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Enhanced Ivermectin Nanoemulsion for Transdermal Treatment of External Parasitic Infestations in Dogs

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Abstract

ECTOPARASITES, such as fleas and mange, are a significant health concern for dogs, affecting their overall health and quality of life. This experimental study aimed to evaluate the efficacy of a Nanoemulsion loaded with ivermectin in the treatment of dogs infested with fleas and mange. Seventeen dogs were included in the trial, divided into three groups: a control group of seven healthy dogs, a group of five dogs suffering from flea infestations, and a group of five dogs with mange infestations. Blood samples were collected before treatment and at weekly intervals over four weeks to assess changes in hematological parameters (CBC), liver function (ALP, AST), and lipid profile (triglycerides, cholesterol, HDL, LDL, albumin, and globulin) before and after treatment at weekly intervals over four weeks. Before treatment, the results of the flea group showed a decrease in HCT, neutrophil, triglyceride and HDL. While in the mange group there was a decrease in Hb, RBCs and HCT. After treatment there was an increase in WBCs count, AST, ALP, albumin, globulin, cholesterol, triglyceride, and HDL in the flea infestation group. On the other hand, the mange infected dogs; showed a significant decrease in Hb, HCT, triglyceride and increase in LDL level compared to premedication levels. In conclusion, the use of ivermectin-loaded Nanoemulsion proved to be highly effective in treating external parasitic infestations, particularly fleas and mange, in dogs, providing a promising therapeutic approach for improving the health and quality of life of affected animals.

Keywords: Nanoemulsion, ivermectin, dogs, fleas, mange.

Introduction

Ectoparasites are a type of arthropods that live on the external surface of the host, they may be found on the skin surface such as fleas, or within the skin layers and hair follicles like Demodex and Sarcoptic mites (sarcoptic mange) [1]. These parasites negatively impact the healthy appearance of the skin, leading to severe itching and fur loss [2]. Dogs typically acquire ectoparasites through direct contact with infected animals, particularly in cases of zoonotic diseases, such as mite infestations, which are more prevalent in young and immunocompromised dogs [3]. Canine sarcoptic mange, caused by *Sarcoptes scabiei* var. *canis*, is characterized clinically by itching, fur loss, erythema, and erosions, with common sites of infection including the ear pinna and limbs, though it can spread across the entire body [4,5]. Flea infestations in dogs often lead to flea allergic dermatitis, which presents with itching, erythema, alopecia, and lesions [6].

The treatment of ectoparasites due to its high efficacy, as it disrupts the parasite's nervous system by binding to GABA- and glutamate-gated channels, the latter being absent in mammals [7,8]. However, the use of ivermectin may result in toxicity, causing neurological symptoms, tachycardia, rapid shallow breathing, and dilated pupils in dogs [9].

Recent advancements in nanotechnology have greatly impacted the medical field, especially in using it as a drug delivery system in different areas of medicine. Nanotechnology offers targeted delivery with the ability to transport a substantial drug load, thus enhancing treatment efficacy with

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minimal or no side effects [10]. Transdermal drug delivery, in particular, is a painless alternative to methods like injection, allowing drugs to be absorbed through the skin into the bloodstream [11,12]. This method also offers advantages such as reducing drug doses, minimizing harmful effects, and avoiding first-pass metabolism [13,14]. Nanotechnology in the veterinary field is showing great promise. For example, zinc oxide nanoparticles have been found to have antiviral effects [15]. Additionally, hydroxyapatite nanogels are being used to effectively treat and repair large bone defects [16]. These advancements suggest a bright future for nanotechnology in veterinary medicine.

The aim of this study is to evaluate the clinical efficacy of a Nanoemulsion loaded with ivermectin as a transdermal drug delivery system for the eradication of ectoparasites in dogs. Additionally, this study will assess the effects of this treatment on hematological parameters, lipid metabolism, and liver function to identify any potential side effects or toxicity

Material and Methods

Animals

This experimental trial was applied on17dogs; upon physical and clinical examination they were grouped into: Apparently healthy group (n= 7 dogs). Fleas' infested group (n= 5 dogs), and Mange infested dogs (n= 5). Both sexes were included with age ranged from 6 to 18 months. They were housed in kennels of private small animal clinics and had different nutritional regime. Infested dogs were treated with 1 ml containing 985.1 µg of nanoemulsion loaded with ivermectin that was applied on the dogs' neck once. Blood samples were collected from all dogs before put on nanoemulsion loaded with ivermectin and after week 1, 2, 3 and 4 from using the medication. The period of experimental study was from December 2022 to July 2023.

Samples

Samples were collected from cephalic vain and separated to two parts: The first part was collected in tubes containing anticoagulant used for automated haematology analysis (Diatro, Hungary). The second one was collected on plain tubes for serum separation to evaluate alkaline phosphatase(ALP) using special kit(ALP- LQ, GPL company, Spain), aspartate aminotransferase (AST) using the kit of(GOT/AST, FL IFC, Chema diagnostica, Italy), lipid profile including triglycerides, total cholesterol (Cholesterol-LQ), HDL (high density lipoprotein), (HDL Cholesterol), and LDL (low density lipoprotein), (LDL Cholesterol D) by kits from Spectrum, Egypt ; and albumin and globulin according to Spinreact company, Spain.

Ivermectin loaded Nanoemulsion

Sample preparation by using solvents and emulsifiers at the same time were a mixture of: Dimethylsulfoxid (DMSO), absolute Ethyl alcohol, Glycerol. This mixture was used for nanoemulcification of cholesterol and loading of ivermectin. Serial dilution is carried out using distilled water according to Jörgensen et al., 2020 [17].

The sample was evaluated with HPLC (Agilent 1260, Germany) as the following: Agilent 1260 infinity HPLC series, equipped with a variable wavelength, UV absorbance detector adjusted at 245nm and an Agilent Zorbax eclipse XDB-C18 column (150 × 4.6 nmcolumn) with temperature was 40◦C. The mobile phase was a mixture of methanol, and water, (85:15 v/v) and the flow rate was 1.0 ml/min. The injection volume was 20µL according to [18].

Statistical analysis

The data were analysed by using SPSS statistics package version 20 (SPSS Inc., Chicago, IL, USA) with one-way ANOVA test the post hoc tests was used is Tukey. and expressed as mean ± SE where P value of less than 0.05 was considered statistically significant.

Results

The results from deep skin scraping under a light microscope confirmed sarcoptic mange infestation (Fig. 1). Clinical and physical examinations of dogs affected by mange revealed common symptoms, including severe pruritus, bruising, erythema, and alopecia, as illustrated in Fig. 2 Following treatment with ivermectin-loaded nanoemulsion, clinical improvement was observed (Fig. 3). Dogs infested with fleas exhibited clinical signs such as intense scratching, alopecia, erythema, crust formation, and papules localized on the head, neck, and lower back regions.

In the haemato-biochemical analysis (Table 1), significant differences were observed between control, flea-infested, and mange-infested dogs prior to treatment. Haemoglobin (Hb) levels were lower in both flea-infested and mange-infested dogs compared to the control group, with the decrease being statistically significant in mange-infested dogs ($p = 0.004$), suggesting a greater impact of mange on haemoglobin levels. Red blood cell (RBC) counts followed a similar trend, with a significant reduction in mange-infested dogs ($p = 0.003$). Haematocrit (HCT) levels were also lower in both infested groups, with a more significant reduction in mange-infested dogs ($p = 0.007$), correlating with the decreased RBC and haemoglobin levels. In terms of mean corpuscular haemoglobin concentration (MCHC), mange-infested dogs exhibited a significant decrease ($p = 0.002$), indicating potential alterations in erythrocyte integrity or haemoglobin

concentration. While platelet counts were reduced in both flea- and mange-infested dogs, these changes were not statistically significant.

White blood cell (WBC) counts increased in flea-infested dogs, though this rise was not statistically significant ($p = 0.86$), suggesting an immune response. Mange-infested dogs also showed an increase in WBCs, albeit less pronounced ($p = 0.38$). Liver function tests, as indicated by aspartate aminotransferase (AST) and alkaline phosphatase (ALP) levels, did not show significant differences between the groups, implying no severe impact on liver function. Additionally, both flea- and mange-infested dogs exhibited lower cholesterol and high-density lipoprotein cholesterol (HDL-C) levels compared to the control group. A significant reduction in triglycerides was noted in flea-infested dogs ($p = 0.01$), indicating potential metabolic disruptions due to infestation.

Post-treatment analysis of flea-infested dogs (Table 2) revealed gradual improvements over time. Haematological indices, including haemoglobin and RBC counts, fluctuated post-treatment but remained statistically non-significant across all time points. A significant increase in platelet count was observed by day 7 post-treatment ($p < 0.05$), which then normalized by day 28, indicating recovery from thrombocytopenia. WBC counts showed a significant decrease on day 7 post-treatment ($p < 0.05$), reflecting a reduction in inflammation, followed by an increase on day 28 ($p < 0.05$), possibly due to secondary infections.

Liver function tests exhibited significant fluctuations post-treatment, particularly in AST and ALP levels, with a marked rise in ALP on day 28 ($p < 0.05$). This suggests possible liver regeneration or stress following treatment. Improvements were also observed in the lipid profile, with cholesterol and HDL-C levels significantly increasing by day 28, indicating enhanced metabolic recovery post-treatment.

In mange-infested dogs (Table 3), more pronounced haematological changes were observed post-treatment. Haemoglobin levels decreased significantly by day 14 and day 28 ($p < 0.05$), indicating persistent anaemia. RBC and haematocrit levels followed similar patterns, with significant fluctuations throughout the treatment period. Platelet counts significantly increased by day 14 and day 21 ($p < 0.05$), reflecting an improvement in thrombocytopenia. Unlike flea-infested dogs, WBC counts remained relatively stable throughout the treatment period, suggesting a steady immune response.

Liver function tests showed significant variability, with a notable drop in AST on day 21 ($p < 0.05$), indicating alleviated liver stress post-treatment. ALP levels fluctuated, with a significant increase on day 14 ($p < 0.05$) and subsequent normalization by day 28. In terms of lipid profile, triglyceride levels significantly dropped by day 7 ($p < 0.05$), and cholesterol levels showed significant changes post-treatment, particularly by day 14, indicating improved lipid metabolism as mange infestation resolved.

Discussion

External parasites such as fleas and mange mites are common causes of discomfort in pets, leading to various clinical symptoms including itching, hair loss, wounds, and an overall unhealthy appearance. These parasites not only affect the skin but can also induce allergic reactions, causing conditions like flea allergy dermatitis. In addition to the visible discomfort, these infestations can lead to more profound systemic effects, particularly blood loss and immune responses.

In both groups of dogs infested with fleas and mange, significant decreases were observed in their complete blood count (CBC), likely due to blood loss from flea feeding [19]. Following treatment, these dogs showed restored levels of Hb, HCT, and Plts, which agrees with previous studies highlighting the positive effects of parasite eradication on blood parameters [20]. The increase in lymphocytes observed in both groups is indicative of an immune response, likely associated with inflammation or blood-borne parasites, further supporting findings from earlier research [21]. Additionally, eosinophilia, commonly linked to skin conditions such as allergies or flea infections, was also noted. This aligns with reports that elevated eosinophil levels can be associated with ectoparasitic infestations or other conditions such as respiratory issues [22, 23]. Some studies concluded that there was no activation or immune response detected in either monocytes or lymphocytes when ivermectin treatment was used [24].

Hepatobiliary enzymes, particularly alanine aminotransferase (ALT) and aspartate aminotransferase (AST), were elevated in both groups compared to the control group, with variations observed throughout the four-week treatment period. This is consistent with the understanding that hepatobiliary enzymes can be affected by various factors, including breed variation, hepatic disorders, and parasitic infections [25]. Ivermectin, the treatment used in this study, is known for its potent activity against a broad range of internal and external parasites, including fleas, ticks, and mites. However, the drug's impact on the neural and neuromuscular systems of parasites can also cause side effects in the host, including an increase in liver serum enzymes [26]. This hepatocellular injury, reflected by elevated ALT and AST levels, may result from ivermectin's effects on hepatic cells, especially in animals with pre-existing liver

conditions or those exposed to hepatotoxic substances [27]. Ivermectin experiences hepatic metabolism, with its breakdown products primarily excreted through feces [28]. This underscores the liver's critical role in processing the drug. To ensure safety and effectiveness, regular liver function tests are highly recommended for patients receiving ivermectin, especially in cases involving high dosages or pre-existing liver conditions. These tests help identify any potential hepatotoxic effects early, allowing for timely intervention and dose adjustments to mitigate risks [29]. Notably, these findings contrast with other studies reporting decreased levels of AST and ALT after ivermectin treatment [30].

Serum proteins, primarily secreted by hepatic cells, play essential roles in transport, immunity, inflammation, and coagulation. Some studies have also suggested that tissues such as the intestines, mammary glands, and lungs can contribute to serum protein production [31]. A slight increase in albumin observed after treatment in week four, particularly in dogs with flea infestations, could be attributed to dehydration or underlying liver conditions [32]. This finding aligns with previous studies that reported increases in total proteins following ivermectin treatment in experimental animals [33, 30]. The concentration of blood proteins is critical for maintaining their biological functions, and both pathological and non-pathological factors can influence serum protein levels [34]. The dogs in this study came from various environments, had different diets, and belonged to different breeds, all of which could have contributed to variations in the lipid profile [35].

Despite being infested with external parasites, most dogs with dyslipidemia appeared clinically healthy without significant symptoms [36]. Following treatment with ivermectin, an increase in cholesterol, HDL, and LDL levels was observed, which agrees with findings from other studies indicating that intradermal administration of ivermectin can elevate these lipid markers in serum, while decreasing triglyceride levels [37]. Flea infestations often cause discomfort and reduced appetite, leading to weight loss. However, after treatment and the eradication of fleas, the dogs regained their weight, as reflected in their improved lipid analysis results [38]. There are also findings that many factors like hormones, such as thyroid hormones, can affect lipid metabolism [39].

The aforementioned results of the formulated ivermectin nanoemulsion could be also attributed to its constituents, Dimethyl Sulfoxide (DMSO), absolute ethyl alcohol, and glycerol play vital roles in optimizing the drug's stability, solubility, and delivery efficiency. DMSO, a potent polar solvent, enhances the solubility of poorly water-soluble compounds and facilitates deeper penetration of nanoemulsion particles through biological barriers such as skin and mucosal membranes. DMSO helps to disrupt the skin's lipid structure, enabling ivermectin to penetrate more easily. Its ability to create a homogenous medium between oil and water phases is crucial in maintaining particle dispersion and ensuring drug stability [40]. Absolute ethyl alcohol, on the other hand, serves both as a solvent and a co-surfactant, aiding in the dissolution of oils and active ingredients while lowering surface tension to promote the formation of nano-sized droplets [41]. This property helps prevent the coalescence of larger droplets, thus improving the emulsification process and enhancing the uniformity of the nanoemulsion. Additionally, glycerol contributes as a humectant and stabilizing agent, preventing phase separation and modulating the viscosity of the system. Its hygroscopic nature also imparts moisturizing properties, which is particularly beneficial in topical and cosmetic applications [42]. Together, these components ensure the nanoemulsion exhibits desirable characteristics such as enhanced solubility, stability, and bioavailability, making it an effective vehicle for the delivery of active compounds. Nanoemulsion Delivery systems for ivermectin improve drug solubility, enhance bioavailability, and allow for targeted delivery. These advancements may lower required doses and enhance safety profiles, particularly for long-term treatments. However, there is limited research on the extended use of these formulations in animals, highlighting the need for studies to understand their safety, pharmacokinetics, and efficacy better.

Conclusion

Treatment of external parasites, particularly with nanoemulsion loaded with ivermectin, not only alleviated clinical symptoms but also led to improvements in blood and biochemical parameters, demonstrating its efficacy in managing parasitic infestations in dogs. However, the potential hepatic side effects of ivermectin warrant careful consideration, especially in dogs with underlying liver conditions.

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Not applicable

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Declaration of Conflict of Interest

The authors declare that there is no conflict of interest.

Ethical of approval

In order to perform this experimental trial, we took the approval of The Institutional Animal Care and Use Committee with ethical approval no. (Vet CU 03162023721).

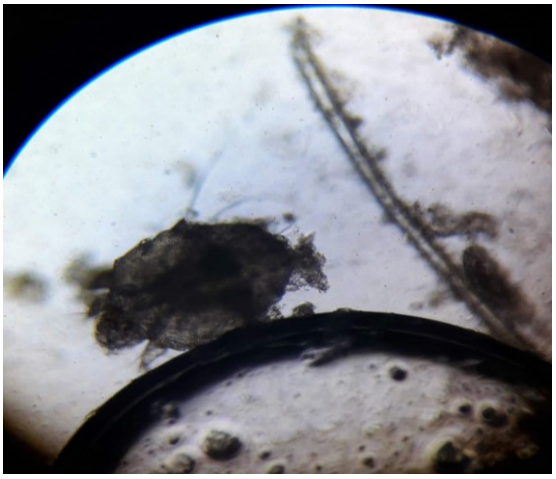

Fig. 1. Showed *Sarcoptic scabie* mange under light microscope using skin scraping technique

Fig. 2 Premedication

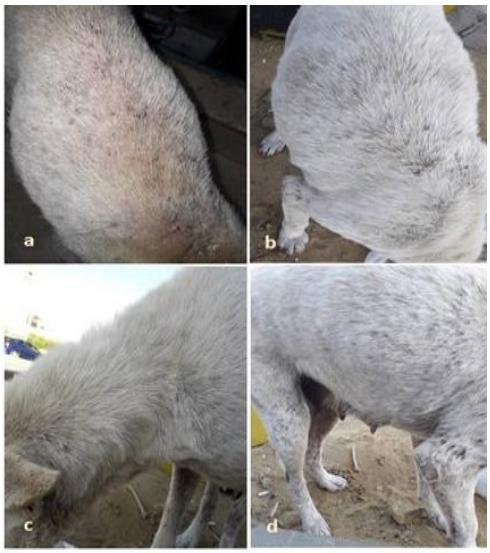

Fig. 3 Post medication

Fig. 2. Represent one-year old balady dog showed clinical signs of sarcoptic mange before treatment. (a,b)showed itching, alopecia, pruritus on the dog's back. (c) Showed erythema, erosion, and hair loss on the dog neck. (d) Showed erythema at the four limps.	**Fig. 3. Post medication with Nanoemulsion loaded with ivermectin. (a) After two weeks of treatment the hair starts to grow with less singe of erythema. (b,c,d) They showed that the clinical signs almost disappeared at week four after applying the treatment of nanoemulsion loaded with ivermectin.**

TABLE 1. Hemato-biochemical analysis of control group compared to pre-medication in dogs infested with flea and mange

Groups / Variables	Control (n=7) mean ± SE	Pre-medication (flea infested dogs) (n=5) mean ± SE	*p* value at 95% confidence interval	Pre-medication (mange infested dogs) (n=5) mean ± SE	*p* value at 95% Confidence interval
Hb (g/dl)	17.58 ± 0.64	13.88 ± 0.48	0.10	13.66 ± 0.73	0.004
RBCs (x10^6 u/L)	7.52 ± 0.28	6.66 ± 0.22	0.06	5.72 ± 0.37	0.003
HCT (%)	49.41 ± 1.80	39.50 ± 1.04[c]	0.04	38.62 ± 2.41	0.007
MCV (fl)	65.86 ± 1.56	58.33 ± 2.31	0.50	67.48 ± 1.36	0.522
MCH (pg)	23.40 ± 0.55	20.04 ± 0.99	0.28	22.60 ± 0.31	0.341
MCHC (g/dl)	35.57 ± 0.15	34.30 ± 0.34	0.06	33.72 ± 0.45[c]	0.002
Plts (x10^3 u/L)	258.50 ± 31.07	119.67± 11.89	0.10	107.00 ± 16.70	0.14
WBCs(x10^{3}u/L)	9.95 ± 0.38	18.66 ± 2.00	0.86	13.56 ± 0.68	0.38
Neutrophils (%)	67.75 ± 5.70	21.83 ± 0.48[c]	0.05	51.33 ± 11.17	0.22
Eosinophils (%)	2.33 ± 0.33	4.67 ± 0.33	1.00	9.00 ± 0.70	0.07
Monocytes (%)	3.92 ± 0.34	3.7 ± 0.6[c]	0.38	5.28 ± 1.43	0.09
Lymphocytes (%)	15.33 ± 0.67	69.33 ± 0.33	0.14	68.66 ± 8.66	0.12
		Liver functions			
AST (U/I)	48.66 ± 2.27	34.60 ± 0.93	0.29	47.33 ± 7.21	0.21
ALP (U/I)	155.66 ± 10.66	34.0 ± 6.0	0.20	176.00 ± 8.717	0.56
Albumin (gm/dl)	3.28 ± 0.13	2.34 ± 0.09	0.97	2.71 ± 0.23	0.36
Globulin (gm/dl)	2.62 ± 0.21	2.36 ± 0.18	0.56	2.46 ± 0.38	0.92
		Lipid profile			
Cholesterol (mg/dl)	178.83 ± 7.14	123.00 ± 9.13	0.66	106.60 ± 10.09	0.47
Triglycerides (mg/dl)	114.50 ± 8.23	36.80 ± 4.33[b]	0.01	85.75 ± 8.68	0.30
HDL_C (mg/dl)	134.77± 5.08	43.53 ± 1.07[c]	0.02	101.33 ± 12.34	0.21
LDL_C (mg/dl)	32.00 ± 3.51	52.26 ± 3.03	0.71	18.66 ± 1.79	0.17

a: p≥ 0.001, b: p≥ 0.01, c: p≥ 0.05

TABLE 2. Results of hemato-biochemical analysis in dog infested with fleas at pre-medication compared to 7, 14, 21- and 28-days post treatment.

Groups / Variables	pre-medication	7 days post treatment	14 days post treatment	21 days post treatment	28 days post treatment
Hb (g/dl)	13.88 ± 0.48 a	12.76 ± 0.27 a	14.28 ± 0.89 a	12.88 ± 0.36 a	13.96 ± 1.04 a
RBCs (x10^6 u/L)	6.66 ± 0.22 a	6.28 ± 0.19 a	7.00 ± 0.05 a	6.20 ± 0.27 a	7.38 ± 0.74 a
HCT (%)	39.50 ± 1.04 a	37.48 ± 1.09 a	40.98 ± 2.41 a	35.74 ± 0.89 a	41.10 ± 2.90 a
MCV (fl)	58.33 ± 2.31 a	61.35 ± 2.79 a	56.77 ± 2.06 a	58.51 ± 2.43 a	57.15 ± 4.83 a
MCH (pg)	20.04 ± 0.99 a	22.94 ± 2.24 a	18.72 ± 0.72 a	21.09 ± 1.44 a	19.39 ± 1.67 a
MCHC (g/dl)	34.30 ± 0.34 a	30.49 ± 3.34 a	34.81 ± 0.17 a	35.72 ± 1.27 a	31.91 ± 1.72 a
Plts (x10^3 u/L)	119.67± 11.89 a	223.00 ± 11.97 b	195.00 ± 14.50 a	195.00 ± 14.50 b	148.20 ± 14.25 a
WBCs(x10^{3}u/L)	18.66 ± 2.00 a	12.75 ± 0.83 b	16.03 ± 1.40 ab	15.18 ± 1.43 ab	21.52 ± 0.77 c

Groups / Variables	pre-medication	7 days post treatment	14 days post treatment	21 days post treatment	28 days post treatment
Neutrophils (%)	21.83 ± 0.48 a	17.33 ± 3.71 a	52.08 ± 2.69 ab	61.45 ± 2.73 b	54.33 ± 8.29 ab
Eosinophils (%)	4.67 ± 0.33 ab	6.50 ± 0.50 ab	5.66 ± 0.66 a	9.00 ± 1.00 b	6.33 ± 0.66 a
Monocytes (%)	3.7 ± 0.69 a	4.80 ± 0.33 ab	4.12 ± 0.19 a	7.86 ± 0.27 b	5.00 ± 1.47 ab
Lymphocytes (%)	69.33 ± 0.33 a	72.66 ± 5.17 a	32.00 ± 2.00 b	22.17 ± 3.40 b	72.66 ± 9.35 a
Liver functions					
AST (U/I)	34.60 ± 0.93 a	53.33 ± 8.33 ab	63.00 ± 3.27 b	42.80 ± 4.93 a	52.50 ± 2.82 b
ALP (U/I)	34.0 ± 6.0 a	75.76 ± 9.14 a	81.33 ± 8.17 a	81.33 ± 3.28 a	110.90 ± 19.55 b
Albumin (gm/dl)	2.34 ± 0.09 a	3.18 ± 0.05 b	2.01 ± 0.03 a	2.07 ± 0.04 a	3.23 ± 0.38 b
Globulin (gm/dl)	2.36 ± 0.18 a	2.24 ± 0.17 a	3.42 ± 0.31 b	2.00 ± 0.26 a	2.90 ± 0.30 ab
Lipid profile					
Cholesterol(mg/dl)	124.00 ± 9.13a	140.40 ± 11.80 ab	137.20 ± 6.87 ab	134.60 ± 8.83 ab	165.10 ± 12.35 b
Triglycerides(mg/dl)	36.80 ± 4.33 ab	40.66 ± 2.33 ab	59.00 ± 8.71 a	49.00 ± 3.86 ab	31.66 ± 6.00 b
HDL_C (mg/dl)	43.53 ± 1.07 a	85.93 ± 7.05 b	73.26 ± 8.40 ab	63.50 ± 2.66 ab	124.60 ± 9.60 c
LDL_C (mg/dl)	52.26 ± 3.03 a	44.60 ± 0.80 a	66.16 ± 5.25 ab	76.20 ± 5.02 b	41.46 ± 4.64 a

* Means having similar lowercase letter within the same row are not significantly different at *P* value less than 0.05 level of probability.

TABLE 3. Hemato-biochemical analysis indog infested with mange at pre-medication compared to 7, 14, 21- and 28-days post treatment.

Groups / Variables	Pre-medication	7 days post treatment	14 days post treatment	21 days post treatment	28 days post treatment
Hb (g/dl)	13.66 ± 0.73a	15.76 ± 0.91 a	12.66 ± 0.31 b	13.32 ± 0.19 ab	11.26 ± 1.15 b
RBCs (x10^6 u/L)	5.72 ± 0.37a	7.09 ± 0.44 a	5.66 ± 0.18 b	5.98 ± 0.08 b	6.39 ± 0.41 ab
HCT (%)	38.62 ± 2.41a	47.25 ± 2.88 a	38.54 ± 1.20 b	41.20 ± 0.59 ab	35.15 ± 2.76 b
MCV (fl)	67.48 ± 1.36a	68.54 ± 2.10 a	68.10 ± 0.45 a	68.38 ± 1.06 a	62.88 ± 6.70 a
MCH (pg)	22.60 ± 0.31a	22.44 ± 0.44 a	22.39 ± 0.21 a	22.37 ± 0.41 a	18.83 ± 1.73 b
MCHC (g/dl)	33.72 ± 0.45a	33.25 ± 0.55 ab	32.89 ± 0.27 ab	33.00 ± 0.60 ab	30.11 ± 2.07 b
Plts (x10^3 u/L)	107.00 ± 16.70 a	214.00 ± 14.00 b	284.66 ± 2.02 bc	282.66 ± 11.66 bc	151.33 ± 12.34 a
WBCs (x10^3 u/L)	13.56 ± 0.68 a	14.56 ± 0.81 a	15.63 ± 0.18 a	15.43± 0.51 a	14.11± 0.42 a
Neutrophils (%)	51.33 ± 11.17 a	12.66 ± 2.72 b	25.00 ± 2.70 a	45.23 ± 4.43 a	40.00 ± 3.60 a
Eosinophils (%)	9.00 ± 0.70 a	3.60 ± 0.73 b	8.80 ± 0.72 a	9.50 ± 0.50a	6.80 ± 0.52 a
Monocytes (%)	5.28 ± 1.43 a	6.60 ± 0.61 a	5.80 ± 0.59 a	6.00 ± 0.57a	3.33 ± 0.33 a
Lymphocytes (%)	68.66 ± 8.66 ac	74.75 ± 2.92 ac	25.00 ± 2.42 b	33.40 ± 3.65 b	68.66 ± 6.96 ac
Liver function					
AST (U/I)	47.33 ± 7.21 ab	61.00 ± 2.04 a	60.32 ± 6.69 a	34.00 ± 2.70 b	48.66 ± 4.84 ab
ALP (U/I)	176.00 ± 8.717 a	159.66 ± 11.25 a	209.00 ± 25.11 b	262.75 ± 39.58 ab	92.10 ± 29.05 a
Albumin (gm/dl)	2.71 ± 0.23 ab	3.02 ± 0.0.31 ab	3.30 ± 0.15 a	1.96 ± 0.14 b	2.87 ± 0.08 ab
Globulin (gm/dl)	2.46 ± 0.38 a	3.02 ± 0.35 a	2.18 ± 0.18 a	2.50 ± 0.31 a	2.42 ± 0.32 a
Lipid profile					
Cholesterol(mg/dl)	106.60 ± 10.09 a	111.66 ± 12.86 ab	165.36 ± 12.50 b	142.40 ± 9.88 ab	135.00 ± 12.47 ab
Triglycerides(mg/dl)	85.75 ± 8.68 a	22.00 ± 1.00 b	42.75 ± 3.19 bc	50.32 ± 5.33 c	45.95 ± 3.06 bc
HDL_C (mg/dl)	101.33 ± 12.34 a	75.93± 10.63 ab	70.40 ± 2.78 b	58.33 ± 6.88 b	94.00 ± 4.79 a
LDL_C (mg/dl)	18.66 ± 1.79 a	15.80 ± 2.91 a	32.65 ± 16.48 a	62.95 ± 9.83 b	35.83 ± 5.99 b

* Means having similar lowercase letter within the same row are not significantly different at *P* value less than 0.05 level of probability

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إيفرمكتين نانوي معزز للعلاج عبر الجلد لحالات الإصابة بالطفيليات الخارجية في الكلاب

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الملخص

ان وجود الطفيليات الخارجية في الكلاب، مثل البراغيث ومرض الجرب، يمثل مصدر قلق صحي كبير يؤثر على رفاهية ومظهر الحيوانات. تهدف هذه الدراسة التجريبية إلى تقييم فعالية نانوإيمولسيون محملة بالإيفرمكتين في علاج الكلاب المصابة بالبراغيث ومرض الجرب. شملت التجربة سبعة عشر كلبًا، تم تقسيمهم إلى ثلاث مجموعات: مجموعة ضابطة تتكون من سبعة كلاب اصحاء، ومجموعة من خمسة كلاب تعاني من إصابات بالبراغيث، ومجموعة من خمسة كلاب مصابة بالجرب. تم جمع عينات من الدم لتقييم التغيرات في المعايير الهيماتولوجية(CBC) ، وظائف الكبدALP) ، (AST، وملف الدهون (الدهون الثلاثية، الكوليسترول، HDL، LDL، الألبومين، والجلوبيولين) قبل وبعد العلاج على فترات أسبوعية لمدة أربعة أسابيع.

أظهرت النتائج انخفاضًا ملحوظًا في الهيماتوكريت(HCT) ، والعدلات، ومستويات الدهون الثلاثية، و HDLفي الكلاب المصابة بالبراغيث، بينما أظهرت الكلاب المصابة بالجرب انخفاضًا كبيرًا في مستويات الهيموغلوبين(Hb) ، وكريات الدم الحمراء(RBCs) ، وحجم الخلايا المعبأة(PCV) ، وتركيز الهيموغلوبين الكروي الوسيط (MCHC) مقارنة بالمجموعة الضابطة. سريريًا، أظهرت النانوإيمولسيون المحملة بالإيفرمكتين تحسنًا ملحوظًا في كلا المجموعتين، مع تأثير ملحوظ بشكل خاص في الكلاب المصابة بالجرب.

في الختام، أثبت استخدام مستحلب محملة بالإيفرمكتين أنه فعال للغاية في علاج إصابات الطفيليات الخارجية، وخاصة البراغيث ومرض الجرب، في الكلاب، مما يوفر نهجًا علاجيًا واعدًا لتحسين صحة وجودة حياة الحيوانات المتأثرة.

الكلمات الدالة : مستحلب النانو، الإيفرمكتين، الكلاب، البراغيث، الجرب.