسجل أي وفيات وسجلت ازالة كاملة للقشور الجلدية مع تحقيق أعلي معدل انخفاض لمؤشر الهدم وانزيم الأكسدة SOD بالإضافة الي نحسن باقي التحاليل بينما المجموعات العلاجية الأخرى سجلت وفيات وبقاء بعض القشور الجلدية لذلك تمت التوصية باستخدام دهان الايفرمكتين 0.1% في علاج جرب الأرانب كعلاج أمن فعال اقتصادي وغير مكلف وليس له أي أضرار أو حساسية للأرانب.

الكلمات الدالة: الأرانب وجرب و ايفرمكتين و كبريت ودلتامثرين