Research Article

Preliminary Evaluation of the Therapeutic Effects of Neem Leaf Extract and Ivermectin in West African Dwarf Goats with Clinical Mange

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Running (short) title: Neem Leaf Extract as a Treatment for Mange in WAD Goats

Abstract

This study investigates the effectiveness of neem (*Azadirachta indica*) extract as a topical treatment for mange in West African Dwarf (WAD) goats, a breed commonly raised in Southern Nigeria and are affected by mange, which undermines animal welfare and productivity. Twelve mange-infected goats were randomly assigned to three treatment groups: T1 (10 ml ivermectin pour-on), T2 (5 ml neem extract + 5 ml ivermectin), and T3 (10 ml neem extract). Treatments were applied over 14 days, and data were collected on skin scrapings, red blood cell (RBC) count, white blood cell (WBC) count and serum biochemical indices. Phytochemical analysis of neem extract revealed notable levels of alkaloids, saponins, and phenols. All groups showed improved skin condition post-treatment, with significant increases in RBC and WBC counts observed in T2 goats ($P<0.05$). Differences in serum biochemical indices, particularly potassium, were also noted. Findings indicate that neem extract can serve as an effective alternative or adjunct treatment to ivermectin for mange control in WAD goats reared in the local environments with poor accesibility to conventional drugs, improving animal health and production outcomes.

Keywords

Neem leaf, Ivermectin, Mange, West African Dwarf goats, Topical, Food security

Abbreviations

WAD: West African Dwarf

RBC: Red Blood cells

WBC: White Blood Cells

DM: Dry Matter

CP: Crude Protein

Introduction

Achieving food security, a central objective of the Sustainable Development Goals, is closely linked to the availability of animal-sourced proteins. This underscores the importance of evaluating and implementing effective strategies to enhance animal production systems [1]. Numerous factors hinder animal productivity, including management challenges, limited feed availability, and the prevalence of pests and diseases [2].

One of the prevalent diseases affecting the West African Dwarf (WAD) goats, in Southern Nigeria is mange [3]. Mange is a parasitic dermatopathy caused by infestation of the skin and hair follicles by mites or lice, affecting a wide range of mammalian hosts, including companion animals, livestock, and occasionally humans. The condition is characterised by clinical signs such as intense pruritus, restlessness, excessive scratching and rubbing, alopecia, fatigue, reduced growth performance, and cutaneous lesions. In livestock, mange presents a significant welfare and economic concern, particularly in severe infestations. Economic losses are attributed to reduced weight gain, compromised skin and fleece quality, anaemia, poor body condition, decreased milk and meat yields, and lowered reproductive efficiency, including suboptimal lambing and kidding rates [4, 5, and 6]. Mange can affect farm animals of all ages, with higher prevalence observed among those reared under poor management conditions. Mange mites are among the most detrimental ectoparasites of livestock, primarily transmitted through direct contact with infested animals [7]. Although a variety of ectoparasiticidal drugs are commercially available for mange treatment, their rising costs and limited accessibility pose challenges for smallholder and subsistence farmers. Despite significant advances in modern veterinary medicine, traditional medicinal practices remain a primary means of disease management in many rural communities [8]. Numerous medicinal plants have been

documented to exhibit antiviral, antifungal, antibacterial, analgesic, and antipyretic activities, suggesting their potential as alternative therapeutic agents for ectoparasitic infections [9]. Most medicinal plants are considered safe, cost-effective, and generally free from issues associated with drug resistance and residual toxicity [10]. Neem (*Azadirachta indica* A. Juss.), a widely recognized multipurpose plant, exhibits a broad spectrum of biological activities. Phytochemicals derived from medicinal plants have shown significant promise due to their diverse biological effects and potential medicinal applications, making them valuable resources for the development of pharmaceuticals, industrial products, and the integrated management of agricultural pests [11]. Neem, in particular, has been described as a panacea for various dermatological conditions [12]. It was reported that 20% crude aqueous extract of neem demonstrated acaricidal efficacy comparable to ivermectin, as it did not induce hepatic and renal toxicity, and also enhanced growth performance in rabbits infested with *Sarcoptes scabiei* var. *cuniculi* [7]. Given its therapeutic potential, it is worthwhile to evaluate the efficacy of neem leaves in the treatment of mange. This study, therefore, investigates the effectiveness of topical neem leaf extract compared to ivermectin in the treatment of mange in infected WAD goats.

Results

Biochemical Composition of Neem Extract

The biochemical composition of the neem extract and ivermectin pour-on is summarized in Table I. The neem extract contained notable levels of alkaloids (0.468%), saponins (0.379%), and phenols (0.189%), with alkaloids being the most abundant active compound. Glycosides (0.185%) and tannins (0.0033%) were present in moderate amounts, while other compounds were found in trace quantities.

Histopathological Changes

Histological analysis of skin samples before treatment (Figures I a, II a, and III a) revealed hyperkeratosis and atrophy, reflecting extensive damage from the mange infection. Post-treatment (Figures I b, II b, and III b), the epidermis of the WAD goat skins appeared normal with moderate cellular infiltration, except for animals treated with neem extract, which exhibited minimal cellular infiltrates.

Haematological changes

Table II presents the haematological indices of the WAD goats before and after topical treatment with neem extract and ivermectin. Before the treatment, significant differences ($P<0.05$) were observed in Red blood cell (RBC), haemoglobin, mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC), platelet count, RDW-CV, and PDW among experimental groups, while white blood cell count (WBC), haematocrit, and mean corpuscular volume (MCV) values showed no significant differences ($P>0.05$). Significant increases ($P<0.05$) in WBC, RBC, MCV, MCH, MCHC were observed across all experimental groups after treatment. However, haemoglobin and haematocrit levels did not

significantly increase (P>0.05), and only platelet distribution width (PDW) and the percentage of large platelets increased significantly in treatments T1 and T2.

Significant changes (P<0.05) in RBC, haemoglobin, haematocrit, RDW-CV, PDW, and mean platelet volume (MPV) were observed in animals treated with the combination of 5 ml neem extract and 5 ml ivermectin (T2). However, no significant differences (P>0.05) were found in WBC, MCV, MCH, MCHC, platelet count, or platelet large cell ratio (PLCR) across treatments. Animals treated with 10 ml ivermectin (T1) and 10 ml neem extract (T3) showed no significant differences (P>0.05) between each other.

Serum Biochemical Indices

Table III presents the serum biochemical indices and mineral levels of the WAD goats before and after topical treatment with neem extract and ivermectin. No significant differences were observed among treatments for most parameters, except for potassium, which showed a significant change after treatment.

Discussion

The biochemical analysis of neem extract revealed significant levels of alkaloids (0.468%), saponins (0.379%), and phenols (0.189%). These compounds have been shown to possess anti-parasitic properties, which could explain the observed effectiveness of neem extract against mange [12]. The biochemical contents, such as saponin and azadirachtin, could have increased the healing rate, and thus the animal can increase its intake of the feed. Saponin is one of the major constituents of neem that is responsible for the treatment of skin diseases. Alkaloids and saponins were responsible for the positive effect of the neem leaf extract on the mange-infected WAD goats. Saponins are reported to have antibiotic, antifungal and antiviral activities [13].

Neem has been traditionally used as an herbal remedy for various parasitic infestations, with studies showing that its active constituents can exert acaricidal, antibacterial, and antifungal activities [14 and 7]. The moderate presence of glycosides (0.185%) and tannins (0.0033%) in neem extract suggest their potential role in enhancing the extract's therapeutic properties, as both tannins and saponins are known for their antimicrobial and anti-inflammatory effects [14]. The ivermectin pour-on, with its active ingredient at 5 mg/ml, aligns with standard concentrations used for treating mange in livestock and was included as a conventional treatment for comparison.

Histopathological examination of skin samples before and after treatment revealed notable improvements, especially in the animals treated with neem extract (Figure III b). Before treatment, all animals (Figures I a, II a and III a) showed signs of hyperkeratosis (a skin condition that occurs when the skin becomes thicker than usual in some places [15] and epidermal atrophy, common indicators of mange infestation [7]. After treatment, the skins of the neem-treated goats showed normal epidermis with minimal cellular infiltrate (Figure III b), suggesting that neem extract not only alleviated the clinical symptoms of mange but also promoted skin recovery. This finding supports previous research indicating the skin-healing and anti-inflammatory properties of neem, which contribute to its effectiveness in treating skin conditions [7].

Haematological changes also provided insights into the systemic effects of the treatments. The significant differences in the haematological parameters and the low values before the treatment, with the exception of WBC, haematocrit and MCV implies that the severity of the mange infection varies among the animals. Across all treatments, significant increases in WBC; RBC, MCV, MCH, and mean corpuscular haemoglobin concentration (MCHC) were observed

after the treatment. These changes suggest an improvement in immune function and red blood cell production, likely in response to the reduction in parasitic load [9]. The increased WBC recorded after the treatment in this study is still within the recommended range for WAD goats - 6.8-20.1×10^3µ/l) reported by [16]. Interestingly, no significant changes were observed in haemoglobin or haematocrit, indicating that these parameters might be less sensitive to the effects of the treatments in the short term. The observed increases in platelet distribution width (PDW) and the percentage of large platelets (PLCR) in the T1 and T2 groups could suggest a heightened thrombopoietic response to infection and subsequent treatment [9].

The values for post-treatment of albumin in this study (3.09-3.16g/dl) are closely related to 2.7-3.9g/dl reported by [17] as the normal range of albumin for goats. Albumin is quantitatively the most important plasma protein synthesized by the liver, and it indicates its health status. The total protein observed in this study (4.90-5.60 g/dl) was lower than that reported by [18] (5.5-9.0g/dl) but consistent with 6.0 -7.0 reported by [19]. Abnormally low protein levels indicate anaemia. Decreased total protein recorded before treatment confirms the activities of the parasitic microorganisms, thus interfering with the normal absorption of nutrients [20]. This confirms the activities of the mites that feed on the blood of the host animal. The significant increase experienced was evident as the neem extract biochemicals inhibited the activities of the mites.

Serum biochemical analyses showed no significant differences in most parameters across treatments, except for potassium, which increased significantly post-treatment. Potassium is essential for maintaining cellular functions, and its increased levels may reflect improved cellular health and metabolic function following treatment [21]. The absence of significant changes in other serum indices suggests that the treatments did not induce major metabolic

disruptions or deficiencies, further highlighting the safety of neem extract and ivermectin as topical treatments for mange.

In conclusion, neem extract proved to be a promising alternative or complementary treatment for mange in WAD goats, offering improvements in blood profile and skin recovery similar to ivermectin. Neem's bioactive compounds, such as alkaloids and saponins, may contribute to its acaricidal and growth-promoting effects. Given its efficacy, affordability, and safety, neem extract represents a valuable tool for managing mange in small ruminant production systems, particularly in resource-limited settings. Future studies should explore the long-term effects and optimal dosages of neem extract in various animal species, as well as its potential in integrated pest management strategies. This research work could be repeated across seasons and with other breeds of goats.

Materials and Methods

Experimental site and location: The experiment was carried out at the Small Ruminant Unit of the Ladoke Akintola University of Technology Teaching and Research Farm, Ogbomoso, Oyo State, Nigeria. The study was conducted following the ethical guidelines for the care and use of animals in research, as approved by the Committee on Research Ethics, Faculty of Agricultural Sciences, Ladoke Akintola University of Technology.

Preparation of the test ingredient: Fresh neem (*Azadirachta indica*) leaves (5 kg) were harvested from trees located within the farm premises. The leaves were allowed to wilt slightly before being homogenized with 10 litres of clean water. The resulting mixture was left to macerate overnight in a dark, enclosed environment to minimize light-induced degradation and prevent fermentation. The extract was subsequently filtered using a muslin cloth to remove the leaves. The extract was then kept in a clean, airtight plastic container. Ivermectin, the

conventional treatment used for comparison, was procured from a certified veterinary pharmacy. The formulation consisted of a mixture of 22,23-dihydroavermectin B1a (≥90%) and 22,23-dihydroavermectin B1b (≤10%). The active ingredient in the ivermectin pour-on was ivermectin at a concentration of 5 mg/ml.

***Experimental animals, housing and management*:** Twelve West African Dwarf (WAD) goats, with an average body weight of 10.22 kg and diagnosed with mange, were sourced from local ruminant farmers within the neighbourhood. The experimental pen was thoroughly cleaned and disinfected, and wood shavings were used as bedding material for the animals. The goats were quarantined for two weeks and allowed a subsequent two-week acclimatization period before the trial began. During the acclimatization phase, the goats were offered *Megathyrsus maximus* as basal diet, supplemented with concentrate feed (Brewers dry grain -20%, cassava peel – 41%, wheat offal-35%, salt – 2%, bone meal- 1% and premix-0.5%), provided with a salt lick, and had free access to water *ad libitum*.

The twelve goats were weighed, balanced by body weight, and randomly assigned to one of three treatment groups; and each animal was tagged for identification. The treatment groups were: Treatment 1 (T1), which received 10 ml of ivermectin pour-on; Treatment 2 (T2), which received a combination of 5 ml of neem extract and 5 ml of ivermectin pour-on; and Treatment 3 (T3), which received 10 ml of neem extract. All treatments were applied topically along the dorsal midline using a syringe (improvised), once a day for two weeks. This is to ensure that the causal organisms are eliminated.

Data collection:

A comprehensive physical examination was performed to diagnose mange infection in the animals. Skin scrapings were collected using sterile surgical blades and immediately preserved in 10% neutral-buffered formalin for histopathological analysis. 10 ml blood samples were collected at both the start and end of the trial from the jugular vein of each animal using sterile needles and syringes. Approximately 5 ml of blood was drawn into sample tubes containing Ethylene Diamine Tetraacetic Acid to prevent coagulation for haematological analysis. Serum biochemical indices were assessed using 5 ml sample collected in plain tubes. The tubes were immediately sealed, gently mixed by repeated inversion or rocking for one minute, and then transported to the laboratory in an ice-packed container to preserve sample integrity. The collected blood samples were analyzed using Haema-autoanalyser B1110 5 plus (Prestige Diagnostics Ltd, United Kingdom).

***Laboratory Procedure and Chemical Analysis*:** The neem extract was evaluated for the presence of alkaloids, tannins, phlobatannins, saponins, flavonoids, terpenes, and steroids using the standard procedures for phytochemical screening and as reported by [22].

Experimental design: The study used a Completely Randomized Design for the experiment.

Statistical analysis: Data were analyzed using a one-way analysis of variance (ANOVA) with SAS software package [23]. In cases where ANOVA revealed significant differences among treatment means, Duncan's Multiple Range Test (DMRT) was used to determine which means differed significantly, with statistical significance set at the 5% level.

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Figure 1.a

The extent of tissue damage as a result of mange infection is evident in the image. The two representative image samples from animals in the treatment revealed hyperkeratosis (thickening of the skin), scabs and inflammation, symptoms of untreated mange.

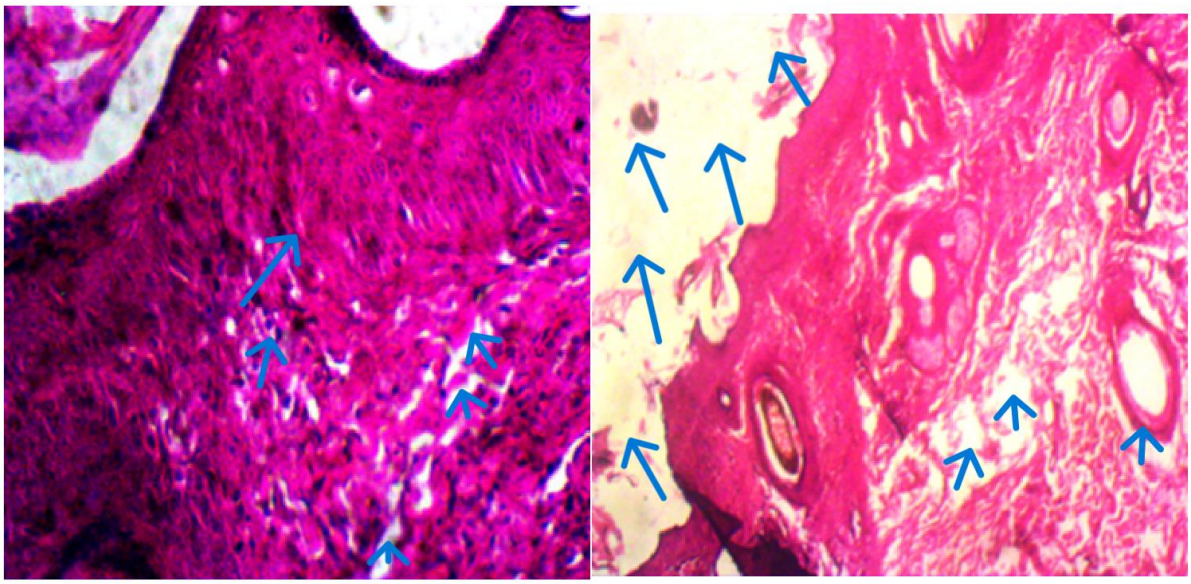

Figure I a: Skin scrapings of the mange infected WAD goats before topical treatment with Ivermectin (T1)

Hyperkeratosis is evident on the skin scraping before the treatment.

Figure 1.b
After the treatment of the mange infected West African dwarf goats with Ivermectin (T1), the histopathological analysis revealed that the epidermis is normal but there is moderate cellular infiltrate in the dermis.

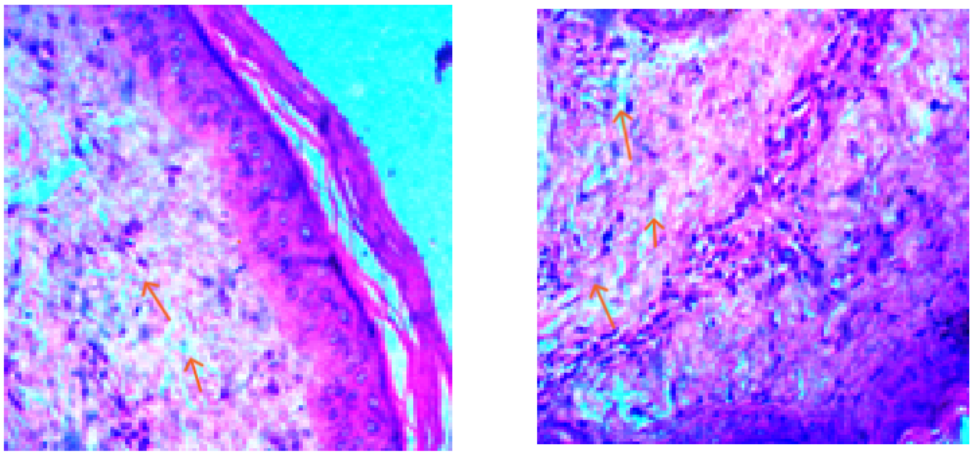

Figure I b: Skin scraping of the mange infected WAD goats after topical treatment with ivermectin (T1)

The epidermis is normal but there is moderate cellular infiltrate in the dermis.

Figure 2.a
The two representative image samples from animals in the treatment revealed scabs, hyperkeratosis (thickening of the skin), inflammation, and alopecia, which are symptoms of untreated mange.

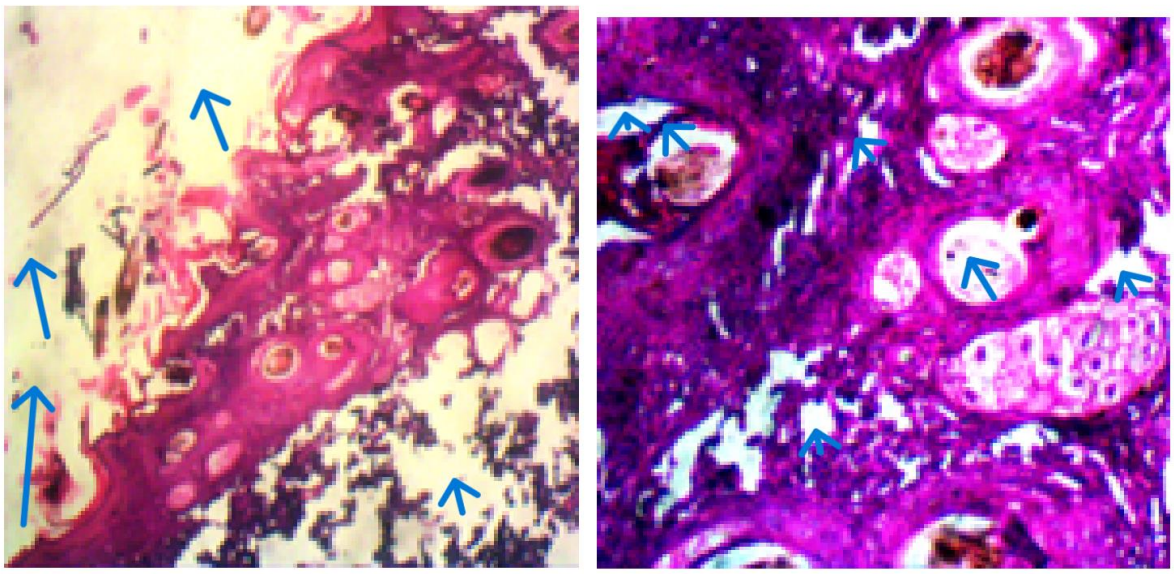

Figure II a: Skin scrapings of the mange infected WAD goats before topical treatment with Ivermectin and Neem leaf extract (T2)

Figure 2.b
After the treatment of the mange infected WAD goats with Ivermectin and neem leaf extract (T2), the histopathological analysis revealed that the epidermis is normal but there is moderate cellular infiltrate and hyperplasia of peri-follicular.

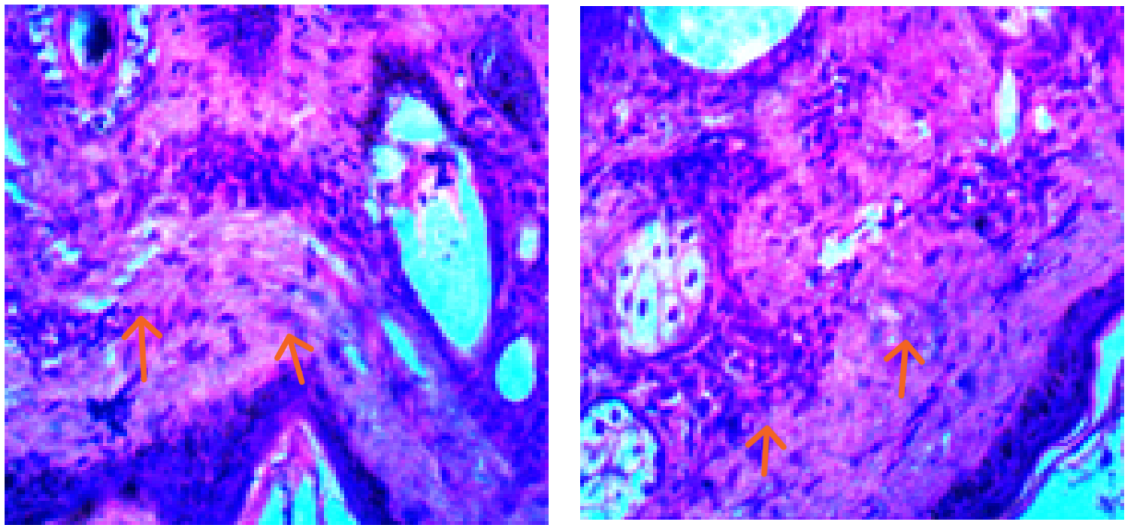

Figure II b: Skin scraping of the mange infected WAD goats after topical treatment with ivermectin and neem leaf extract (T2)

After the treatment of the mange infected WAD goats with Ivermectin and neem leaf extract (T2), the histopathological analysis revealed that the epidermis is normal but there is moderate cellular infiltrate and hyperplasia of peri-follicular.

Figure 3.a

The two representative image samples from animals in the treatment revealed atrophy of the epidermis, hyperkeratosis (thickening of the skin), scabs, inflammation, and alopecia, which are symptoms of untreated mange.

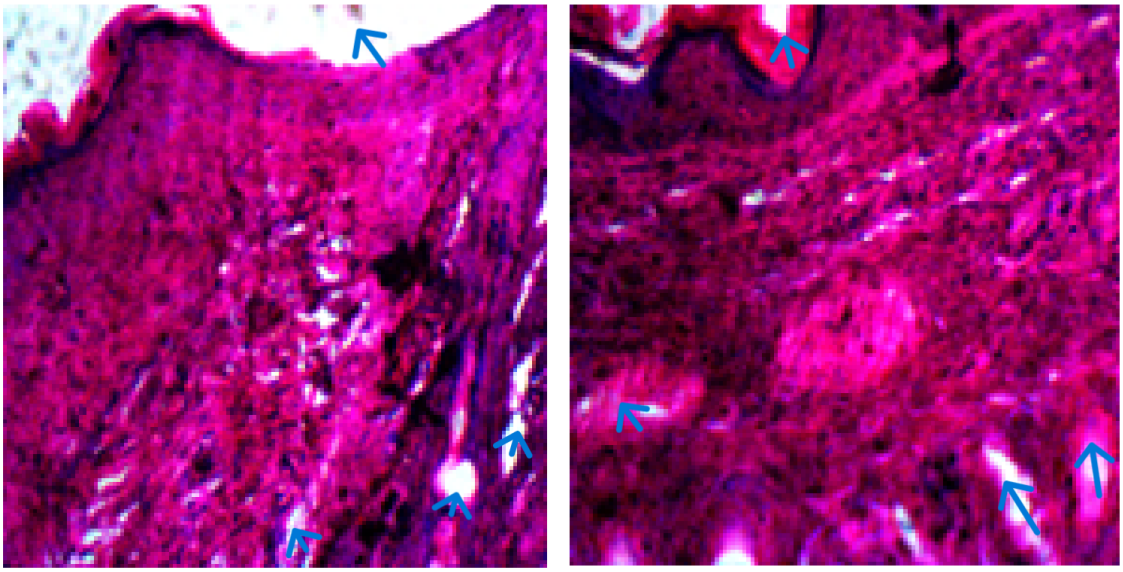

Figure III a: Skin scrapings of the mange infected WAD goats before topical treatment with Neem leaf extract (T3)

There is hyperkeratosis before the animals were exposed to the treatment.

Figure 3.b
After the treatment of the mange infected WAD goats with neem leaf extract (T3), the histopathological analysis revealed that the epidermis is normal with a few cellular infiltrates in the dermis.

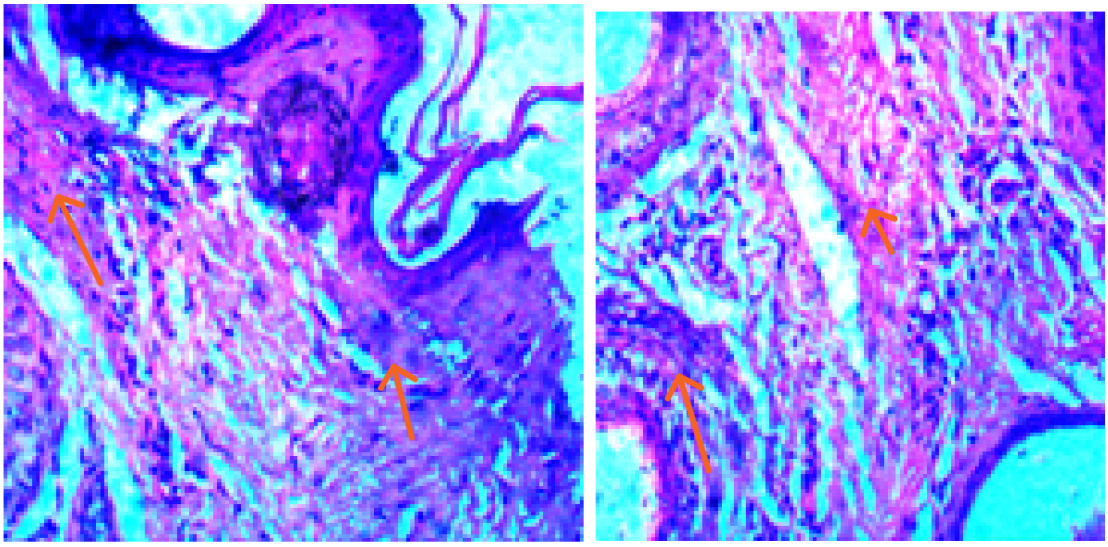

Figure III b: Skin scraping of the mange infected WAD goats after topical treatment with neem leaf extract (T3)

The epidermis is normal with a few cellular infiltrates in the dermis.

Table I: Biochemical composition of the neem extract

Parameters	Observation Qualitative	Phyto Quantitative (%)
Neem extract		
Alkaloids	+++	0.4680±0.05
Tannin	++	0.0033±0.03
Phlobatannin	+	0.0011±0.04
Saponin	+++	0.3790±0.07
Flavonoids	+	0.0014±0.05
Terpenes	+	0.0080±0.10
Steroids	+	0.0012±0.08
Anthraquinones	+	0.0026±0.05
Phenol	+++	0.1890±0.02
Chalcones	+	0.0006±0.02
Glycosides	++	0.1850±0.02
Cardenolides	+	0.0050±0.01

KEY: +++ = PRESENT in an appreciable amount, ++ = PRESENT in a moderate amount, + = PRESENT in a trace amount

Table II: Haematological Indices of the West African Dwarf Goats Before and After Mange Topical Treatment with Neem Extract and Ivermectin

Parameter		T1(10ml ivermectin)	T2(5ml ivermectin+5ml neem extract	T3(10ml neem extract)	SEM
White blood	Before	6.85^{y}	9.90^{y}	8.73^{x}	0.65
Cell Count	After	18.00^{x}	17.13^{x}	19.83^{y}	0.88
(* $10^{3}\mu$L)	SEM*	0.85	1.85	3.13	
Red blood	Before	1.71^{by}	3.12^{ax}	1.39^{bx}	0.26
Cell Count	After	12.02^{bx}	14.03^{ay}	12.37^{by}	0.33
(*10^{6} μL)	SEM*	0.39	0.53	0.30	
Haemoglobin	Before	5.20^{b}	8.90^{a}	4.5^{b}	0.64
g/dL	After	6.48^{b}	11.58^{a}	7.10^{b}	0.82
	SEM*	0.62	1.12	0.61	
Haematocrit	Before	14.05	20.38	14.77	1.64
(%)	After	23.58^{ab}	33.40^{a}	21.13^{b}	2.36
	SEM*	3.07	4.78	1.94	
MCV (fl)	Before	10.77^{y}	10.79^{y}	10.15^{y}	0.16
	After	17.13^{x}	18.00^{x}	17.17^{x}	0.29
	SEM*	0.25	0.70	0.62	
MCH	Before	3.22^{aby}	2.45^{by}	3.53^{ay}	0.20
(Pg)	After	7.28^{x}	7.70^{x}	7.13^{x}	0.16
	SEM*	0.03	0.07	0.32	
MCHC	Before	28.10^{b}	23.28^{cy}	32.53^{a}	1.33
(%)	After	32.08	31.48^{x}	31.40	0.94
	SEM*	3.67	1.17	2.22	
Platelet count	Before	134.33^{by}	188.65^{ay}	124.48^{by}	9.95
(* $10^{3}\mu$L)	After	290.47^{x}	320.27^{x}	311.87^{x}	8.23
	SEM*	17.43	9.46	18.93	
RDW-CV	Before	20.35^{a}	21.85^{a}	18.17^{b}	0.55
	After	18.64^{b}	22.18^{a}	19.17^{b}	0.57
	SEM*	0.76	0.88	0.68	
PDW	Before	10.35^{by}	11.95^{ay}	10.46^{b}	0.25
	After	13.05^{bx}	16.85^{ax}	12.60^{b}	0.75
	SEM*	0.67	1.10	0.90	
PLCR	Before	66.25^{a}	69.40^{a}	56.90^{b}	2.10
	After	59.85	69.78	62.71	2.10
	SEM*	4.38	2.88	2.27	
MPV	Before	14.10^{ab}	14.78^{a}	13.23^{b}	0.24
	After	13.63^{b}	15.25^{a}	14.07^{ab}	0.29
	SEM*	-0.58	0.42	0.24	

abc- means with different superscripts in the same row are significantly different (P< 0.05); xy= means with different superscripts in the same sub –column are significantly different (t<0.05); SEM= standard error of mean among the treatments; SEM*= standard error of mean for the values before and after the treatment.

Table III: Serum Biochemical Indices and minerals of the West African Dwarf goats before and after mange topical treatment with Neem extract and Ivermectin

Parameter		T1 10ml ivermectin	T2 5ml neem extract+5ml ivermectin	T3 10ml neem extract	SEM
Total protein (g/dl)	Before	4.30	3.64^{y}	4.44	0.25
	After	5.21	5.50^{x}	4.92	0.18
	SEM*	0.56	0.53	0.46	
Albumin (g/dl)	Before	1.64^{y}	1.65y	1.61^{y}	0.05
	After	3.09^{x}	3.39^{x}	3.16^{x}	0.17
	SEM*	0.27	0.24	0.46	
Globulin (g/dl)	Before	2.66	1.98	2.83	0.25
	After	2.11	2.11	1.77	0.11
	SEM*	0.34	0.56	0.31	
Aspartate Aminotransferase (u/l)	Before	188.03	192.49	187.46^{x}	13.78
	After	168.08	190.42	152.80^{y}	8.47
	SEM*	16.57	48.23	9.69	
Alanine Aminotransferase (u/l)	Before	46.64^{x}	50.21	46.45^{x}	4.43
	After	16.43^{y}	20.75	19.97^{y}	1.07
	SEM*	3.36	3.44	3.00	
Alkaline Phosphatase (u/l)	Before	53.63^{y}	45.41^{y}	56.17^{y}	5.44
	After	123.05^{x}	137.00^{x}	163.67^{x}	8.99
	SEM*	13.13	19.24	29.54	
Albumin-globulin Ratio	Before	0.65^{y}	1.24	0.58^{y}	0.22
	After	1.50^{x}	1.66	1.88^{x}	0.16
	SEM*	0.06	0.58	0.05	
Minerals					
Sodium (Mmol/l)	Before	105.02	106.34	105.47	0.46
	After	148.33	139.89	130.70	7.79
	SEM*	16.29	11.24	14.38	
Potassium (Mmol/l)	Before	1.99	2.30	2.43	0.17
	After	3.33^{a}	2.25^{b}	2.73^{ab}	0.20
	SEM*	0.35	0.77	0.46	
Phosphorus (100mg/ml)	Before	1.88	2.06	1.75	0.08
	After	1.80	2.03	2.05	0.07
	SEM*	0.24	0.28	0.46	

abc- means with different superscripts in the same row are significantly different (P< 0.05); xy= means with different superscripts in the same sub –column are significantly different (t<0.05); SEM= standard error of mean among the treatments; SEM*= standard error of mean for the values before and after the treatment.