Int. j. adv. multidisc. res. stud. 2025; 5(4):1069-1093

Received: 14-06-2025
Accepted: 24-07-2025

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Efficacy of Ethnoveterinary Plant Extract Sprays for Wound Healing in Rabbits (*Oryctolagus cuniculus*)

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DOI: https://doi.org/10.62225/2583049X.2025.5.4.4723
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Abstract
The study was conducted to determine the efficacy of ethnoveterinary plant extract sprays for wound healing in rabbits in a reliable Rabbit Farm in Pagsanjan, Laguna, Philippines. Twenty-four (24) heads of rabbits were randomly distributed into four Treatments: T1 - Control (Ivermectin), T2 -Neem + Hagonoy + Guava + Citronella Oil + Emulsifier, T3 - Makabuhay + Hagonoy + Guava + Citronella Oil+ Emulsifier, and T4 - Akapulco + Hagonoy + Guava + Emulsifier, with the use of Complete Randomized Design.
The results revealed that there are no significant differences in the physical appearance in terms of length and total wound area on the specific anatomical part of the rabbit such as ear, nose, head and both forelegs and hind Legs. On day 10, the wound width on the left foreleg showed a significant difference with a p-value of 0.0300, highlighting Treatment 4, which had the smallest wound size at 0.47 mm. The analysis revealed a significant difference in wound contraction on the left ear on day 10, with a pvalue of 0.0429. A significant difference among Treatment groups was recorded in terms of days of healing wound. The results appeared that T2 had the highest wound healing rate in the Right Hind Leg during the observation. Mortality showed no significant differences among Treatments resulting in 12.5% mortality rate. In terms of Hematological test result, WBC, LYM%, GRAN%, RBC, HGB, HCT, MCV, MCH, MCHC and MPV revealed no significant differences in all Treatments. Platelet counts (PLT) showed a significant difference among treatments whereas T1 and T2 revealed a significant decline in platelet level while T3 and T4 showed an increase in platelet counts. This implies that all treatments have the same effect comparable to the control group.

Keywords: Ethnoveterinary Plants, Rabbit, Wound Area, Wound Contraction, Hematological Test

Introduction

The rabbit (*Oryctolagus cuniculus*) is a member of the order Lagomorpha and family Leporidae. Rabbit farming, also known as cuniculture, involves breeding and raising domestic rabbits for various purposes such as meat, fur, wool, laboratory use, and as household pets (Staff, 2023). With appropriate management practices, rabbit production is considered a sustainable and profitable venture that requires minimal space and can be conducted in backyards, farms, or even urban households (Veneracion, 2017).

However, rabbits are highly susceptible to a range of diseases, particularly parasitic infections. Ectoparasites such as ticks, mites, and lice, along with helminths like roundworms, tapeworms, and flukes, contribute significantly to rabbit morbidity and mortality, resulting in considerable economic losses (Singh *et al*., 2017) [56]. Mange, caused by burrowing and non-burrowing mites, is a highly contagious condition in rabbits, leading to skin lesions, irritation, and decreased productivity (Abd El-Ghany, 2022) [4]. The severity of infestation is clinically graded from absent to severe, depending on the extent and intensity of skin abnormalities. Moreover, some ectoparasites are vectors of zoonotic diseases, posing serious public health concerns.

In light of these challenges, ethnoveterinary medicine has emerged as an alternative approach, particularly in rural and resource-limited areas. Medicinal plants such as *Chromolaena odorata* (hagonoy), *Tinospora cordifolia* (makabuhay), *Azadirachta indica* (neem), *Cassia alata* (akapulko), and *Psidium guajava* (guava) are traditionally used for treating wounds, skin infections, and parasitic conditions in animals (Shah, 2017; Osuala, 2023; Hashilkar *et al*., 2016; Chundran *et al*., 2015; Nasution *et al*., 2019; Fernandes *et al*., 2010) [54, 42, 23, 13, 40, 19].

This study aimed to evaluate the wound-healing efficacy of selected ethnoveterinary plant extracts when applied as topical sprays on skin wounds of rabbits. Furthermore, proper blood collection techniques, such as using the marginal ear vein with anesthetic precautions (Smith, 2013) [57], were employed to monitor health parameters during the experiment.

Materials and Methods

The research employed Complete Randomized Design (CRD) as well. Idrees (2019) [25] defines a completely randomized design as the most basic type of design where Treatments are assigned to experimental units completely at random. Treatments were as follows: T1- Control (Ivermectin)(100ml) T2- Neem(33ml) + Guava leaves(33ml) + Hagonoy(33ml) + Citronella oil(0.5ml) + Polysorbate 20(0.5ml) T3- Makabuhay (33ml) + Guava leaves(33ml) + Hagonoy(33ml) + Citronella oil(0.5ml) + Polysorbate 20(0.5ml) T4- Akapulko (33ml) + Guava leaves(33ml) + Hagonoy(33ml) + Citronella oil(0.5ml) + Polysorbate 20(0.5ml).

The subject of the study consisted of twenty-four (24) heads of rabbit treated by different ethnoveterinary plant extract sprays for wound healing in rabbits in terms of physical appearance, wound area, wound contraction, days of healing wounds, mortality, result of hematological test before and after applying the Treatment in terms of WBC, LYM%, GRAN%, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, MPV, and most effective to use. It includes site selection, Securing of Institutional Animal Care and Use Committee (IACUC) Certification, purchasing of materials, plant extraction, phytochemical analysis, blood collection in rabbits, application of Treatment.

The researchers formulated various ethnoveterinary plant spray extracts, which include:T2- Neem (33ml) + Guava leaves (33ml) + Hagonoy (33ml) + Citronella oil (0.5 ml) + Emulsifier (0.5 ml) T3- Makabuhay (33ml) + Guava leaves (33ml) + Hagonoy (33ml) + Citronella oil (0.5 ml) Emulsifier (0.5 ml) T4- Akapulko (33ml) + Guava leaves (33ml) + Hagonoy (33ml) + Citronella oil (0.5 ml) + Emulsifier (0.5 ml), specifically designed for wound healing in rabbits. The treatments were applied using a spray method twice a day, covering all parts with affected area enhanced efficacy and achieved better results. Based on the study of Mandal & Rahaman, (2022) [33], Ethnoveterinary medicine, rooted in traditional knowledge, utilizes medicinal plants for animal healthcare, with plant combinations often formulated to enhance therapeutic efficacy. A common practice is the use of a 1:1 ratio, balancing active compounds from two plants to maximize synergistic effects while minimizing side effects. For instance, garlic and ginger are paired for antimicrobial properties, while neem and turmeric are combined for anti-inflammatory and antiseptic benefits. This approach reflects traditional wisdom and aims to optimize animal health, though further scientific validation is needed to support the effectiveness of such formulations (Mandal & Rahaman, 2022) [33]. Before applying the treatments, the researchers went to the University of the Philippines, Los Baños Institute of Chemistry to test the phytochemical analysis of different formulation of extract including the presence of alkaloids, cardiac glycosides, flavonoids, phenolics/tannins, and saponins. All of the treatments showed a positive presence of the following parameters except treatment 4 which showed a negative presence of alkaloids.

Analysis of Variance (ANOVA) and Analysis of Covariance (ANCOVA) were used to arrange and statistically analyze the acquired data in Complete Randomized Design (CRD). A total of 24 rabbits was subjected to the data collection procedure throughout the experiment. Data on the performance of rabbit were collected in terms of physical appearance, such as wound area, wound contraction, days of healing wounds, and mortality. The result of hematological test before and after applying the Treatment, including WBC, LYM%, GRAN%, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, MPV were collected to determine the significant differences among the Treatments and identify the most effective one.

Results and Discussion

Wound Area

The collected data focused on evaluation of average length and width of wound area gathered every other day from day 2,4,6,8,10,12 and 14 from a total of 24 samples.The results are shown in the tables below.

Left Ear

The average wound area length on the left ear of rabbits was assessed every other day from days 2 to 14, as shown in Table 4. The Analysis of Variance (ANOVA) revealed no significant differences among the treatments during this period. The highest recorded p-value was 0.5688, while the lowest was 0.0599. This indicates that Treatment 1, which involved the commercial antiparasitic treatment (Ivermectin), had effects on wound length compared to those of other treatments throughout the observation period. All p-values exceeded the conventional significance threshold of 0.05, suggesting that the treatments similarly influenced wound healing. It is noteworthy that Treatments 1 and 3 demonstrated the highest results on day 14, both achieving a value of 0, indicating complete wound healing. This observation emphasizes the efficacy of these treatments in promoting wound healing by that time point. Adewunmi *et al*., (2001) [1] found that ethnoveterinary medicine leverages traditional knowledge of plants promote animal health, particularly in wound healing. Numerous studies have highlighted the effectiveness of various ethnoveterinary plants, such as Aloe vera and Calendula officinalis, which exhibit significant antimicrobial properties. These plants help prevent infections in wounds, thereby facilitating a quicker healing process. Additionally, many ethnoveterinary plants possess anti-inflammatory compounds that can alleviate pain and swelling, further enhancing the recovery of injured animals.

Table 1: Average length of wound area taken every other day (left ear)

Average length of wound in left ear (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	162.08	156.32	120.63	68.17	28.85	6.43	0.00
T2	171.88	153.35	115.37	69.27	26.95	5.23	0.87
T3	164.23	157.85	119.62	74.90	32.75	0.92	0.00
T4	186.02	181.18	135.65	77.88	35.88	8.80	2.23
Analysis of Variance							
F=value	0.72	1.72	0.96	0.89	3.75	2.03	0.78
P=value	0.5688^{ns}	0.3793^{ns}	0.4560^{ns}	0.4846^{ns}	0.0599^{ns}	0.1887^{ns}	0.5399^{ns}
CV (%)	12.94	12.64	12.73	11.65	11.49	75.19	267.70

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The average width of the wound area in the left ear was measured every other day from days 2 to 14, as shown in Table 5. The Analysis of Variance (ANOVA) indicated no significant differences among the treatments during this period. The highest recorded value was 0.9382, while the lowest was 0.4449. This suggests that all treatments had similar effects on the width of the wound area in the left ear throughout the observation period. Notably, treatments 1 and 3 achieved the highest results on day 14, both indicating a value of 0, which signified a complete wound healing by that time. Furthermore, all treatments exhibited effects compared to the control treatment, which is Ivermectin, confirming their efficacy in promoting wound healing.

The healing properties of these plants are often attributed to their ability to promote cell proliferation and tissue regeneration. For instance, extracts from Turmeric, which contains the active compound curcumin, have been shown to reduce inflammation and accelerate wound closure. While traditional practices provide valuable insights into the use of these plants, further scientific research is essential to validate their efficacy and understand the underlying mechanisms. This can lead to the development of new, effective treatments for wound healing in veterinary medicine based on ethnoveterinary knowledge (Adewunmi *et al*., 2001) [1].

Table 2: Average width of wound area taken every other day (left ear)

Average width of wound in left ear (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	40.32	39.22	30.65	19.00	8.17	1.92	0.00
T2	42.30	27.32	21.05	12.43	5.70	1.73	0.1667
T3	29.87	29.00	22.95	15.08	6.17	0.17	0.00
T4	40.62	39.47	30.72	12.77	5.43	1.88	0.333
Analysis of Variance							
F=value	0.13	0.17	0.17	0.18	0.15	1.00	0.78
P=value	0.9382^{ns}	0.9168^{ns}	0.9161^{ns}	0.9039^{ns}	0.9271^{ns}	0.4449^{ns}	0.5391^{ns}
CV (%)	70.55	81.96	81.77	82.27	87.09	102.66	268.05

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The average wound area in the left ear of rabbits was measured every other day, from days 2, 4, 6, 8, 10, 12, to 14, as presented in Table 6. The Analysis of Variance (ANOVA) indicated no significant differences among the treatments during this period. The highest recorded p-value was 0.9442, while the lowest was 0.4290. This suggests that all treatments had effects on the wound area similar to the control treatment, which is Ivermectin. Notably, Treatments 1 and 3 exhibited the highest results on day 14, both achieving a value of 0. This indicates the complete wound healing by this time. Overall, it can be concluded that all treatments demonstrated comparable effects on wound healing in the left ear throughout the observation period.

Phan *et al*., (2001) [48] demonstrated that hagonoy leaf extracts (*Chromolaena odorata*) are beneficial for wound treatment, with crude ethanol extracts shown to be potent antioxidants that protect fibroblasts and keratinocytes.

Table 3: Average wound area taken every other day (left ear)

Average wound area in left ear (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	6859.64	6408.20	3832.99	1297.36	238.82	17.63	0.00
T2	7845.74	4370.00	2535.90	880.24	145.52	16.95	0.87
T3	5717.43	5361.55	3203.04	1362.93	243.35	0.92	0.00
T4	8211.45	7737.84	4502.39	993.85	196.93	21.05	2.90
Analysis of Variance							
F=value	0.12	0.22	0.22	0.16	0.19	1.03	0.82
P=value	0.9442^{ns}	0.8781^{ns}	0.8789^{ns}	0.9214^{ns}	0.8993^{ns}	0.4290^{ns}	0.5197^{ns}
CV (%)	77.23	88.76	88.20	88.87	87.39	108.51	278.41

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Right Ear

The average wound area length in the right ear was measured every other day from days 2, 4, 6, 8, 10, 12, to 14, as shown in Table 7. The Analysis of Variance (ANOVA) indicated no significant differences among the treatments during this period. The highest recorded p-value was 0.8784, while the lowest was 0.3977. This suggests that all treatments had comparable effects on the width of the wound area in the right ear throughout the observation period. Notably, Treatments 1, 2, and 4 achieved the highest results on day 14, all reaching a value of 0. This indicates a complete wound healing by this time. Furthermore, all treatments exhibited effects similar to those of the anti-parasitic control (Ivermectin), demonstrating their effectiveness in promoting wound healing.

Farrar & Farrar (2020) [18] found that the essential oils have gained recognition for their potential benefits in wound healing, thanks to their diverse therapeutic properties. Many essential oils, such as tea tree oil and lavender oil, exhibit strong antimicrobial effects, which can help prevent infections in wounds. These oils contain compounds that inhibit the growth of bacteria and fungi, making them effective in maintaining a clean wound environment. Additionally, essential oils like chamomile and eucalyptus possess anti-inflammatory properties that can help reduce swelling and redness around wounds, promoting a more favorable healing process.

Table 4: Average length of wound area taken every other day (right ear)

Average length of wound in right ear (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	162.23	158.48	122.48	78.98	32.72	4.48	0.00
T2	155.73	144.90	114.37	68.13	28.77	6.12	0.00
T3	163.65	159.68	123.03	76.67	34.40	3.12	1.13
T4	170.05	166.58	130.45	71.62	29.85	1.77	0.00
Analysis of Variance							
F=value	0.22	0.82	0.68	0.98	1.12	0.97	1.00
P=value	$0.^{8784ns}$	0.5184^{ns}	0.5908^{ns}	0.4487^{ns}	0.3977^{ns}	0.4512^{ns}	0.4411^{ns}
CV (%)	13.25	11.02	11.30	11.60	13.48	84.45	346.41

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The average width of the wound area in the right ear was assessed every other day from days 2 to day 14, as detailed in Table 8. The Analysis of Variance (ANOVA) revealed no significant differences among the treatments during this timeframe. The highest p-value recorded was 0.4328, while the lowest was 0.4160. This suggests that all treatments had a comparable impact on the wound width in the right ear throughout the study period. Notably, Treatments 1, 2, and 4 showed the best results on day 14, achieving a value of 0, which indicates fully complete wound healing by this point. Additionally, all treatments exhibited effects similar to the control (Ivermectin), thereby affirming their effectiveness in facilitating wound healing.

Beyond their antimicrobial and anti-inflammatory effects, essential oils can also provide pain relief and support tissue regeneration. Oils such as peppermint and clove are known for their analgesic properties, helping to alleviate discomfort associated with injuries. Furthermore, certain essential oils, like frankincense and myrrh, have been shown to encourage the regeneration of skin cells and accelerate the healing of damaged tissues. By incorporating essential oils into wound care routines—whether through topical application or diffusion—individuals may enhance their recovery while benefiting from the soothing and aromatic qualities of these natural substances (Farrar & Farrar, 2020) [18].

Table 5: Average width of wound area taken every other day (right ear)

Average width of wound in right ear (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	34.60	33.60	27.35	16.60	6.92	0.98	0.00
T2	32.23	31.45	24.47	16.25	6.98	1.67	0.00
T3	43.18	41.26	32.50	19.75	8.23	1.77	0.2167
T4	27.80	26.83	20.80	11.95	5.28	0.73	0.00
Analysis of Variance							
F=value	1.02	1.01	1.06	1.07	0.84	1.02	1.00
P=value	0.4328^{ns}	0.4373^{ns}	0.4194^{ns}	0.4160^{ns}	0.5084^{ns}	0.4342^{ns}	0.4411^{ns}
CV (%)	32.16	32.35	31.66	33.31	33.32	67.69	

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The average wound area in the right ear was measured every other day, from days 2, 4, 6, 8, 10, 12, to 14, as presented in Table 9. The Analysis of Variance (ANOVA) indicated no significant differences between the treatments throughout this period. The highest recorded value was 0.6285, while the lowest was 0.4963. This suggests that all treatments had similar effects on wound area in the right ear. Notably, on day 14, all of the wounds completely healed by this time. Furthermore, all treatments exhibited effects compared to anti-parasitic control (Ivermectin), underscoring their effectiveness in promoting wound healing.

Based on the study of Chundran *et al.* (2015) [13], neem leaves (Azadirachta indica) contain active compounds such as nimbidin and sodium nimbidate, which possess anti-inflammatory, antibacterial, antifungal, and antiviral properties that aid the healing process. Additionally, these leaves provide essential nutrients that play a vital role in collagen formation and the development of new capillaries.

Table 6: Average wound area taken every other day (right ear)

Average wound area in right ear (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	5857.74	5547.49	3457.95	1369.17	238.22	9.25	-
T2	5100.99	4616.94	2845.41	1135.73	208.66	12.34	-
T3	7072.58	6707.01	4058.59	1538.07	285.65	8.51	-
T4	4934.57	4666.32	2841.35	901.62	164.69	2.89	-
Analysis of Variance							
F=value	0.61	0.73	0.68	0.87	0.87	0.79	-
P=value	0.6285^{ns}	0.5637^{ns}	0.5900^{ns}	0.4976^{ns}	0.4963^{ns}	0.5343^{ns}	-
CV (%)	37.70	36.95	37.13	41.78	42.14	93.28	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Nose

The average length of the wound area in the nose was systematically measured every other day, from days 2, 4, 6, 8, 10, 12, and continuing through day 14, as illustrated in Table 10. The Analysis of Variance (ANOVA) conducted during this period revealed no significant differences among the various treatments applied. The highest recorded value in this analysis was 0.9793, while the lowest was noted at 0.2999. This outcome indicates that all treatments exhibited a similar effect on the wound length in the nose throughout the observation period. Notably, on day 10, the results showed that Treatment 3 had already achieved complete wound healing, making it stand out among all the treatments. By day 14, it was further observed that the average length of the wound area in the nose had completely healed across all treatments, demonstrating their effectiveness over time. This complete healing signifies a successful response to the interventions applied. Moreover, it is essential to highlight that all treatments showed effects comparable to those of the control treatment, Ivermectin. This similarity reinforces the notion that these alternative treatments can be as effective as established methods in promoting wound healing.

Ivermectin, traditionally recognized for its antiparasitic properties, has demonstrated significant potential in enhancing wound healing. Studies indicate that ivermectin can modulate inflammatory responses, crucial for effective wound repair. By adjusting the levels of cytokines and eicosanoids, ivermectin helps balance inflammation, promoting a conducive environment for healing. Additionally, it influences growth factors like Transforming Growth Factor-Beta 1 (TGF-β1) and Vascular Endothelial Growth Factor (VEGF), which are vital for tissue regeneration and angiogenesis (Cairns *et al.*, 2018) [12].

Table 7: Average length of wound area taken every other day (nose)

Average length of wound in nose (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	21.62	20.9	16.20	8.93	1.85	0.1667	-
T2	23.13	22.12	17.13	10.88	0.98	0.2333	-
T3	22.73	21.80	16.60	7.77	0.00	0.00	-
T4	23.12	22.40	17.32	6.73	1.60	0.00	-
Analysis of Variance							
F=value	0.06	0.05	0.05	0.44	1.45	0.68	-
P=value	0.9793ns	0.9850ns	0.9832ns	0.7295ns	0.2999ns	0.5861ns	-
CV (%)	22.21	23.01	22.96	54.05	107.03	248.33	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The average width of the wound area in the nose was measured every other day from days 2, 4, 6, 8, 10, 12, to 14, as illustrated in Table 11. The Analysis of Variance (ANOVA) indicated no significant differences among the treatments throughout this period. The highest recorded value was 0.6458, while the lowest was 0.2850. This finding suggests that all treatments had a similar effect on the width of the wound area in the nose. Notably, on day 10, the results showed that Treatment 3 had already healed completely among all the treatments. By day 14, it is important to highlight that Treatments 2, 3, and 4 had achieved a complete healing, while Treatment 1 still exhibited a wound width of 0.1667 mm. This observation underscores a difference in healing outcomes among the treatments. Furthermore, all treatments demonstrated effects comparable to those of the control treatment, which was Ivermectin. This similarity indicates that each treatment was generally effective in influencing wound width, reinforcing their potential as viable options for promoting healing in this context. Overall, the results emphasize the consistent efficacy of the treatments across the observed timeframe, with most achieving complete healing by day 14.

According the study of Cairns *et al*., (2018) [12], ivermectin has been observed to promote peripheral nerve regeneration during wound healing. Research suggests that it can induce dermal fibroblasts to adopt a glial-like phenotype, enhancing nerve growth within the wound area. This property is particularly beneficial in preventing loss of sensation at the wound site, a common issue in impaired wound healing. The combined effects of modulating inflammation, influencing growth factors, and promoting nerve regeneration position ivermectin as a promising agent in wound management strategies.

Table 8: Average width of wound area taken every other day (nose)

Average width of wound in nose (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	16.72	16.05	12.40	6.10	1.70	0.1667	0.1667
T2	17.32	16.43	12.82	7.20	1.02	0.1667	0.00
T3	20.98	20.17	15.37	4.73	0.00	0.00	0.00
T4	17.28	16.65	12.93	4.17	0.68	0.00	0.00
Analysis of Variance							
F=value	0.93	0.94	0.72	0.58	1.51	0.67	1.00
P=value	0.4701ns	0.4661ns	0.5666ns	0.6458ns	0.2850ns	0.5957ns	0.4411ns
CV (%)	19.47	19.72	20.49	56.13	122.56	244.95	346.41

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The average wound area in the nose was measured every other day from days 2, 4, 6, 8, 10, 12, to 14, as shown in Table 12. The Analysis of Variance (ANOVA) showed no significant differences among the various treatments during this time. The highest recorded value was 0.9379, while the lowest was 0.4499. This suggests that all treatments had a similar impact on the wound area in the nose throughout the study period. Notably, by day 10, the results indicated that Treatment 3 had already achieved complete healing among all the treatments. Importantly, by day 14, the average wound area in the nose had completely healed for all treatments. These finding highlights that all treatments were effective and performed similarly to the control treatment, which is Ivermectin. The results indicate that each treatment played a significant role in promoting wound healing, underscoring their potential as effective options for managing wounds in this context.

Hashilkar *et al*. (2016) [23] found that Makabuhay (Tinospora cordifolia) significantly promotes wound healing, improving contraction and reducing healing time in excision wounds, increasing breaking strength in incision wounds, and enhancing granuloma dry weight and cellular infiltration.

Table 10: Average wound area taken every other day (nose)

Average wound area in nose (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	373.76	347.94	207.71	68.56	3.82	0.1667	-
T2	399.10	363.49	220.59	82.17	2.83	0.2333	-
T3	546.03	504.05	293.20	62.63	0.00	0.00	-
T4	400.12	372.81	224.83	57.80	1.89	0.00	-
Analysis of Variance							
F=value	0.48	0.46	0.37	0.13	0.98	0.68	-
P=value	0.7056ns	0.7209ns	0.7784ns	0.9379ns	0.4499ns	0.5861ns	-
CV (%)	45.69	46.58	46.40	73.98	133.46	248.33	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.

ns not significant
*Significant at p ≤ 0.05
**highly significant at p ≤ 0.01

Head

The Analysis of Variance (ANOVA) shows that the average length of the wound area in the head was measured every other day from days 2, 4, 6, 8, 10, 12, to 14, as presented in Table 13. The analysis indicated that there were no significant differences among the treatments during this period. The highest recorded value was 0.7056, while the lowest was 0.4499. This finding suggests that all treatments had similar effects on the length of the wound area in the head throughout the observation period. Notably, by day 12, Treatments 2 and 4 had already a complete wound healing among all treatments, showcasing their effectiveness in promoting recovery. Furthermore, by day 14, the average wound area in the head had completely healed across all groups. It is important to highlight that all treatments demonstrated effects comparable to those of the control treatment, Ivermectin. This similarity indicates that each treatment was effective in promoting wound healing to a similar extent as the anti-parasitic control, reinforcing the overall efficacy of the treatments applied.

Based on findings of Sychrová *et al*., (2022) [61], flavonoids, a diverse group of polyphenolic compounds found in plants, play a significant role in wound healing due to their anti-inflammatory, antioxidant, and antimicrobial properties. These bioactive compounds help modulate the wound-healing process by reducing oxidative stress, which can delay healing, and by neutralizing free radicals in the wound environment. Additionally, flavonoids exhibit anti-inflammatory activity by inhibiting pro-inflammatory cytokines and enzymes such as cyclooxygenase and lipoxygenase, creating a conducive environment for tissue repair. Their antimicrobial effects further help prevent infections, which can impede wound closure. These mechanisms collectively promote fibroblast proliferation, collagen synthesis, and re-epithelialization, leading to enhanced wound healing.

Table 11: Average length of wound area taken every other day (head)

Average length of wound in head (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	34.45	33.40	25.54	9.67	1.60	0.5000	-
T2	18.62	16.97	13.07	1.98	0.03	0.0000	-
T3	25.57	24.92	19.24	8.18	1.37	0.1667	-
T4	22.53	21.83	16.89	5.07	0.95	0.0000	-
Analysis of Variance							
F=value	3.38	4.11	3.80	0.58	0.64	0.80	-
P=value	0.0748ns	0.0488ns	0.0582ns	0.6425ns	0.6099ns	0.5279ns	-
CV (%)	25.09	24.30	24.86	124.46	151.32	273.86	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at p ≤ 0.05
**highly significant at p ≤ 0.01

The Analysis of Variance (ANOVA) conducted on the average width of the wound area in the head, measured every other day from days 2 to day 14, indicating that there were no significant differences among the treatments during this period. The highest recorded value was 0.8634, while the lowest was 0.3898. All observed values were above the conventional significance level of 0.05, implying that all treatments produced comparable effects on wound width throughout the observation period. Notably, by day 12, results showed that Treatments 2 and 4 had already a complete wound healing among all the treatments. By day 14, the average width of the wound area had completely resolved for all treatments. This outcome demonstrates that each treatment was effective in promoting healing, achieving a complete resolution of the wounds. Additionally, all treatments exhibited effects similar to those of the control treatment, Ivermectin, reinforcing their efficacy in facilitating wound healing. Overall, these findings underscored the effectiveness of the treatments in managing wound recovery throughout the study period.

Recent studies highlight flavonoids' potential in modern wound management. For example, quercetin, a flavonoid found in many fruits and vegetables, has been shown to enhance wound contraction and collagen deposition in animal models. Similarly, flavonoids like catechins, found in green tea, and epigallocatechin gallate (EGCG) have been reported to accelerate wound healing through their angiogenic and antioxidative properties. The incorporation of flavonoids into topical formulations, such as creams and hydrogels, has also shown promise in improving wound-healing outcomes in clinical settings. These findings underscore the potential of flavonoids as natural agents in developing therapeutic strategies for effective wound care.

Table 12: Average width of wound area taken every other day (head)

Average width of wound in head (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	22.22	21.48	18.47	9.55	1.82	0.3333	-
T2	24.47	25.67	13.02	1.68	0.58	0.0000	-
T3	22.83	22.15	19.18	8.07	0.60	0.1667	-
T4	19.33	18.77	16.85	4.57	0.32	0.0000	-
Analysis of Variance							
F=value	0.24	0.39	1.14	0.70	1.11	0.73	-
P=value	0.8634ns	0.7614ns	0.3898ns	0.5761ns	0.4004ns	0.5607ns	-
CV (%)	33.81	35.62	26.46	122.45	133.07	258.20	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at p ≤ 0.05
**highly significant at p ≤ 0.01

The average wound area in the head was measured every other day, on days 2, 4, 6, 8, 10, 12, and 14, as presented in Table 15. The Analysis of Variance (ANOVA) indicated no significant differences between the treatments across these days. The highest recorded p-value was 0.7071, while the lowest was 0.1891. Each of these values exceeded the accepted significance level of 0.05, suggesting that all treatments had similar effects on wound area compared to the anti-parasitic control (Ivermectin). Notably, by day 12, the results showed that Treatments 2 and 4 had already a complete wound healing among all the treatments. By day 14, it was further observed that the average wound area in the head had completely resolved for all groups. This outcome underscored the effectiveness of all treatments in promoting healing, demonstrating results compared to the control treatment. Overall, these findings highlight the successful application of the treatments in facilitating wound recovery throughout the observation period.

According to Kandimalla *et al*. (2016) [27], citronella oil was studied for its effects on healing Candida-infected wounds in a diabetic mouse model. The oil exhibited both antifungal and anti-inflammatory properties, which the researchers suggested contributed to accelerated wound healing.

Table 13: Average wound area taken every other day (head)

Average wound area in head (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	743.26	697.54	463.93	185.74	5.64	0.500	-
T2	535.45	520.48	205.21	20.03	0.12	0.0000	-
T3	585.77	553.42	373.61	98.94	1.51	0.1667	-
T4	551.23	518.54	363.21	69.98	0.90	0.0000	-
Analysis of Variance							
F=value	0.57	0.48	2.02	0.94	1.19	0.80	-
P=value	0.6508ns	0.7071ns	0.1891ns	0.4657ns	0.3724ns	0.5279ns	-
CV (%)	36.21	37.19	37.23	132.60	191.42	273.86	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Left Foreleg

The average length of the wound area in the left foreleg was measured every other day, specifically on days 2, 4, 6, 8, 10, 12, and 14, as shown in Table 16. The Analysis of Variance (ANOVA) indicated that there were no significant differences among the treatments during this period. The highest recorded p-value was 0.8825, while the lowest was 0.3406. These findings suggest that all treatments produced effects comparable to those of the control treatment, Ivermectin. Notably, on day 12, the results showed that Treatment 2 had the highest healing rate in wound length (0.18mm) among all the treatments. This highlights its effectiveness in promoting wound recovery compared to the others. Importantly, by day 14, the length of the wound area in the left foreleg demonstrated complete healing across all treatments. This outcome underscores the effectiveness of each treatment in facilitating wound recovery, indicating that they all achieved comparable results in terms of wound healing compared to the control group. Overall, the data reflect a consistent trend where all treatments contributed positively to the healing process without significant variation among them.

Alkaloids, naturally occurring compounds found in various medicinal plants, play a significant role in enhancing wound healing. Their anti-inflammatory properties help reduce swelling and pain at the wound site, creating a conducive environment for healing. Additionally, alkaloids exhibit antimicrobial activity, effectively combating potential infections that can impede the healing process. By mitigating inflammation and preventing microbial growth, alkaloids facilitate a more efficient and rapid wound repair process (Alkaloids | Definition, Examples & Structure Video, 2023) [9].

Table 14: Average length of wound area taken every other day (Left Foreleg)

Average length of wound in Left Foreleg (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	52.05	49.70	38.68	27.15	5.93	1.10	-
T2	48.43	51.73	39.87	27.60	5.47	0.18	-
T3	43.40	41.73	31.97	22.60	2.95	0.42	-
T4	50.33	48.18	37.32	24.65	3.65	1.10	-
Analysis of Variance							
F=value	0.22	0.23	0.26	0.25	0.94	1.30	-
P=value	0.8825ns	0.8764ns	0.8554ns	0.8600ns	0.4658ns	0.3406ns	-
CV (%)	28.65	32.88	32.33	34.14	56.70	102.50	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The average width of the wound area in the left foreleg of rabbits was measured every other day, on days 2, 4, 6, 8, 10, 12, and day 14, as presented in Table 15. The Analysis of Variance (ANOVA) indicated that there were no significant differences among the treatments across most of these days. However, notably, day 10 stood out with a recorded p-value of 0.0300, suggesting a significant difference compared to the other days in the observation period. The highest recorded value during this analysis was 0.6958, while the noteworthy p-value of 0.0300 on day 10 indicates a unique response at this time point. This finding implies that on day 10, the effects of the treatments on wound width were more pronounced than on other days especially in treatment 4 with the smallest width of wound (0.47mm). Despite this significant observation, overall results suggest that all treatments exhibited effects on wound width compared to control treatment, Ivermectin. Throughout the observation period, all treatments had similar effects on the width of the wound area in the left foreleg. By day 14, the average width of the wound area had completely healed. This outcome underscores the effectiveness of all treatments applied in this study and highlights their equivalency to Ivermectin in promoting wound healing.

Furthermore, alkaloids contribute to wound healing by promoting cell proliferation and collagen synthesis, essential components in tissue regeneration. By stimulating the production of new cells and extracellular matrix components, they aid in restoring the structural integrity of damaged tissues. This multifaceted approach not only accelerates wound closure but also enhances the quality of the healed tissue, reducing the likelihood of scarring and improving overall functional recovery (Alkaloids | Definition, Examples & Structure Video, 2023) [9].

Table 15: Average width of wound area taken every other day (Left Foreleg)

Average width of wound in Left Foreleg (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	15.93	15.27	11.87	8.23	1.95	0.6000	-
T2	13.05	13.47	10.33	7.13	2.28	0.1667	-
T3	13.70	13.22	10.17	7.00	1.30	0.2167	-
T4	13.80	13.42	10.28	7.10	0.47	0.6667	-
Analysis of Variance							
F=value	0.79	0.49	0.52	0.56	0.70	0.98	-
P=value	0.5327ns	0.6958ns	0.6803ns	0.6589ns	0.0300*	0.4488ns	-
CV (%)	17.30	17.01	18.15	18.32	41.19	109.09	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The Analysis of Variance (ANOVA) conducted on the average wound area in the left foreleg, measured every other day on days 2, 4, 6, 8, 10, 12, and 14, indicated that there were no significant differences among the treatments during this period. The highest recorded value was 0.8955, while the lowest was 0.1896. This finding suggests that all treatments produced effects on the wound area comparable to those of the control treatment, Ivermectin. Notably, on day 12, the results showed that Treatment 2 had the highest healing rate of wound area in the left foreleg, measuring at 0.18 mm among all treatments. Throughout the observation period, it was evident that all treatments had similar effects on the width of the wound area in the left foreleg. Importantly, by day 14, the average wound area had completely healed. This outcome highlights the efficacy of all treatments applied in this study and reinforces their equivalency to Ivermectin in promoting effective wound healing. Overall, these results underscore the potential of each treatment as viable options for facilitating recovery in similar contexts.
According to the study of Nasution *et al.* (2019) [40], Akapulko (*Cassia alata L*) is recognized as a herbal medicine with a spicy and warm taste, believed to heal itching and skin damage and wound healing. This research aimed to analyze the optimization of Cassia alata leaf extract for burn healing.

Table 16: Average wound area taken every other day (Left Foreleg)

Average wound area in Left Foreleg(mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	820.48	750.87	455.75	221.58	14.91	1.33	-
T2	637.17	702.68	417.59	202.74	12.77	0.18	-
T3	638.76	591.27	349.19	168.82	6.54	0.54	-
T4	706.31	657.55	390.11	179.08	4.33	1.47	-
Analysis of Variance							
F=value	0.42	0.20	0.24	0.25	2.02	1.07	-
P=value	0.7456ns	0.8955ns	0.8683ns	0.8560ns	0.1896ns	0.4133ns	-
CV (%)	32.96	39.22	39.67	42.19	63.35	117.32	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Right Foreleg

The average length of the wound area in the right foreleg was measured every other day, on days 2, 4, 6, 8, 10, 12, and day 14, as shown in Table 19. The Analysis of Variance (ANOVA) indicated no significant differences among the treatments during this period. The highest recorded value was 0.9209, while the lowest was 0.4540. This finding suggests that all treatments had comparable effects on the length of the wound area in the right foreleg throughout the observation period. Notably, on day 12, the results showed that Treatment 4 had the highest healing rate in wound area, with a value of 0.1833mm wound length among all treatments. Importantly, by day 14, the average length of the wound area in the right foreleg had completely healed. This outcome emphasizes that all treatments provided similar results to those of the control treatment, Ivermectin, confirming their effectiveness in promoting wound healing.
Flávia *et al*., (2018) [21] found that the cardiac glycosides, traditionally used for treating heart conditions, have shown promise in enhancing wound healing by stimulating collagen synthesis in dermal fibroblasts. Collagen is essential for wound repair, providing structural support and facilitating tissue regeneration. Studies have demonstrated that compounds like digitoxigenin and digoxin can significantly increase collagen production, thereby accelerating the wound healing process. For instance, research published in the Journal of Applied Physiology reported that cardiotonic steroids, including digoxin, induced an eightfold increase in collagen synthesis by human dermal fibroblasts, suggesting their potential utility in wound care.

Table 17: Average length of wound area taken every other day (Right Foreleg)

Average length of wound in Right Foreleg (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	31.02	29.70	22.93	13.80	4.33	0.4333	-
T2	41.12	42.67	32.58	22.77	6.50	0.5167	-
T3	27.77	26.55	20.52	12.45	3.67	0.4000	-
T4	29.08	27.73	21.15	17.55	5.10	0.1833	-
Analysis of Variance							
F=value	0.74	0.97	0.95	0.92	0.57	0.16	-
P=value	0.5580ns	0.4540ns	0.4597ns	0.4755ns	0.6482ns	0.9209ns	-
CV (%)	37.89	41.43	41.02	50.22	56.79	160.94	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The average width of the wound area in the right foreleg was measured every other day on days 2, 4, 6, 8, 10, 12, and 14, as shown in Table 20. The Analysis of Variance (ANOVA) indicated that there were no significant differences among the treatments during this period. The highest recorded value was 0.9935, while the lowest was 0.4650. This finding suggests that all treatments produced comparable results, demonstrating no significant differences in their effects on the width of the wound area in the right foreleg. Notably, on day 12, the results revealed that Treatment 4 had the highest healing rate in width of wound area, measuring just 0.1667mm among all treatments. This underscores its effectiveness in promoting recovery compared to the other treatments. Importantly, by day 14, the width of the wound area in the right foreleg had completely healed across all treatments. This outcome highlights that all treatments exhibited effects similar to those of the control treatment, Ivermectin. Thus, it can be concluded that each treatment was effective in promoting wound healing to a degree comparable to that of the anti-parasitic control.

In vivo studies further support these findings. A feasibility study on topical digitoxigenin application in rats with full-thickness excisional wounds showed that short-term treatment significantly decreased wound size compared to controls. The study also developed a digitoxigenin formulation for topical administration, which demonstrated effective drug release and enhanced wound healing. These results indicate that cardiac glycosides could be developed into therapeutic agents for improving wound healing outcomes (Flávia *et al*., 2018) [21].

Table 18: Average width of wound area taken every other day (right foreleg)

Average width of wound in Right Foreleg (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	14.37	13.82	10.52	6.25	1.88	0.3333	-
T2	14.37	14.92	11.53	8.02	2.12	0.4333	-
T3	12.17	11.70	9.02	5.62	1.92	0.4000	-
T4	10.37	9.83	7.40	6.60	2.02	0.1667	-
Analysis of Variance							
F=value	0.76	0.88	0.94	0.32	0.03	0.14	-
P=value	0.5478^{ns}	0.4898^{ns}	0.4650^{ns}	0.8135^{ns}	0.9935^{ns}	0.9335^{ns}	-
CV (%)	32.36	33.13	33.49	47.25	55.94	165	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The average wound area in the right foreleg was measured every other day, on days 2, 4, 6, 8, 10, 12, and day 14, as shown in Table 21. The Analysis of Variance (ANOVA) indicated that there were no significant differences among the treatments during this period. The highest recorded value was 0.8766, while the lowest was 0.5244. This finding suggests that all treatments produced similar effects on the wound area in the right foreleg throughout the observation period. Notably, on day 12, the results revealed that Treatment 4 had the highest healing rate in wound area, measuring just 0.1833 mm among all treatments. By day 14, it was evident that the wound area had completely healed across all treatments. This outcome emphasizes that all treatments were effective and demonstrated results comparable to those of the control treatment, Ivermectin. Thus, it can be concluded that each treatment contributed equally to promoting wound healing in this study.

According to the study of Osuala 2023 [42] Hagonoy (*Chromolaena odorata*), a highly invasive plant from the Asteraceae family, is commonly known as Siam weed, devil weed, and French weed. Despite its classification as one of the world's worst invasive species, it is traditionally used for wound healing due to its ability to quickly stop bleeding.

Table 19: Average wound area taken every other day (right foreleg)

Average wound area in Right Foreleg (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	451.05	415.18	244.	104.06	10.21	0.4333	-
T2	637.18	667.62	394.51	191.82	14.82	0.7033	-
T3	427.08	393.16	234.54	110.55	10.04	0.4867	-
T4	449.62	406.48	233.15	136.43	12.80	0.1833	-
Analysis of Variance							
F=value	0.55	0.81	0.84	0.73	0.25	0.22	-
P=value	0.6644^{ns}	0.5244^{ns}	0.5075^{ns}	0.5629^{ns}	0.8602^{ns}	0.8766^{ns}	-
CV (%)	46.72	53.93	53.69	59.69	66.35	172.79	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Left Hind Leg

The average length of the wound area in the left hind leg was measured every other day, on days 2, 4, 6, 8, 10, 12, and day 14, as shown in Table 22. The Analysis of Variance (ANOVA) indicated that there were no significant differences among the treatments throughout this period. The highest recorded value was 0.9708, while the lowest was 0.3026. This outcome suggests that all treatments had comparable effects on the length of the wound area in the left hind leg. Notably, on day 12, the results showed that Treatment 2 had the highest healing rate in wound area in the left hind leg, measuring at 1.10 mm among all treatments. This highlights its effectiveness in promoting wound recovery compared to the others. Importantly, all treatments demonstrated similar efficacy to the control treatment, which was Ivermectin. This equivalence indicates that each treatment was effective in promoting healing. By day 14, it is noteworthy that the wound area had completely healed across all treatments, underscoring the overall success of the interventions applied in this study.

According to the study of Dai & Mumper, (2010) [14], phenolics and tannins, both plant-derived compounds, offer significant benefits in wound healing due to their biological activities. Phenolics are known for their potent antioxidant properties, which help to neutralize free radicals and reduce oxidative stress, thereby protecting cells from damage during the healing process. They also exhibit anti-inflammatory effects, which can help to manage the inflammatory phase of wound healing, reducing redness and swelling. This enables faster tissue repair and minimizes excessive scar formation. Additionally, phenolics promote collagen synthesis, an essential protein for tissue regeneration, thus aiding in wound closure. The antimicrobial properties of phenolics further contribute to preventing infections at the wound site, which is critical for effective healing.

Table 20: Average length of wound area taken every other day (left hind leg)

Average length of wound in Left Hind Leg (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	39.22	37.87	29.43	10.47	5.83	1.58	-
T2	42.45	44.08	35.65	5.32	6.02	1.10	-
T3	61.38	58.62	45.75	14.93	8.00	1.32	-
T4	36.80	35.52	27.23	9.57	5.03	1.35	-
Analysis of Variance							
F=value	1.44	1.21	1.30	1.33	0.28	0.08	-
P=value	0.3026ns	0.3668ns	0.3386ns	0.3314ns	0.839ns	0.9708ns	-
CV (%)	35.97	37.13	36.46	9.57	66.53	92.44	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The Analysis of Variance (ANOVA) was used to determine the average width of the wound area in the left hind leg, measured every other day from days 2 to 14, indicated no significant differences among the treatments during this period. The highest recorded value was 0.9322, while the lowest was 0.1786. This finding implies that all treatments produced similar effects on the width of the wound area in the left hind leg. Notably, on day 12, the results showed that Treatment 2 had the highest healing rate in terms of wound width, measuring at 0.77 mm among all treatments. Throughout the observation period, it was evident that all treatments yielded outcomes comparable to those of the control treatment, which was Ivermectin. Importantly, by day 14, the width of the wound area had completely healed across all treatments. This result highlights the effectiveness of each treatment in promoting healing, demonstrating that they all functioned similarly to Ivermectin in facilitating wound recovery.

Tannins, on the other hand, are recognized for their astringent properties that help tighten and protect the wound area. By forming a protective layer over the wound, they reduce the risk of infection and encourage tissue regeneration. Tannins also support wound contraction, which is a vital aspect of the healing process, enabling the wound to close more rapidly. These compounds have shown promising effects in promoting cell growth and accelerating tissue repair. Combined, phenolics and tannins offer a multifaceted approach to wound healing by reducing inflammation, promoting collagen production, preventing infection, and stimulating tissue regeneration (Dai & Mumper, 2010) [14].

Table 21: Average width of wound area taken every other day (left hind leg)

Average width of wound in Left Hind Leg (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	20.20	19.40	14.93	10.47	2.57	1.00	-
T2	15.88	13.83	10.70	5.32	1.70	0.77	-
T3	31.88	30.60	23.60	14.93	4.95	1.20	-
T4	21.23	20.35	15.78	9.57	3.62	1.13	-
Analysis of Variance							
F=value	2.10	2.47	2.36	1.33	1.42	0.14	-
P=value	0.1786ns	0.1360ns	0.1474ns	0.3314ns	0.3070ns	0.9322ns	-
CV (%)	36.42	36.56	37.30	58.85	63.49	85.88	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The Analysis of Variance (ANOVA) was used to determine the average wound area in the left hind leg, measured every other day from day 2 to 14, indicated that there were no significant differences among the treatments during this period. The highest recorded value was 0.8337, while the lowest was 0.1966. This finding implies that all treatments resulted in similar effects on the wound area in the left hind leg, demonstrating an equivalent outcome to that of the control treatment, which was Ivermectin. Notably, on day 12, results showed that Treatment 2 had the highest healing rate in the width of the wound area, measuring 2.16 mm among all treatments. Throughout the observation period, it became evident that each treatment had a comparable impact on wound healing. By day 14, the wound area had completely healed across all treatments, underscoring the effectiveness of all treatments applied in this study. This consistent performance across treatments reinforces their efficacy in promoting wound healing, aligning closely with the results observed with Ivermectin.

The study of Sujarwo *et al*., 2016 [70] determined the leaves of the neem tree (Azadirachta indica) have a wide spectrum of applications in traditional medicine, particularly in the Indian subcontinent. Key uses include Treatment of skin diseases and use as an insect repellent.

Table 22: Average wound area taken every other day (left hind leg)

Average wound area in Left Hind Leg (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	798.65	740.31	443.09	216.78	18.13	2.63	-
T2	687.90	617.52	385.39	165.86	15.73	2.16	-
T3	2409.61	2184.24	1316.00	615.52	55.84	4.81	-
T4	953.57	882.29	523.86	250.54	27.32	3.10	-
Analysis of Variance							
F=value	1.97	2.05	2.02	1.59	1.44	0.29	-
P=value	0.1966ns	0.1857ns	0.1891ns	0.2670ns	0.3019ns	0.8337ns	-
CV (%)	81.92	79.53	79.63	90.36	90.89	117.64	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Right Hind Leg

The average length of the wound area in the right hind leg was evaluated every other day from day 2 to day 14, as illustrated in Table 25. The Analysis of Variance (ANOVA) demonstrated that there were no significant differences among the treatments during this period. The highest recorded value was 0.675, while the lowest was 0.1090, indicating that all treatments produced effects on wound length comparable to those of the control treatment, Ivermectin. Notably, on day 12, the results showed that Treatment 4 had the lowest healing rate in the width of the wound area, achieving a measurement of 66.51 mm among all treatments. Throughout the observation period, it became clear that each treatment had a similar impact on the length of the wound area in the right hind leg. Remarkably, by day 14, the average length of the wound area had completely healed for all treatments. This finding reinforces the effectiveness of all treatments tested in promoting wound healing, confirming their equivalency to Ivermectin in facilitating recovery.

Based on the study of s, Liu *et al*., (2022) [31], saponins, a class of naturally occurring compounds found in various plants, have demonstrated significant therapeutic effects in wound healing. They exhibit antimicrobial properties, which help prevent infection at the wound site by inhibiting the growth of bacteria, fungi, and viruses. Additionally, saponins possess anti-inflammatory effects, reducing inflammation and pain associated with wounds, and accelerating the healing process. Saponins also promote the formation of collagen, an essential protein for wound closure and tissue regeneration. By stimulating angiogenesis (the formation of new blood vessels), saponins help improve blood supply to the wound site, facilitating nutrient and oxygen delivery for faster healing.

Table 23: Average length of wound area taken every other day (right hind leg)

Average length of wound in Right Hind Leg (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	25.32	24.23	18.73	13.87	3.12	99.71	-
T2	27.92	26.80	20.47	7.67	1.52	99.71	-
T3	67.30	63.95	49.13	42.47	13.83	99.85	-
T4	63.07	59.95	47.20	38.02	11.80	66.51	-
Analysis of Variance							
F=value	2.66	2.66	2.75	2.79	3.55	1.00	-
P=value	0.1193^{ns}	0.1198^{ns}	0.1122^{ns}	0.1090^{ns}	0.675^{ns}	0.4412^{ns}	-
CV (%)	51.72	51.34	50.93	70.28	74.78	31.49	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The average width of the wound area in the right hind leg was measured every other day from day 2 to 14, as presented in Table 26. The Analysis of Variance (ANOVA) indicated that there were no significant differences among the treatments during this period. The highest recorded value was 0.4411, while the lowest was 0.0604. On day 14, the results indicated that Treatments 1, 2, and 3 achieved the highest healing rate in the width of the wound area, with a measurement of 0mm, signifying a complete wound healing. In contrast, Treatment 4 still exhibited a wound width of 0.2000mm among all treatments. This suggests that all treatments had effects on wound width that were comparable to those of the control treatment, which was Ivermectin. Throughout the observation period, it became evident that all treatments yielded similar outcomes regarding the width of the wound area in the right hind leg. By day 14, all treatments contributed to effective healing, demonstrating their equivalence to Ivermectin in promoting wound recovery. This finding reinforces the notion that each treatment applied in this study was effective in facilitating wound healing.

Furthermore, saponins are known to enhance the permeability of cell membranes, which can improve the delivery of other active compounds to the wound, making them valuable in topical formulations for wound care. Their ability to reduce edema (swelling) and support the regeneration of healthy tissue further contributes to their role in wound healing. Overall, saponins' combination of antimicrobial, anti-inflammatory, and tissue-regenerating properties makes them promising candidates for use in wound healing applications (Liu *et al*., 2022) [31].

Table 24: Average width of wound area taken every other day (right hind leg)

Average width of wound in Right Hind Leg (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	17.75	17.13	13.22	7.00	1.10	0.97	0.00
T2	16.77	18.07	14.00	2.95	0.22	0.38	0.00
T3	28.28	27.33	21.15	15.13	3.98	2.33	0.00
T4	29.23	28.30	22.05	12.43	3.72	2.73	0.2000
Analysis of Variance							
F=value	1.88	1.45	1.53	2.81	3.74	2.43	1.00
P=value	0.2117^{ns}	0.2991^{ns}	0.2788^{ns}	0.1081^{ns}	0.0604^{ns}	0.1405^{ns}	0.4411^{ns}
CV (%)	36.60	37.52	36.85	60.18	74.78	77.00	346.41

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The Analysis of Variance (ANOVA) conducted on the average wound area in the right hind leg, measured every other day from day 2 to day 14, indicated that there were no significant differences among the treatments throughout this period. The highest recorded value was 0.4411, while the lowest was 0.1535. This finding suggests that all treatments had effects on the wound area that were comparable to those of the control treatment, Ivermectin. Notably, by day 14, Treatments 1, 2, and 3 achieved the highest healing rate in terms of wound width, with a measurement of 0, indicating that these wounds completely healed. In contrast, Treatment 4 still exhibited a wound width of 0.5000 mm among all treatments. Throughout the observation period, it became clear that all treatments produced similar outcomes regarding the average wound area in the right hind leg. By day 14, the data indicated that all wounds had demonstrated significant healing, confirming the efficacy of each treatment applied. This consistency in results reinforces the notion that all treatments, including Ivermectin, effectively promoted wound healing in the rabbits studied.

Based on the study of Shah, (2017) [54], ethnoveterinary plants are crucial for animal healthcare in developing countries, where farmers use them to treat common ailments like mild diarrhea, skin diseases, intestinal worms, wounds, and reproductive disorders.

Table 25: Average wound area taken every other day (right hind leg)

Average wound area in Right Hind Leg (mm)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	421.15	388.08	230.54	108.10	6.74	0.47	0.00
T2	462.24	481.48	285.27	63.33	1.97	0.18	0.00
T3	2448.25	2255.59	1329.95	816.69	72.40	1.32	0.00
T4	2232.77	2054.68	1270.91	671.75	66.69	1.15	0.5000
Analysis of Variance							
F=value	2.30	2.21	2.33	2.28	1.83	1.78	1.00
P=value	0.1535^{ns}	0.1645^{ns}	0.1508^{ns}	0.1564^{ns}	0.2196^{ns}	0.2286^{ns}	0.4411^{ns}
CV (%)	90.21	89.72	87.80	106.49	130.79	90.18	346.41

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Wound Contraction

The collected data focused on the evaluation of the wound contraction average gathered every other day from day 2,4,6,8,10 and 14, for a total of 24 samples. The results are shown in the tables below:

Ear

The Analysis of Variance (ANOVA) conducted on the average wound contraction measurements from the left ear of rabbits, collected every other day from days 2, 4, 6, 8, 10, 12, and 14, revealed that there were generally no statistically significant differences among the treatment means at most of these time points leading up to day 14. However, it is important to highlight that day 10 showed a significant difference, with a p-value of 0.0429. This indicates that on this particular day, the treatments had a notably different effect compared to the other days observed. While the highest recorded p-value was 0.5509 and the lowest was the aforementioned 0.0429, the significance of day 10 stood out in this analysis. This suggests that the wound contraction effects of the treatments were more pronounced on this day compared to others in the observation period. Despite this notable difference on day 10, it is essential to recognize that overall, throughout the entire observation timeframe, all treatments still demonstrated comparable effects to the control treatment, Ivermectin. This equivalency across most time points reinforces the idea that each treatment was effective in promoting wound healing. By day 14, the data illustrated a consistent pattern of healing across all groups, indicating that all administered treatments were beneficial in facilitating both contraction and healing of wounds in the left ear.

A study by Fernandes *et al*. (2010) [19] demonstrated that guava leaf extract (Psidium guajava) significantly accelerated wound healing in rat oral mucosa, with improvements evident as early as the third day of treatment compared to corticosteroids.

Table 26: Average wound contraction taken every other day (left ear)

Average wound contraction in left ear (%)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	0.6967	6.52	43.45	79.75	96.24	99.62	100
T2	0.6300	9.56	46.79	80.67	96.99	99.73	99.94
T3	0.6133	7.53	44.55	77.83	95.90	99.95	100
T4	0.2233	5.14	45.12	80.03	96.14	99.62	99.95
Analysis of Variance							
F=value	0.75	2.98	3.88	1.90	4.35	1.23	0.67
P=value	0.5509^{ns}	0.0963^{ns}	0.0556^{ns}	0.2077^{ns}	0.0429^{*}	0.4983^{ns}	0.5928^{ns}
CV (%)	79.25	25.96	2.72	80.03	0.4053	0.2448	0.0677

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Average measurements of wound contraction from the right ear were collected every other day, specifically on days 2, 4, 6, 8, 10, 12, and 14. The results, as summarized in Table 29, provide valuable insights into the healing process over time. An Analysis of Variance (ANOVA) performed on this data revealed that there were no significant differences among the treatment means at the various time points leading up to day 14. The highest measurement occurred on day 10 with a p-value of 0.9099, while the lowest was recorded on day 2 with a p-value of 0.1623. Importantly, all treatments exhibited effects similar to that of the control treatment throughout the healing stages. Notably, by day 14, the average wound contraction in the right ear had achieved complete healing.

The study of Abbas *et al*. (2018) [3] examinef the acaricidal and insecticidal properties of essential oils against ectoparasites in livestock, showing them to be safer and more economical alternatives to chemical treatments. It highlights their effectiveness in controlling ticks and mites, enhancing veterinary health management strategies.

Table 27: Average wound contraction taken every other day (right ear)

Average wound contraction in right ear (%)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
T1	0.1933	5.14	38.45	75.98	95.70	99.84	-
T2	0.3133	6.91	42.95	77.73	95.98	99.77	-
T3	0.5200	6.00	43.95	78.25	95.76	99.84	-
T4	0.9300	6.56	43.37	78.06	96.04	99.93	-
Analysis of Variance							
F=value	02.23	1.19	0.88	0.86	0.18	0.63	-
P=value	0.1623ns	0.3741ns	0.4905ns	0.5011ns	0.9099ns	0.6164ns	-
CV (%)	76.71	19.99	11.03	2.51	0.7176	0.1492	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at p ≤ 0.05
**highly significant at p ≤ 0.01

Nose

Average measurements of wound contraction from the nose of rabbits were taken every other day from days 2, 4, 6, 8, 10, 12, to 14. An Analysis of Variance (ANOVA) performed on this data revealed no statistically significant differences among the treatment means at any of the time points leading up to day 14. The highest recorded p-value was 0.8642, while the lowest was 0.3505. All values exceeded the conventional significance level of 0.05, indicating that there were no meaningful differences in wound contraction among the various treatments throughout the healing process. Importantly, on day 10, Treatment 3 reached a total wound contraction and was completely healed among all treatments. Despite the lack of significant differences, all treatments exhibited effects similar to those of the control group, which was treated with Ivermectin. This suggests that all treatments performed similarly in promoting wound healing. Notably, by day 14, the average wound contraction in the nose had achieved complete healing, underscoring the overall effectiveness of the treatments employed in this study.

According to Abille, (2015) [5], Akapulko (*Cassia alata*) demonstrates various pharmacological activities, including antioxidant, antimicrobial, and anti-inflammatory effects, supporting its traditional uses. It is particularly effective against fungal skin infections like Tinea versicolor and Tinea corporis, as well as in treating constipation.

Table 28: Average wound contraction taken every other day (nose)

Average wound contraction in nose (%)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	1.17	8.25	45.03	83.78	99.06	99.96	-
T2	1.04	7.60	44.22	79.91	99.40	99.95	-
T3	0.91	8.95	47.31	89.84	100.00	100.00	-
T4	1.19	7.89	44.89	86.86	99.52	100.00	-
Analysis of Variance							
F=value	0.24	1.26	1.20	1.01	1.19	0.68	-
P=value	0.8642ns	0.3505ns	0.3687ns	0.4356ns	0.3747ns	0.5885ns	-
CV (%)	43.05	10.97	4.68	8.59	0.6216	0.0577	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at p ≤ 0.05
**highly significant at p ≤ 0.01

Head

The average measurements of wound contraction from the rabbits' heads were taken every other day, specifically on days 2, 4, 6, 8, 10, 12, and 14. These results, outlined in Table 31, provide valuable insights into the progression of the healing process over time. The Analysis of Variance (ANOVA) conducted on this data showed no statistically significant differences among the treatment means at the various time points leading up to day 14. Notably, all treatments exhibited effects similar to those of the control treatment, which was Ivermectin. By day 14, it was observed that Treatments 1 and 3 had completely healed, while Treatments 2 and 4 still displayed a percentage wound contraction of 66.67%. This outcome indicates that Treatments 1 and 3 were significantly more effective in promoting wound contraction compared to Treatments 2 and 4. Overall, the analysis suggests that all treatments performed comparably to the control, underscoring their effectiveness in facilitating wound healing. The findings highlight that the various treatments utilized in this study had a similar impact on wound contraction as observed with Ivermectin, although some treatments achieved complete healing, while others did not, by the end of the observation period.

The leaves of the neem tree (*Azadirachta indica*) are widely used in traditional medicine, especially in the Indian subcontinent, primarily for treating skin diseases and as an insect repellent (Sujarwo *et al*., 2016) [70].

Table 29: Average wound contraction taken every other day (head)

Average wound contraction in head (%)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	1.23	7.27	38.59	76.36	99.32	99.94	100.00
T2	0.41	4.48	44.35	66.67	66.67	66.67	66.67
T3	0.87	6.29	34.73	84.28	99.77	99.98	100.00
T4	0.66	4.56	24.19	58.94	66.56	66.67	66.67
Analysis of Variance							
F=value	1.45	0.70	0.44	0.22	0.65	0.67	0.67
P=value	0.2982ns	0.5764ns	0.7295ns	0.8810ns	0.6038s	0.5965ns	0.5957ns
CV (%)	62.85	49.87	62.41	57.38	49.10	49.00	48.99

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at p ≤ 0.05
**highly significant at p ≤ 0.01

Foreleg

Average measurements of wound contraction in the left foreleg of rabbits were recorded every other day from days 2, 4, 6, 8, 10, 12, to 14. The findings, illustrated in Table 32, provide insight into the healing progression over time. An Analysis of Variance (ANOVA) performed on this data indicated no statistically significant differences among the treatment means at the various time points leading up to day 14. The highest p-value was 0.7865, while the lowest was 0.1940. This outcome suggests that there were no meaningful differences in wound contraction between the treatments during the different stages of healing. Notably, on day 12, Treatment 3 exhibited the smallest percentage of wound contraction at just 66.52%, compared to the other treatments, which demonstrated higher rates of wound contraction. Importantly, by day 14, it was observed that the average wound contraction in the left foreleg had completely healed across all treatments. This outcome underscores the effectiveness of each treatment in promoting wound recovery, indicating that they all contributed positively to the healing process without significant disparity among them. Additionally, all treatments exhibited effects similar to those of the control treatment, which was Ivermectin. This similarity reinforces the effectiveness of the various treatments in facilitating wound healing throughout the observation period.

According to Vaisakh and Pandey (2012) [66], Chromolaena is used traditionally for its many medicinal properties, especially for external uses as in wounds, skin infections, inflammation etc. Studies have demonstrated that the leaf extract has antioxidant, anti-inflammatory, analgesic, antimicrobial, cytoprotective and many other medicinally significant properties

Table 30: Average wound contraction taken every other day (left foreleg)

Average wound contraction in Left Foreleg (%)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	0.71	9.12	45.16	73.24	98.35	99.70	-
T2	0.89	10.63	47.11	74.78	98.14	99.91	-
T3	1.22	8.51	46.21	74.35	99.19	66.52	-
T4	0.50	7.48	45.02	74.91	99.40	99.78	-
Analysis of Variance							
F=value	0.63	1.99	1.28	0.49	2.07	1.00	-
P=value	0.6145^{ns}	0.1940^{ns}	0.4547^{ns}	0.6978^{ns}	0.7865^{ns}	0.4405^{ns}	-
CV (%)	79.80	18.12	3.26	2.53	0.7520	31.49	-

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.

Means with the same letter are not significantly different.

ns not significant

*Significant at $p \leq 0.05$

**highly significant at $p \leq 0.01$

The average wound contraction measurements from the right foreleg of rabbits were recorded every other day, specifically on days 2, 4, 6, 8, 10, 12, and 14. These findings, summarized in Table 33, provide valuable insights into the progression of the healing process over time. The Analysis of Variance (ANOVA) conducted on this data indicated no statistically significant differences among the treatment averages at the various time points leading up to day 14. On day 14, Treatments 1 and 2 achieved the highest percent of wound contraction, reaching a complete 100% healing compared to the other treatments, which exhibited lower percentages of wound contraction. It is noteworthy that all treatments exhibited effects similar to those of the control treatment, Ivermectin. This suggests that each treatment was comparably effective in promoting wound contraction during the initial phases of healing. While the highest recorded value among the treatments was observed on day 14, the lowest values were noted earlier in the observation period. Overall, these results imply that the treatments did not significantly influence wound contraction during the early stages of recovery, reinforcing the idea that they functioned similarly to the control treatment throughout this timeframe.

Tinospora crispa, locally known as "makabuhay" or "papaitan" in the Philippines Traditional uses of certain plants include treating hypertension, wounds, intestinal worms, skin infections, stimulating appetite, and repelling mosquitoes. Scientific studies have revealed various biological activities, particularly in the stems, such as antioxidant properties from methanolic extracts, immunomodulatory effects from isolated fractions, anti-inflammatory effects from aqueous extracts, and analgesic and antimicrobial activities. The roots also display antimicrobial properties.

Table 31: Average wound contraction taken every other day (right foreleg)

Average wound contraction in Right Foreleg (%)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	1.23	9.00	46.44	78.70	97.99	99.91	100.00
T2	0.79	8.87	46.22	74.07	98.06	99.90	100.00
T3	1.00	6.06	30.82	48.52	64.96	66.59	66.67
T4	0.22	3.33	15.99	49.18	65.17	66.64	66.67
Analysis of Variance							
F=value	1.17	1.39	1.72	0.85	0.68	0.67	0.67
P=value	0.3786^{ns}	0.3133^{ns}	0.2405^{ns}	0.5061^{ns}	0.5863^{ns}	0.5961^{ns}	0.5957^{ns}
CV (%)	84.84	57.96	55.19	48.14	48.87	49.00	66.67

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.

Means with the same letter are not significantly different.

ns not significant

*Significant at $p \leq 0.05$

**highly significant at $p \leq 0.01$

Hind Leg

The average wound contraction in the left hind leg of rabbits was measured every other day from day 2, as shown in Table 34. The Analysis of Variance (ANOVA) indicated that there were no significant differences among the treatment means on days 2, 4, 6, 8, 10, and 14. The highest recorded value was 0.9708, while the lowest was 0.4388. This finding suggests that all treatments produced effects similar to those observed in the control group, which used Ivermectin. Notably, by day 14, Treatments 1, 2, and 3 achieved a total wound contraction rate of 100%, indicating complete healing. In contrast, Treatment 4 exhibited a lower wound contraction rate of only 66.67%. Overall, the results indicate that there were no significant differences in wound contraction during the early stages of healing across all treatments. This consistency implies that each treatment, including the commercial antiparasitic treatment (Ivermectin), had comparable impacts on wound healing in the rabbits throughout the observed period.

Based on recent research (*Citronella Oil Benefits, How to Use, Side Effects and Safety*, 2019) citronella oil may have the potential to speed up the healing of wounds. Antibacterial and antifungal activity of ten essential oils and found that citronella oil was effective against all 12 fungi that were tested. The same study found that citronella oil managed to inhibit 15 of 22 bacteria, while eucalyptus, lemongrass, peppermint, and orange oils were effective against all 22 bacterial strains.

Table 32: Average wound contraction taken every other day (left hind leg)

Average wound contraction in Left Hind Leg (%)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	0.92	8.22	45.09	73.35	97.81	1.58	100.00
T2	0.77	7.73	42.12	79.51	98.07	1.10	100.00
T3	0.78	8.48	45.20	77.58	98.22	1.32	100.00
T4	1.15	6.07	30.54	49.18	65.28	1.32	66.67
Analysis of Variance							
F=value	0.015	0.43	0.81	0.85	1.01	0.08	1.00
P=value	0.9254ns	0.7366ns	0.5224ns	0.5061ns	0.4388ns	0.9708ns	0.4411ns
CV (%)	86.73	37.54	32.79	35.60	31.48	92.44	31.49

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

The Analysis of Variance (ANOVA) conducted on the average wound contraction measurements from the right hind leg of rabbits revealed no significant differences among the treatment means from days 2, 4, 6, 8, 10, and 14. The highest p-value recorded was 0.6843, while the lowest was 0.1275. These results indicate that all treatments exhibited effects on wound contraction similar to those of the control treatment, Ivermectin. Notably, by day 14, Treatment 3 demonstrated the lowest percentage of wound contraction at 66.67% compared to the other treatments. Throughout the healing process, it was observed that the treatments did not produce significant variations in wound contraction during the initial stages of healing. This consistency suggests a reliable efficacy across all treatments when compared to the control. The data collectively imply that each treatment provided comparable outcomes in promoting wound healing, reinforcing the notion that they function similarly to Ivermectin in this context.

Makabuhay (*Tinospora cordifolia*) significantly promotes wound healing in all the three models viz. enhanced wound contraction and decreased days for complete epithelization in excision wound; increased breaking strength in resutured incision wound; increased granuloma dry weight and cellular infiltration in granulation tissue (Hashilkar *et al*., 2016) [23].

Table 33: Average wound contraction taken every other day (right hind leg)

Average wound contraction in Right Hind Leg (%)							
Treatment	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day14
T1	1.23	9.01	45.88	75.75	98.47	1.39	100.00
T2	1.13	8.65	45.94	88.87	99.58	0.42	100.00
T3	0.62	7.42	30.25	44.08	64.86	5.01	66.67
T4	0.60	8.42	44.47	71.36	31.19	3.94	99.99
Analysis of Variance							
F=value	2.57	0.51	1.01	2.09	1.08	1.46	1.00
P=value	0.1275ns	0.6843ns	0.4380ns	0.1794ns	0.4115ns	0.2963ns	0.4411ns
CV (%)	39.74	19.64	31.58	32.11	31.19	114.12	31.49

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Days of Healing Wound

The data collected focused on evaluation of average days of healing wound gathered from beginning to end of the study. The results show in the table below. The collected data focused on the evaluation of average days of healing wounds gathered from the beginning to the end of the study. The Analysis of Variance (ANOVA) results for the days of wound healing indicate significant differences in treatment means across various time points. The results indicate that Treatment 3 had the highest healing rate in the left ear, with an average healing rate of 12.33%. For the right ear, both Treatment 1 and Treatment 4 achieved an average healing rate of 13.00%. In the nose, T3 recorded an average healing rate of 9.33%. T4 was noted for having the highest average healing rate in the head at 6.67%, while in the left foreleg, T4 also demonstrated an average healing rate of 11.33%. The right foreleg had its highest average healing rate with T3 at 11.33%, and in the left hind leg, Treatment 2 achieved an average of 11.67%. Finally, T2 also recorded a healing rate of 9.33% for the right hind leg. Notably, the highest p-value recorded was 0.8400, while Treatment 2 showed a significant difference, achieving a p-value of 0.041 and exhibiting the highest healing rate for the right hind leg, which resulted in a slightly smaller wound size compared to other treatments. Throughout the study, it became evident that all treatments had effects similar to those of the control group, which utilized Ivermectin. This suggests that both Treatment 1 and Treatment 2 could potentially yield comparable outcomes in wound healing. The findings imply that Treatment 2 may serve as a viable alternative to Ivermectin for effective wound management.

Taderera (2017) found that ethnoveterinary plants significantly enhance wound healing in rabbits with mange by promoting angiogenesis and epithelial migration.

Table 34: Average Days of Healing Wound

Average Days of Healing (%)								
Treatment	Left ear	Right Ear	Nose	Head	Left Foreleg	Right Foreleg	Left Hind Leg	Right Hind Leg
T1	13.33	13.00	11.67	10.67	12.67	12.00	13.67	11.33
T2	13.17	13.67	11.00	9.33	12.33	12.67	11.67	9.33
T3	12.33	13.50	9.33	11.00	11.67	11.33	12.00	13.67
T4	14.00	13.00	10.00	6.67	11.33	12.33	12.67	13.17
Analysis of Variance								
F=value	2.05	0.55	1.33	0.79	1.90	0.28	0.49	4.40
P=value	0.1854ns	0.6631ns	0.3300ns	0.5331ns	0.2073ns	0.8400ns	0.6981ns	0.0417*
CV (%)	6.28	6.05	14.81	40.78	6.36	15.48	17.44	13.70

T1-ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Hematological Test

The data collected focused on the evaluation of Hematological Test gathered before and after applying the treatments in the study. The results are shown in the tables below.

White Blood Cells (WBC)

The Analysis of Covariance (ANCOVA) was employed to analyze the data regarding the White Blood Cell (WBC) counts for rabbits before and after applying four different treatments. Among the treatments, Treatment 1 exhibited the most significant increase in WBC count, rising from 5.2 (µL) to 11.15 (µL). This substantial increase indicates a robust immune response or reaction to the treatment, showcasing its effectiveness in enhancing the immune system's activity. Treatment 2 showed a minimum microliter amount of WBC, T3 and 4 experienced the most considerable decrease in WBC count of almost 6 microliters after the application. This notable decline may suggest a negative response to the treatment, potentially indicating adverse effects on the rabbits' immune function. Throughout the study, it became evident that while Treatment 1 significantly boosted WBC levels, T2, T3, and T4 decreases. The ANCOVA analysis revealed that the overall differences in WBC counts among the treatments were not statistically significant, with a p-value of 0.1806, which is greater than the conventional threshold of 0.05 for significance. This finding implies that despite these individual variations, all treatments generally had effects comparable to those of the control group, which utilized Ivermectin and still on the standard level of WBC counts.

According to A. Barbul (1978) [2], White blood cells (WBCs) play a crucial role in the immune system, serving as the body's defense against infections and aiding in wound healing. They are essential for identifying and neutralizing pathogens, such as bacteria and viruses, and for orchestrating the inflammatory response.

Table 35: White Blood Cells (WBC) Microliter (µL) before and after application of the treatments

Parameter	Treatment				
	T1	T2	T3	T4	Standard
Before	5.2	8.65	11.55	13	5.2 - 13.5
After	11.15	8.45	5.45	7.75	
Analysis of Covariance					
Sources of Variation	DF	SS	MS	F	P. Value
Regression	2	15.9907	7.9954	14.8259	0.1806^{ns}
Variation	1	0.5393	0.5393		
Total	3	16.53			

T1 - ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapµLco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Lymphocytes (LYM)

The The Analysis of Covariance (ANCOVA) was employed to analyze the data presented in Table 38, which details the hematological test results for lymphocytes before and after the application of various treatments. Among the treatments, Treatment 1 exhibited the most significant increase in lymphocyte percentage (LYM%), rising from 21% before treatment to an impressive 47.6% after treatment. This substantial increase indicates a strong positive response to the intervention, highlighting Treatment 1's effectiveness in enhancing immune response. Treatment 3 also showed a notable improvement, with LYM% increasing from 11.3% to 28.3%, indicating a beneficial effect of this treatment as well. Treatment 2 and 4 displayed minimal change, as a result T2, T3 and T4 failed to reach the standard amount of LYM% of 35.2-75.6%. Despite these varying outcomes, the ANCOVA analysis revealed a p-value of 0.6020, indicating that the differences in LYM% across the treatments were not statistically significant. Overall, these findings highlight the distinct responses elicited by each treatment regarding lymphocyte levels, showcasing Treatment 1 as the most effective in increasing lymphocyte percentage.

According to study of M Schäffer, & A Barbul. (1998) [32], lymphocytes are crucial for the resolution phase and optimal tissue repair. Injury can lead to generalized immunosuppression, reducing T lymphocyte numbers and impairing their function, which increases susceptibility to infections. This impairment also affects antibody-producing B lymphocytes due to their reliance on helper T cells. Therapeutic strategies that enhance lymphocyte function may improve healing outcomes by restoring effective immune responses.

Table 36: Lymphocytes (LYM) Percentage (%) before and after application of the treatments

Parameter	Treatment				
	T1	T2	T3	T4	Standard
Before	21	19.35	11.3	15	35.2 - 75.6
After	47.6	17.4	28.3	15.7	
Analysis of Covariance					
Sources of Variation	DF	SS	MS	F	P. Value
Regression	2	411.6507	205.8253	0.8796	0.6020^{ns}
Variation	1	233.9993	233.9993		
Total	3	645.65			

T1 - ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapµLco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Granulocytes

The Analysis of Covariance (ANCOVA) examining the granulocyte percentage (GRAN%) in rabbits after various treatments provides valuable insights into the effects of these interventions on immune function. The standard reference range for GRAN% in rabbits is 20.0% to 59.3%. Treatment 1 exhibited a significant decrease in GRAN%, dropping from 66.45% to 46.55%. This suggests a potential impact on the granulocyte levels in rabbits, as the initial value exceeded the normal range but later fell within it. This decrease may indicate a modulation of immune response, warranting further investigation into its implications. In contrast, Treatment 2 showed a slight increase in GRAN%, rising from 69.95% to 72.8%, which remains above the standard range. This suggests that the treatment may not be beneficial and could contribute to an abnormal immune response if continued. Similarly, Treatment 4 increased from 72.75% to 76.9%, also staying above the standard range, raising concerns about its potential long-term effects on immune health. Treatment 3 experienced a decline in GRAN%, decreasing from 80% to 61%, which while closer to the upper limit of the standard range. Despite these differences across treatments, the statistical analysis yielded a p-value of 0.5967, indicating that the variations in GRAN% among treatments were not statistically significant overall, suggesting that no treatment consistently demonstrated a significant advantage over others when compared to the control group.

Schirmacher P. (2001) [51] found that granulocyte-macrophage colony-stimulating factor (GM-CSF) significantly enhances wound healing by promoting keratinocyte proliferation, increasing granulation tissue formation, and facilitating angiogenesis. It regulates the expression of other critical cytokines involved in inflammation and tissue repair, creating a supportive environment for healing.

Table 37: Granµlocytes (GRAN) Percentage (%) before and after application of the treatments

Parameter	Treatment				
	T1	T2	T3	T4	Standard
Before	66.45	69.95	80	2.75	20.0 - 59.3
After	46.55	72.8	61	76.9	
Analysis of Covariance					
Sources of Variation	DF	SS	MS	F	P. Value
Regression	2	358.6713	179.3357	0.9044	0.5967^{ns}
Variation	1	198.2905	198.2905		
Total	3	556.9619			

T1 - ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapµLco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at p ≤ 0.05
**highly significant at p ≤ 0.01

Red Blood Cells (RBC)

The Analysis of Covariance (ANCOVA) conducted the analysis of Red Blood Cell (RBC) levels in rabbits following various treatments reveals significant variations in their effects, with the standard reference range for RBC being 5.00 to 7.60 microliter. Treatment 1 showed the most considerable decrease in RBC levels, dropping from 5.86 to 4.59, indicating a negative impact on the rabbits' blood health and suggesting ineffectiveness in promoting healthy RBC levels. In contrast, Treatment 3 experienced a slight increase in RBC levels, rising from 4.735 to 4.875, which may indicate a positive response and potential enhancement of RBC production or overall blood health. Treatment 2 also exhibited a minor decrease from 4.39 to 4.17, while Treatment 4 observed a slight reduction from 4.805 to 4.69, reflecting minimal changes in RBC levels for both treatments. Despite these fluctuations, the statistical analysis yielded a p-value of 0.6271, indicating that the differences in RBC levels among the treatments were not statistically significant, suggesting that the observed changes do not imply meaningful impacts on the overall health of the rabbits involved in the study.

According to Kulzhan Berikkhanova *et al*. (2016) [29], Red blood cells (RBCs) enhance wound healing in rabbits by promoting tissue repair, preventing infections, and accelerating epithelialization. Encapsulating cytokines and antibiotics in RBC ghosts further target inflammation, leading to quicker wound closure and improved tissue regeneration compared to free drug treatments.

Table 38: Red Blood Cells (RBC) Microliter (µL) before and after application of the treatments

Parameter	Treatment				
	T1	T2	T3	T4	Standard
Before	5.86	4.39	4.735	4.805	5.00 - 7.60
After	4.59	4.17	4.875	4.69	
Analysis of Covariance					
Sources of Variation	DF	SS	MS	F	P. Value
Regression	2	0.1622	0.0811	0.1051	0.6271^{ns}
Variation	1	0.1051	0.1051		
Total	3	0.2673			

T1 - ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapµLco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at p ≤ 0.05
**highly significant at p ≤ 0.01

Hemoglobin (HGB)

The Analysis of Covariance (ANCOVA) presented in Table 41 details the analysis of Hemoglobin (HGB) levels in rabbits following various treatments reveals significant findings, particularly when considering the standard reference range of 105 to 170 grams per deciliter. Treatment 1 exhibited the most substantial decrease in HGB, falling from 101 g/dL to 87.5 g/dL, indicating a negative impact on hemoglobin concentration and placing it below the normal range. Treatment 2 also showed a decline, with HGB levels dropping from 84 g/dL to 81.5 g/dL, while Treatment 3 experienced a reduction from 97 g/dL to 93.5 g/dL. Treatment 4 had a slight decrease as well, moving from 96.5 g/dL to 91 g/dL. Despite these reductions across all treatments, the statistical analysis revealed a p-value of 0.3736, which exceeds the conventional significance threshold of 0.05, suggesting that there were no statistically significant differences in HGB levels among the treatments. Overall, while all treatments resulted in decreased hemoglobin levels, none demonstrated significant differences in their effects on HGB concentrations compared to one another.

According to Elg, F. and Hunt, S. (2018) [17], hemoglobin therapy significantly enhances wound healing by improving oxygen delivery to chronic and non-healing wounds. This treatment reduces wound size, accelerates healing rates, and alleviates pain, leading to better overall wound conditions. Clinical studies indicate that using hemoglobin alongside standard care increases the likelihood of healing and enhances patients' quality of life, making it a valuable addition to wound management strategies.

Table 39: Hemoglobin (HGB) Grams per deciliter (g/dL) before and after application of the treatments

Parameter	Treatment				
	T1	T2	T3	T4	Standard
Before	101	84	97	96.5	105 - 170
After	87.5	81.5	93.5	91	
Analysis of Covariance					
Sources of Variation	DF	SS	MS	F	P. Value
Regression	2	69.8569	34.9285	3.0827	0.3736^{ns}
Variation	1	11.3306	11.3306		
Total	3	81.1875			

T1 - ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapμLco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at p ≤ 0.05
**highly significant at p ≤ 0.01

Hematocrit (HCT)

The analysis of Hematocrit (HCT) levels in rabbits following various treatments indicates significant variations in response, with the standard reference range for HCT being 31.0% to 46.0%. Treatment 1 exhibited the most substantial decrease in HCT, falling from 42.65% to 31.7%, which suggests a significant reduction in red blood cell volume and may indicate adverse effects on the rabbits' health. Treatment 3 also showed a decrease, albeit less pronounced, from 34.75% to 33.9%, while Treatment 4 experienced a minor decline from 33.3% to 32.7%. In contrast, Treatment 2 demonstrated only a slight decrease from 30.2% to 29.8%, reflecting minimal change in HCT levels. The p-value of 0.5326 indicates that these differences were not statistically significant, suggesting that the treatments did not have a meaningful impact on HCT levels overall within the study context.

According to Ouaknine-Orlando, B. *et al.* (1999) [43], hematocrit levels significantly influence wound healing in rabbits. Lower hematocrit can enhance bleeding time and reduce thrombosis, promoting better blood flow to healing tissues. A study demonstrated that reducing hematocrit from 36% to 23% eliminated cyclic arterial thrombosis and increased bleeding time, which may improve healing conditions. Maintaining optimal hematocrit is essential, as both anemia and excessively high levels can negatively affect recovery outcomes.

Table 40: Hematocrit (HCT) Percentage (%) before and after application of the treatments

Parameter	Treatment				
	T1	T2	T3	T4	Standard
Before	42.65	30.2	34.75	33.3	31.0 - 46.0
After	31.7	29.8	33.9	32.7	
Analysis of Covariance					
Sources of Variation	DF	SS	MS	F	P. Value
Regression	2	6.4445	3.2222	1.2624	0.5326^{ns}
Variation	1	2.5524	2.5524		
Total	3	8.9969			

T1 - ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapμLco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at p ≤ 0.05
**highly significant at p ≤ 0.01

Mean Corpuscular Volume (MCV)

The Analysis of Covariance (ANCOVA) was employed to analyze the data of Mean Corpuscular Volume (MCV) in rabbits following various treatments, with a standard reference range of 56.8 to 66.5, revealed significant trends. Treatment 1 exhibited the most substantial decrease in MCV, falling from 72.6 to 69.0, indicating a notable reduction in red blood cell volume and suggesting a pronounced effect on red blood cell parameters. Treatment 2 showed a minor decrease from 72.8 to 72.4, reflecting minimal fluctuation in MCV levels, while Treatment 3 also experienced a slight decline, decreasing from 69.8 to 69.4. In contrast, Treatment 4 demonstrated a slight increase in MCV, rising from 69.45 to 69.7, indicating minimal change but still remaining above the standard range. The overall statistical analysis yielded a p-value of 0.3952, suggesting that the variations in MCV across treatments were not statistically significant, reinforcing the conclusion that none of the treatments had a meaningful impact on MCV levels in this study.

According to Hsieh, Y.-P. *et al.* (2017) [24], Mean Corpuscular Volume (MCV) is a valuable screening tool for vitamin B12 deficiency, particularly in macrocytic anemia, as elevated MCV can indicate the need for further serum B12 testing. However, its sensitivity is limited (17% to 30%), meaning many deficient cases may be missed if MCV is used alone. Thus, while MCV can suggest further investigation, it should not be the sole criterion for diagnosing B12 deficiency.

Table 41: Mean Corpuscular Volume (MCV) femtoliters (fL) before and after application of the treatments

Parameter	Treatment				
	T1	T2	T3	T4	Standard
Before	72.6	72.8	69.8	69.45	56.8 - 66.5
After	69.0	72.4	69.4	69.7	
Analysis of Covariance					
Sources of Variation	DF	SS	MS	F	P. Value
Regression	2	5.9376	2.9688	2.7008	0.3952^{ns}
Variation	1	1.0992	1.0992		
Total	3	7.0369			

T1 - ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapμLco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at p ≤ 0.05
**highly significant at p ≤ 0.01

Mean Corpuscular Hemoglobin (MCH)

The ANCOVA analysis of Mean Corpuscular Hemoglobin (MCH) levels in rabbits following various treatments reveals significant changes relative to the standard reference range of 20.1% to 25.1%. Treatment 1 showed a notable increase in MCH, rising from 17.3 pg to 18.95 pg, which indicates an improvement in hemoglobin content per red blood cell, thereby enhancing the rabbits' hematological status. Conversely, Treatment 3 experienced a marked decrease in MCH, falling from 20.45 pg to 19.1 pg, highlighting a significant reduction in hemoglobin levels within the red blood cells. Treatment 4 also exhibited a decrease, with MCH declining from 20 pg to 19.35 pg. These contrasting results between Treatments 1 and the others underscore the variability in treatment effects on MCH levels; however, the overall statistical analysis yielded a p-value of 0.8999, indicating that these changes were not statistically significant across the treatments when evaluated collectively.

Mean Corpuscular Hemoglobin (MCH) is a key parameter in a complete blood count (CBC) that measures the average hemoglobin content in red blood cells. It aids in diagnosing conditions like anemia and thalassemia by indicating the blood's oxygen-carrying capacity. Abnormal MCH levels can signal nutrient deficiencies and are essential for improving diagnostic accuracy and patient management in various medical fields.

Table 42: Mean Corpuscular Hemoglobin (MCH) Picograms (pg) (one trillionth of a gram) before and after application of the treatments

Parameter	Treatment				
	T1	T2	T3	T4	Standard
Before	17.3	19.1	20.45	20	20.1 - 25.1
After	18.95	19.5	19.1	19.35	
Analysis of Covariance					
Sources of Variation	DF	SS	MS	F	P. Value
Regression	2	0.034720149	0.0174	0.1174	0.8999^{ns}
Variation	1	0.147779851	0.1478		
Total	3	0.1825			

T1 - ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapµLco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Mean Corpuscular Hemoglobin Concentration (MCHC)

The Analysis of Covariance (ANCOVA) was utilized to analyze the hematological test results before and after the application of various treatments, as presented in Table 42. The findings reveal distinct responses in Mean Corpuscular Hemoglobin Concentration (MCHC) among the treatments. Treatment 1 demonstrated a significant increase in MCHC, rising from 240 before treatment to 275 after treatment, indicating a notable improvement in hemoglobin concentration relative to red blood cell volume. In contrast, Treatment 2 experienced a slight decrease in MCHC, dropping from 278 to 272, while Treatment 3 also showed a minor reduction from 279 to 275. Treatment 4 reflected a similar trend, with MCHC decreasing from 289 to 278. Among these treatments, Treatment 1 stood out with the most significant increase in MCHC, suggesting its effectiveness in enhancing hemoglobin levels. Conversely, Treatments 2, 3, and 4 exhibited decreases in MCHC, with Treatment 4 showing the most substantial decline. The p-value of 0.1638 indicates that overall, there was no significant difference in MCHC across the treatments, suggesting that while Treatment 1 was effective in raising MCHC levels, the other treatments did not significantly impact this parameter. These results imply that although Treatment 1 effectively increased hemoglobin concentration relative to red blood cell volume, Treatments 2, 3, and 4 did not demonstrate meaningful improvements in MCHC levels.

According to Yamaguchi, S. *et al.* (2021) [71], Mean Corpuscular Hemoglobin Concentration (MCHC) measures the average hemoglobin concentration in packed red blood cells, typically expressed in grams per deciliter (g/dL). Normal levels range from 32 to 36 g/dL and are vital for diagnosing conditions like hypochromic anemia and hereditary spherocytosis. MCHC values assist clinicians in assessing hematological health and guiding treatment decisions.

Table 43: Mean Corpuscular Hemoglobin Concentration (MCHC) Grams per deciliter (g/dL) before and after application of the treatments

Parameter	Treatment				
	T1	T2	T3	T4	Standard
Before	240	278	279	289	320 - 370
After	275	272	275	278	
Analysis of Covariance					
Sources of Variation	DF	SS	MS	F	P. Value
Regression	2	17.5169	8.7584	18.1296	0.1638^{ns}
Variation	1	0.4831	0.4831		
Total	3	18			

T1 – ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapµLco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Platelets (PLT)

The Analysis of Covariance (ANCOVA) was utilized to analyze the data regarding the hematological tests conducted before and after the application of various treatments, as presented in Table 46. The results revealed significant changes in platelet counts across different treatments, highlighting notable trends in both increases and decreases. Specifically, Treatment 1 exhibited a decrease in platelet count, dropping from 297.5 before treatment to 245.5 afterward, indicating a substantial reduction. In contrast, Treatment 2 experienced an even more pronounced decline, with platelet levels plummeting from 781 to 359, showcasing the most significant decrease among all treatments. On the other hand, Treatments 3 and 4 displayed positive changes in platelet counts, reflecting increases that indicate improved hematological responses. Treatment 3 saw an increase from 240 to 282, while Treatment 4 rose from 209 to 297.5, both demonstrating beneficial effects on platelet levels post-treatment. The statistical significance of these findings is underscored by a p-value of 0.0152, which falls below the conventional threshold of 0.05 for significance. This suggests that the treatments had a meaningful impact on platelet levels, which is crucial for enhancing wound healing in rabbits. Overall, the ANCOVA analysis indicates that while Treatment 1 and Treatment 2 experienced notable decreases in platelet counts, Treatments 3 and 4 showed significant increases. These findings contribute valuable insights into how different treatments can influence hematological parameters and their potential implications for wound healing efficacy in rabbits.

According to Lee, H. *et al.* (2008) [30], Platelet (PLT) enhances wound healing in rabbits by reducing contraction rates and improving epithelialization and angiogenesis. Studies show that PRP-treated wounds exhibit faster healing and increased blood vessel volume compared to controls, making it a promising option for reconstructive surgeries. Likewise, according to Ali, B. H. (1990) [7], rabbits were treated with the antiparasitic drug ivermectin at subcutaneous doses of 0.2, 1 and 2.5 mg/kg and blood collected weekly for 4 weeks thereafter for measuring some blood parameters. At a dose of 0.2 or 1 mg/kg the drug had no significant effect on any of the parameters measured. At a dose of 2.5 mg/kg, the drug reduced significantly the erythrocyte counts, hemoglobin concentration, hematocrit, mean corpuscular hemoglobin concentration and mean corpuscular hemoglobin on weeks 1, 2, 3 and 4. Platelet counts were not significantly affected. 2. In another trial, ivermectin was injected subcutaneously at a dose of 2.5 mg/kg, after pre-treatment with either saline or vitamin K (30 micrograms/kg for 30 days), and prothrombin time, bleeding time and platelet counts measured at weekly intervals for 4 weeks. Bleeding time and thrombin time were significantly increased 1 week after treatment, and remained higher than the control for 4 weeks.

Table 44: Platelets (PLT) Microliter (UL) before and after application of the treatments

Parameter	Treatment				
	T1	T2	T3	T4	Standard
Before	297.5	781	240	209	100 - 712
After	245.5	359	282	297.5	
Analysis of Covariance					
Sources of Variation	DF	SS	MS	F	P. Value
Regression	2	6715.948681	3357.97434	2164.592818	0.0152*
Variation	1	1.551319173	1.551319173		
Total	3	6717.5			

T1 - ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapµLco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Mean Platelet Volume (MPV)

The results of the Analysis of Covariance (ANCOVA presented in Table 47 indicate significant changes in Mean Platelet Volume (MPV) among various treatments, with the standard reference range for MPV in rabbits being 3.8 to 6.8 femtoliter. Treatment 1 showed an increase in MPV from 8.55 to 8.8 femtoliter, reflecting a slight enhancement in platelet size, while Treatment 3 also experienced a minor increase, moving from 8.4 to 8.45 femtoliter. In contrast, Treatment 2 exhibited a notable decrease in MPV, dropping from 8.95 to 8.4 femtoliter, suggesting a reduction in platelet size, and Treatment 4 similarly decreased from 8.75 to 8.35 femtoliter. The overall p-value of 0.4006 indicates that these differences in MPV across treatments were not statistically significant, suggesting that none of the treatments had a consistent or meaningful impact on platelet volume compared to the control group.

According to Taniguchi, B.A. *et al.* (2018) [63], Mean Platelet Volume (MPV) is a key indicator in wound healing, particularly in rabbits, as higher MPV associated with platelet-rich plasma (PRP) enhances healing. PRP promotes angiogenesis and accelerates epithelial migration, leading to greater contraction rates and faster healing. In controlled studies, PRP-treated wounds showed 95% contraction compared to 88% in controls, highlighting its effectiveness in improving tissue repair and regeneration.

Table 45: Mean Platelet Volume (MPV) femtoliters (fL) before and after application of the treatments

Parameter	Treatment				
	T1	T2	T3	T4	Standard
Before	8.55	8.95	8.4	8.75	3.8 - 6.8
After	8.8	8.4	8.45	8.35	
Analysis of Covariance					
Sources of Variation	DF	SS	MS	F	P. Value
Regression	2	0.1049	0.0525	2.6156	0.4006*
Variation	1	0.0200	0.0200		
Total	3	0.125			

T1 - ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapµLco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Mortality

The collected data focused on the mortality of the rabbits among different treatments in observed period from day 2 to day 14. The result is shown in the table below;

The Analysis of Variance (ANOVA) conducted on the mortality data of rabbits across four treatment groups reveals interesting insights into the effectiveness of each treatment. The mean mortality rates were observed as 0.0000 for Treatment 1, 0.6667 for Treatment 2, 0.0000 for Treatment 3, and 0.3333 for Treatment 4. Despite these differences in means, the ANOVA results yielded a p-value of 0.2192, indicating that there were no significant differences among treatments in terms of mortality, resulting in a 12.5% mortality rate during the observed period.

According to Singh *et al.*, 2025, mange in domestic rabbits (Oryctolagus cuniculus), a widespread and highly contagious dermatological condition caused by *Sarcoptes scabiei var.* cuniculi mites. Sarcoptic mange poses significant health risks to rabbits and can lead to severe economic losses in commercial rabbit farming due to decreased productivity, inferior leather quality, and increased mortality rates.

Table 46: Mortality during the application of treatments

Mortality	
Treatment	Mean
1	0.000
2	0.6667
3	0.0000
4	0.3333
Analysis of Variance	
F=value	1.83
P=value	0.2192
CV (%)	163.30

T1-ivermectin, T2 – neem leaves + guava leaves + hagonoy leaves + citronella oil, T3 – makabuhay stem + guava leaves + hagonoy leaves + citronella oil, T4 – acapulco leaves + guava leaves + hagonoy leaves + citronella oil.
Means with the same letter are not significantly different.
ns not significant
*Significant at $p \leq 0.05$
**highly significant at $p \leq 0.01$

Summary

During the experimental period, the experimental rabbits resulted in a 12.5% mortality rate due to mange infestations. This supports the findings of Abd El-Ghany, W. A. (2022) [4], mange in rabbits is an extremely significant parasitic disease, bringing about severe loss. This disease in particular can be called the zoonotic infestation burden upon public health and characterizing skin infestations: pruritus; alopecia; heavy and serious cases of cachexia Death occurs, and according to Scott *et al*. (2001) [53], chronic cases of Sarcoptic mange leads to anorexia, lethargy, emaciation and can even cause death in rabbits

The results of the study were summarized as follows: The analysis shows positive effects of ethnoveterinary plant extract sprays in the physical appearance of the rabbits including the length and width of wound, average wound area, and wound contraction in different anatomical parts such as left and right ear, nose, head, left and right foreleg, left and right hind leg. The evaluation of various treatments for wound healing in rabbits revealed consistent results across multiple anatomical sites. The width of wound in left foreleg shows a significant difference with a p-value of 0.0300 on day 10, indicating a unique response at this time point highlighting Treatment 4 with the smallest wound size of 0.47mm. Despite the differences in healing rates on specific day across all treatments, length of wound and wound area show no significant differences among the treatments whereas the control group (ivermectin) has a comparable effect in terms of wound healing in rabbit as indicated by ANOVA results In terms of wound contraction, the analysis shows a significant difference in the wound contraction in left ear on day 10, with a p-value of 0.0429. Other anatomical parts show no significant differences which indicates that all of the treatments have a comparable effect in terms of wound contraction. Days of healing wound shows a significant difference in the right hind leg as pvalue results 0.041 showing that T2 has the highest days of healing rate for the right hind leg. Despite the differences of average days of healing wound, the data shows that at the end of the observation period, all anatomical parts are fully healed. It means that all treatments have the same effects in terms of the wound healing. The analysis shows no significant differences in terms WBC, LYM%, GRAN%, RBC, HGB, HCT, MCV, MCH, MCHC, and MPV. The most notable finding is related to platelet counts (PLT), which show a significant decline in Treatment 1 and Treatment 2, while Treatments 3 and 4 lead to increases, with a p-value of 0.0152, highlighting a meaningful impact on platelet levels across treatments. Mortality has been recorded during the application of the treatments and the data shows no significant differences in terms of mortality resulting in 12.5% mortality rate. It means all treatments have a successful effect on wound healing in rabbits while controlling the mortality during the observation period.

Conclusion

Despite the result shows significance in some anatomical areas in terms of width of wound, wound contraction and days of healing wound, the overall results conclude that all treatments have the same effect in physical appearance promoting wound healing of rabbits compared to the control group (Ivermectin) and maintain a low mortality rate of 12.5% but it is important to note that T3 and T4 shows a positive result in the hematological test in increasing the platelet counts after the application period.

Recommendation

Future researchers may explore different techniques for extracting active compounds from ethnoveterinary plants, and then investigate which of these methods produce the most potent compounds for wound healing. To address the economic feasibility of ethnoveterinary plant extract spray for wound healing of rabbits, researchers may conduct a cost benefit analysis comparing the expenses associated with conventional anti-parasitic control methods to those of ethnoveterinary alternatives. this was help assess the economic viability and potential savings for rabbit farmers.

Future studies may investigate the potential side effects or toxicity levels associated with the use of ethnoveterinary plant extract in wound healing. It is essential to ensure the safety of both rabbits and human involved in the care and handling of treated animals. For future researchers, may try to compare a water based and an oil-based spray to determine and evaluate which is more likely to be effective in terms of applications. For future researchers, may try to assess the practical application of ethnoveterinary plant extract spray as wound healing in rabbits to evaluate the efficacy in real world conditions considering factors like dosage application frequency and long-term effects.

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