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Wound healing effects of *Commiphora swynnertonii* resin formulations using rat as model animal

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Commiphora swynnertonii **(Burceraceae) is commonly used for the treatment of various ailments, including arthritis, wounds, and skin conditions. In this study, the effects of various formulations of the tree resin on wound healing were evaluated in rats through skin contracture and histological changes. Body weights were also monitored during the experiments. Tree resins were prepared at 0, 2.5, 5, 10, 15, and 30% v/v concentrations to create various formulations of two products, namely wound gel and wound spray. The formulations were applied on wounds cut on rats' skins at cervical regions and monitored for 34 days. Wound contraction diameters were measured in millimeters, and fibrous tissue formation was assessed under the microscope. Both formulations sped up wound healing by contractions and fibroblast migration in dose-dependent manners, with (R2 = 95.6; P <0.01) for spray and (R2 = 69.7; P<0.05) for the gels. This study indicates that wound spray and gel formulations from the plant resin accelerate wound healing without affecting weight.**

Key words: *Commiphora swynnertonii*, resin, wound healing activity, rats.

INTRODUCTION

Wound healing is a highly coordinated cascade of events following tissue injury (Maxson et al., 2021). For successful wound healing, the process must pass through four highly programmed phases: coagulation, inflammation, proliferation, and remodeling in that order (Heil et al., 2017). These phases are important because the coagulation phase controls bleeding, while inflammation supplies materials (cells, etc.) needed for successful healing. The proliferative phase generates fibroblasts and endothelial cells, which facilitate angiogenesis, collagen deposition, granulation tissue formation, wound contracture, and re-epithelialization. Remodeling, on the other hand, ensures the realignment of the neo-collagen fibers to provide tensile strength comparable to the original tissues (Agyare et al., 2016). Delayed wound healing can be attributable to several factors such as repeated trauma, poor perfusion hence low oxygen supply, and excessive inflammation that perpetuate the chronicity of wounds through induced oxidative stress and tissue damage (Harding et al.,

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Table 1. Five *C. swynnertonii* wound gel formulations (F1-F5) prepared by addition of varying amounts of gelling agent, buffer, preservative, glycerine and distilled water.

Ingredient	F1	F2	F3	F4	F5
Resin (ml)	25	50	100	150	300
Gelling agent (g)	10	10	10	10	10
Buffer agent(g)	1.2	1.2	1.2	1.2	1.2
Preservative (g)	5	5	5	5	5
Glycerine (ml)	50	50	50	50	50
Distilled water (ml)	[1]q.s	q.s	q.s	q.s	q.s
Total (ml)	1000	1000	1000	1000	1000

[1] = Quantum satis (q.s.) that is the amount which is enough to top to 1000 ml.

2005).

Chronic wounds such as tropical ulcers are increasing in many developing countries. They are frequently associated with disease conditions like diabetes mellitus, road accidents, poor surgical interventions, as well as chronic diseases (Harding et al., 2005; Kevin et al., 2020). Treatment options are limited and expensive, leading to increased dependency on traditional medicines. In Tanzania, for instance, some well-documented and commonly used medicinal plant remedies include: *Azadirachta indica, Sida rhombifolia, Balanites aegyptiaca, Trichodesma zeylanicum, Melanthera scandens, Commiphora swynnertonii, Rytigynia celastroides* and *Hugonia castaneifolia* (McMillen et al., 2008; Moshi et al., 2010; Yadav and Panghal, 2010; Bakari et al., 2012; Muanza et al., 2018). However, their biological activities and efficacy are not scientifically well known.

Previous studies with experimental animals have demonstrated that resinous extracts from C. *swynnertonii*, one of the commonly used plant remedies, exhibit various biological activities ranging from antimicrobial activity, lowering blood sugar, lowering blood cholesterol (Bakari et al., 2012; Bakari et al., 2017; Maghembe et al., 2017), and increasing white blood cell (WBC) counts. The latter effect suggests that the extracts could also facilitate fast wound healing. The current study, therefore, focused on investigating the wound healing effects of two topical formulations (wound gel and wound spray) using varying concentrations of C. *swynnertonii* resin, using Wistar rats as a model experimental animal.

MATERIALS AND METHODS

Preparation of *C. swynnertonii* formulations

Wound gel

There are five different wound healing formulations (F1–F5) from varying concentrations of resins of C. *swynnertonii*. The trees from the family Burseraceae in Arusha were identified by a botanist (Kayombo, 2009). Resins from the trees were collected in clean plastic containers by incising the tree barks to the sapwood to allow the resin to drip. Three collection points per tree in ten trees were made to collect enough resin for experiments. The resin was transported in clean, closed containers under room temperature to Sokoine University for experiments. The resin was apportioned into aliquots of 25, 50, 100, 150, and 300 ml, and each aliquot was mixed with 10g of gelling agent, 1.2 g of buffer, 5 g of preservative, 50 ml of glycerine, and the mixture was made up to 1000 ml with distilled water as shown in Table 1. The ingredients were homogeneously mixed at room temperature to make the wound gel product and stored at room temperature away from direct sunlight.

Wound spray

Five different formulations (C1-C5) were prepared from *C. swynnertonii* using varying amount (ml) resin. The resin was apportioned into aliquots of 25, 50, 100, 150 and 300 ml and each aliquot were mixed with 5 g of preservative, 50 ml of glycerine and the mixture water topped to 1000 ml with ethanol as shown in Table 2.

Preparation and maintenance of Wistar rats as model experimental animals

A total of 280 mature Wistar rats, five weeks of age and weighing between 100 to 200 g were used for the study. The animals were kept in bio-secured small experimental house and in sanitary cages. They were provided with *ad libitum* potable water and broiler mash feeds. The house ambient temperature and humidity during the study were similar to the surrounding environment with average of 26°C for temperature and 66% for humidity. Light and dark hours in the house were similar with 12 h of light and 12 h of darkness.

Experiment setup by animal grouping

Two parallel animal trials were conducted to validate the effect of the C. *swynnertonii* resin products (wound gel and wound spray) produced as formulations of different concentrations on wound healing (Table 3). The rats were randomly divided into two major groups, each with fifty rats designated as Group GA for one group and Group GB for the other. Group GA was used for wound gel formulation trials, while Group GB rats were used for wound spray formulation trials. These two major groups were further subdivided

Table 2. Five *C. swynnertonii* wound spray formulations (C1 – C5) prepared by addition of various proportions of *C. swynnertonii* resin, stabilizer, preservative and absolute ethanol.

Ingredient	C1[1]	C2	C3	C4	C5
Resin (ml)	25	50	100	150	300
Stabilizer (g)	10	10	10	10	10
Preservative (g)	5	5	5	5	5
Absolute ethanol (ml)	q.s[1]	q.s	q.s	q.s	q.s
Total (ml)	1000	1000	1000	1000	1000

[1] = Quantum satis (q.s.) that is the amount which is enough to top to 1000 ml.

Table 3. Grouping and treatment allocation.

Variable		Sub group (n=7)	Treatment received	Resin (%)
Trial 1	GA (gel)	GA0	Untreated*	0
		GA1	Gentamycin cream	0
		GA2	WG1	2.5
		GA3	WG2	5.0
		GA4	WG3	10.0
		GA5	WG4	15.0
		GA6	WG5	30.0
Trial 2	GB (spray)[1]	GB0[2]	Untreated*	0
		GB1	OTC spray[3]	0
		GB2	WS2[4]	2.5
		GB3	WS3	5.0
		GB4	WS4	10.0
		GB5	WS5	15.0
		GB6	WS6	30.0

*These groups were left untreated to allow uninterrupted healing process. 1= Group B rats, 2 = Subgroup B rats, 3 = Oxytetracycline, 4 = Wound spray.

into 7 subgroups referred to as groups one to group seven (GA0-GA6) for GA and (GB0 –GB6) each with 20 rats. Sub-groups GA0 and GB0 from each group were used as negative controls and did not receive any resin formulation but were treated with distilled water as a placebo. For positive controls, GA1 and GB1 were treated with Gentamycin cream and oxytetracyclines (OTC) spray, respectively, as standard antimicrobial drugs.

Wound creation

All rats were weighed and then anesthetized by intramuscular injection of ketamine hydrochloride (40 mg/kg) plus xylazine hydrochloride (5 mg/kg). The back cervical region of the animals was shaved and disinfected methylated spirit followed iodine tincture. Ten mm of skin were excised from the prepared areas to create aseptic wounds. These surgically inflicted wounds were of full thickness type extending up to the subcutaneous tissue.

Evaluation of wound healing

Wound healings were evaluated by monitoring wound contractions (Kuria et al., 2015), body weights and cutaneous histopathological changes with time. Wound contractions as indicators of healing were calculated using the formula below:

Wound contracture (%) = 100 × (1^{st} day wound size – n^{th} day wound size)/ (First day wound size)

For histopathology, two rats from each subgroup were humanely sacrificed for collection of skin tissue samples. Tissue collection and processing were done as described by Drury et al. (1976). Body weight measurements of the rats were taken using top loading balance in grams on days 0, 2, 6, 9 and 14 of the experiment.

Ethical clearance

All procedures involving the animals were adhered to guidelines and procedures reviewed and approved by the Institutional Ethical Clearance committee number RPGS/R/ETHICS/2023/26 from the Directorate of the Post graduate, Research and Consultancy Committee of Sokoine University of Agriculture.

Data analysis

Body weight and wound contracture data were subjected to One

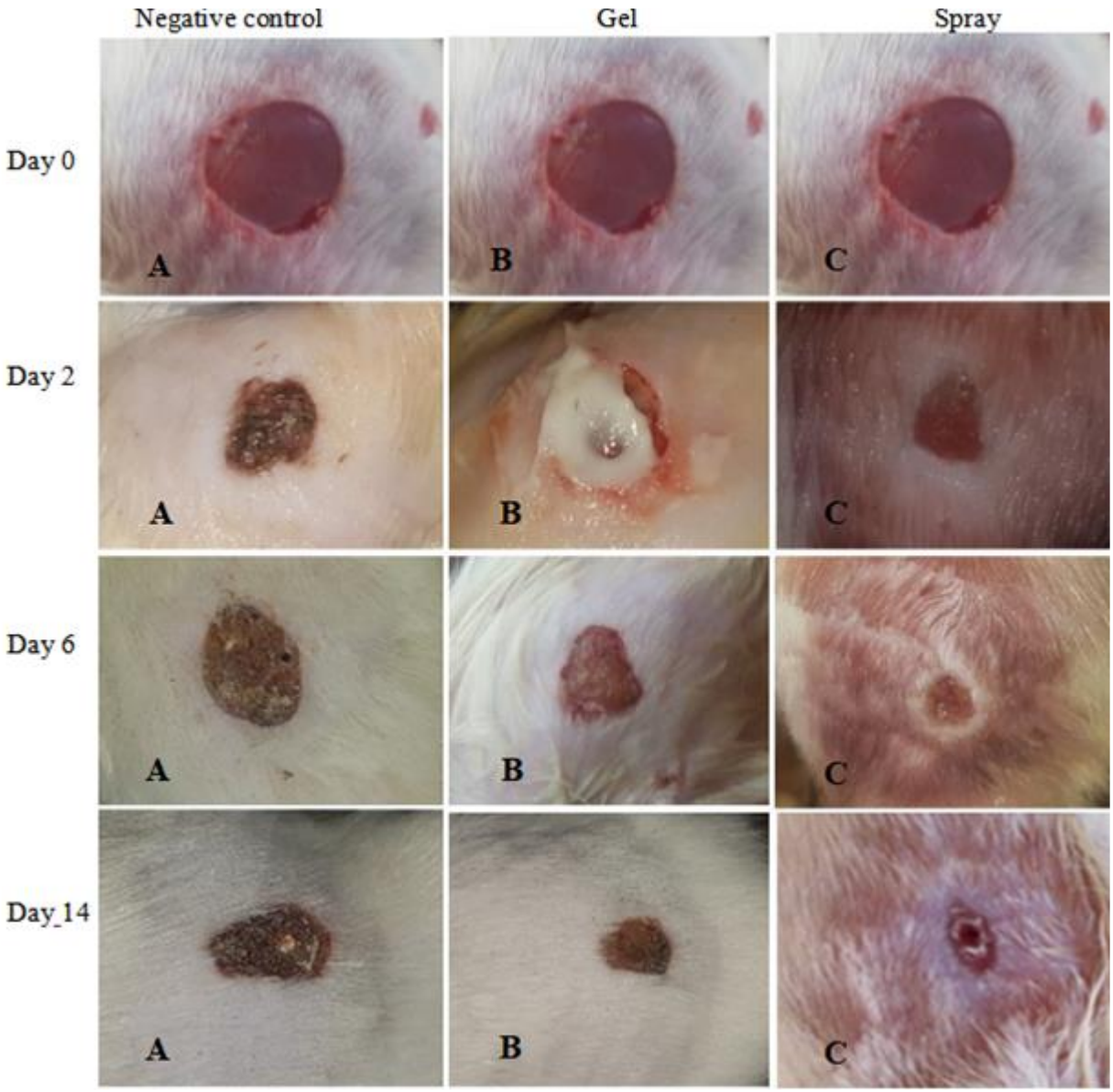

Figure 1. Pictures of wound healing indicated by contractures following treatment with gel and spray formulation. Down the picture columns, wound contractions appearances at different days from day 0 to day 14 on treatments with gel and spray formulations at 30% concentration compared with control groups.

Way ANOVA, using MS Excel. Group means (± SEM) were compared using Student's *t-test* comparison method; *p* values ≤ 0.05 were considered significant.

RESULTS AND DISCUSSION

This study evaluated effects of *C. swynnertonii* resin formulations for two products (wound gel and spray) on cutaneous wounds healing of skin excised Wistar rats. Results from this study showed that, following skin excision and treatment of the rats with both *C. swynnertonii* resin products, both similarly accelerated wound healing with no significant difference ($p>0.05$) between them. However, there were significant differences ($p<0.05$) among the formulations within the two product lines. Reduction in wound size was significant in G3, G4 and G5 as compared to negative control G0 for both products.

The wound sizes contracted from ten to two millimeters by day 14 after wound creation (Figure 1). Wound areas for rats treated with wound spray were observed to decrease significantly ($p < 0.001$) from day 6 to 14 post excision compared to wounds in the control groups, where the sizes reduced on average from 10.2 to 2.5 mm. Furthermore, the contracture was 100% by day 14

Table 4. Percentage wound contractures with time following treatment of the different groups of rats with different formulations of wound spray and wound gel products.

Product formulation	Treatment time (days)					
	Group	Day 0	Day 2	Day 6	Day 9	Day 14
Wound gel	GA0	0	12	36	48	54
	GA1	0	57	74	85	100
	GA2	0	26	42	50	68
	GA3	0	20	60	77	84
	GA4	0	45	65	79	91*
	GA5	0	43	59	74	91*
	GA6	0	46	66	81	100*
Wound spray	GB0	0	12	36	48	54
	GB1	0	46	61	72	91
	GB2	0	33	50	71	79*
	GB3	0	48	63	76	81*
	GB4	0	34	52	68	95*
	GB5	0	42	55	78	100*

*= $p < 0.05$ and (Significant against negative control).

post-wound creation (Table 4) for G5 and G6 for those treated with higher concentrations of wound spray and wound gel. The wound contractures were observed to increase in a dose-dependent manner ($R^2 = 95.6$; $p < 0.01$) for spray and ($R^2 = 69.7$, $p < 0.05$) for gel. The wound contractures for the formulations and the positive controls were higher compared to untreated groups (G0). For positive controls, OTC spray and Gentamycin cream (brands and registered trademarks) have shown higher wound healing compared to untreated negative control. The fast wound healing ability of different medicinal plants revealed the efficacy of the medication which was attributed to the presence of different phytochemical constituents such as phenolic compounds, alkaloids, saponins, tannins, flavonoids, anthraquinones, and cardiac glycosides, terpenes, sesquiterpenes, esters cumunic aldehyde, eugenol, steroids, resin acids, and proteins (Beara et al., 2009; Vitale et al., 2022). According to Cedillo-Cortezano et al. (2024), these different phytochemicals work individually or synergistically to achieve wound healing through anti-inflammatory, antioxidant, and antibacterial properties, and they promote collagen synthesis and facilitate protective cell regeneration. The compounds have also been reported to promote fast wound healing by multiple mechanisms, such as wound contracture, increased rate of epithelialization, and prevention of secondary bacterial infection that would have complicated and delayed wound healing (Li et al., 2011; Lodhi and Singhaim, 2013). Studies done by Nagar et al. (2016) on ethanolic extract of *Cestrum nocturnum* leaves showed better venerability of collagen synthesis attributed to the presence of phenolic compounds. They showed too that flavonoids in the extracts prevented secondary wound infections as they are known to have potent antiviral and antibacterial activities. A previous work by Bakari et al. (2012) with *C. swynnertonii* have also demonstrated significant increase in fibroblasts proliferation and migration to the wound area in 24 to 48 h of experiment after (3- (4, 5-Dimethylthiazol-2-yl)-2, 5-diphenyl Tetrazolium Bromide (MTT) and wound scratch assays. The increased proliferation and migration of fibroblasts led to increased synthesis of collagen and extracellular matrix components in building and repairing the structural components of the skin thus facilitated healing of the wound (Figure 2).

Compared to the control groups, mean body weights of rats in all groups increased significantly ($p<0.05$) probably due to the soothing effect of the resin formulated products that reduces stress to the treated rats compared to the controls (Table 5). The control group rats were observed to leak their wounds more frequently than the treated rats.

Conclusion

This study has demonstrated that *C. swynnertonii* resin products speeds up wound healing, as evidenced by an increased cell proliferation rate and wound closure. Treatment with these products does not affect the growth rate of the rats. Further studies are needed to elucidate the mode of action of the formulated products on wound healing.

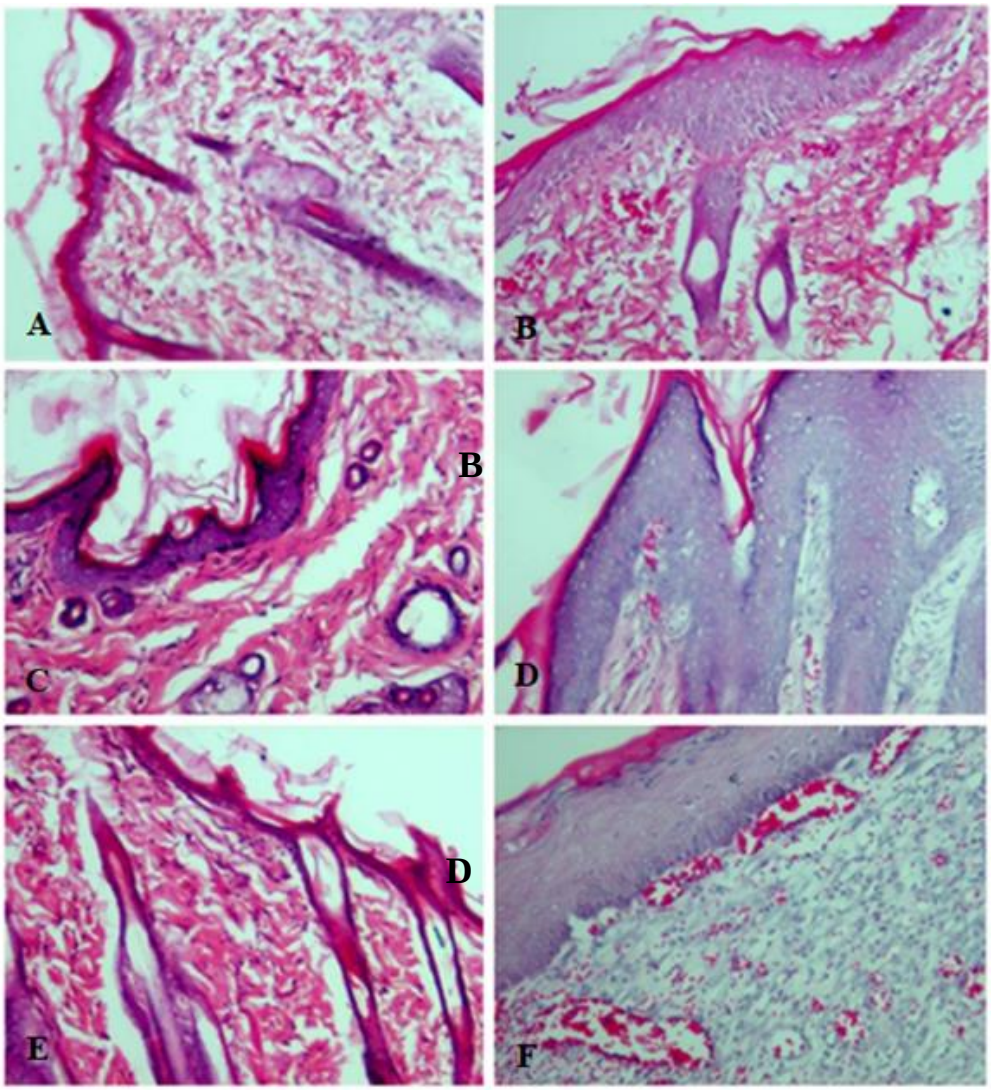

Figure 2. Histological sections (stained with H&E, 100 x magnification) of wound tissue from rats treated with *C. swynnertonii* gel. Day 0: [A] normal dermal cover hair follicle; Day 2: [B] neutrophils infiltration, subcutaneous dermal haemorrhages, missing epidermal cover; Day 6: [C&D] heavy clot plug of blood and neutrophils; Day 9: [E] complete epithelial restoration, sub-epidermal congestion, mononuclear cells infiltration, fibrotic tissues; Day 14: [F] complete epithelial restoration, fibrosis and revascularization.

Table 5. Body weight (mean ± SEM) changes following wound excision and treatment, using either spray or gel containing varying concentrations of *C. swynnertonii* resin.

Group (n = 7)	Treatment time (days)				
	0	2	6	9	14
Gel formulation					
GA0 - untreated	114.5 ± 1.7	129.4 ± 3.4	141.3 ± 2.7	145.3 ± 3.9	148.4 ± 4.6
GA1 - Gentamycin	108.5 ± 1.9	119.4 ± 2.7	125.6 ± 3.8	134.2 ± 5.2	137.3 ± 7.3
GA2 - WG1	104.2 ± 0.9	113.3 ± 1.7	122.3 ± 3.0	126.0 ± 2.5	128.8 ± 2.9
GA3 - WG2	124.8 ± 1.8	141.5 ± 2.7*	147.8 ± 1.8*	163.7 ± 2.5*	169.8 ± 1.1*
GA4 - WG3	115.7 ± 2.1	126.9 ± 2.9	136.3 ± 3.7	143.9 ± 5.4	150.9 ± 6.1
GA5 - WG4	131.6 ± 3.3	140.9 ± 4.1*	153.4 ± 7.2*	171.1 ± 9.5*	171.9 ± 9.1*
GA6 - WG5	118.1 ± 2.5	142.4 ± 3.2*	155.4 ± 5.1*	179.6 ± 7.2*	187.6 ± 5.9*

Table 5. Contd.

Spray formulation					
GB0 - untreated	114.5 ± 1.7	129.4 ± 3.4	141.3 ± 2.7	145.3 ± 3.9	148.4 ± 4.6
GB1 - OTC spray	129.3 ± 2.1	124.1 ± 3.1	121.5 ± 5.9	128.6 ± 8.1	138.7 ± 9.9
GB2 - WSP 1	108.5 ± 1.9	129.4 ± 2.7	135.6 ± 3.8	144.2 ± 5.2	157.2 ± 7.3*
GB3 - WSP 2	104.2 ± 0.9	113.3 ± 1.7	122.3 ± 3.0	126.0 ± 2.5	128.9 ± 2.9
GB4 - WSP 3	124.8 ± 1.8	141.5 ± 2.7*	147.8 ± 1.8*	163.7 ± 2.5*	169.8 ± 1.1*
GB5 - WSP 4	115.7 ± 2.1	126.9 ± 2.9	136.2 ± 3.7	143.9 ± 5.3	150.9 ± 6.1
GB6 - WSP 5	131.6 ± 3.3	140.9 ± 4.2*	153.4 ± 7.2*	171.1 ± 9.5*	171.9 ± 9.1*

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

REFERENCES

Agyare C, Boakye YD, Bekoe EO, Hensel A, Dapaah SO, Appiah T (2016). Review: African medicinal plants with wound healing properties. Journal of ethnopharmacology 177: 85-100.

Bakari GG, Max RA, Mdegela RH, Phiri, ECJ, Mtambo MMA (2012). Effect of extracts from *Commiphora swynnertonii* (Burrt) against selected microbes of animal health importance. Journal of Medicinal Plants Research 6(9):1795-1799.

Bakari GG, Ceaser G, Max RA, Mbasa GK (2017). Effect of resin from *Commiphora swynnertonii* on white blood cell and selected haematopoietic organs in albino mice (*Mus musculus*). African Journal of Biotechnology 16(28):1561-1566.

Beara IN, Lesjak MM, Jovin ED, Balog KJ, Anackov GT, Orcić DZ, Mimica-Dukić NM (2009). Plantain (*Plantago L*.) species as novel sources of flavonoid antioxidants. Journal of agricultural and food chemistry 57(19):9268-9273

Cedillo-Cortezano M, Martinez-Cuevas LR, López JAM, Barrera López IL, Escutia-Perez S, Petricevich VL (2024). Use of Medicinal Plants in the Process of Wound Healing: A Literature Review. Pharmaceuticals 17(3):303.

Drury RA, Wallington EA, Cancerson R (1976). Carlton's Histopathological Techniques. 4th Edition, Oxford University Press, Oxford, London, New York.

Harding KG, Moore K, Phillips TJ (2005). Wound chronicity and fibroblast senescence—implications for treatment. International Wound Journal 2(4):364-368.

Heil N, Bravo K, Montoya A, Robledo S, Osorio E (2017). Wound healing activity of *Ullucus tuberosus*, an Andean tuber crop. Asian Pacific Journal of Tropical Biomedicine 7(6):538-543

Kevin LH, Manoli I, Edorta S, Rosa MH (2020). Chronic wounds: Current status, available strategies and emerging therapeutic solutions. Journal of Controlled Release 328:532-550.

Kuria JM, Maria JM, Gathumbi PK, Kiama SG (2015). Influence of *Aspilia pluriseta* Schweinf (Asteraceae) on the healing of dermal excision wounds (mouse model) and skin sensitization activity (Guinea pig model). African Journal of Pharmacology and Therapeutics 4(3):112-117.

Li K, Diao Y, Zhang H, Wang S, Zhang Z, Yu B (2011). Tannin extracts from immature fruits of Terminalia chebula Fructus Retz. promote cutaneous wound healing in rats. BMC complementary and alternative medicine 11:1-9.

Lodhi S, Singhaim AK (2013). Wound healing effect of flavonoid rich fraction and luteolin isolated from *Martynia annua* Linn. on streptozotocin induced diabetic rats. Asian Pacific Journal of Tropical Medicine 6(4):253-259.

Maghembe RS, Bakari GG, Max RA, Balthazary ST (2017). Effect of *Commiphora swynnertonii* resin on liver functions and levels of plasma glucose and lipids in carbon-tetrachloride treated chickens. International Journal of Nutrition and Metabolism 9(7):58-66.

Maxson S, Lopez EA, Yoo D, Danilkovitch-Miagkova A, Leroux MA (2021). Concise review: role of mesenchymal stem cells in wound repair. Stem Cells Translational Medicine 1(2):142-149.

McMillen H (2008). Conserving the Roots of Trade: Local Ecological Knowledge of Ethnomedicines from Tanga, Tanzania Markets. Ph.D. Thesis. University of Hawaii.

Moshi MJ, Innocent E, Magadula JJ, Otieno DF, Weisheit A, Mbabazi PK (2010). Brine shrimp toxicity of some plants used as traditional medicines in Kagera Region, north western Tanzania. Tanzania Journal of Health Research 12(1):1-5.

Muanza DN, Euler KL, Williams L, Newman DJ (2018). Screening for antitumor and anti-HIV activities of nine medicinal plants from Zaire. International Journal of Pharmacognosy 33(2):98-106.

Nagar HK, Srivastava AK, Srivastava R, Kurmi ML, Chandel SL, Mahendra SR (2016). Pharmacological Investigation of the Wound Healing Activity of *Cestrum nocturnum* (L.) Ointment in Wistar Rats. Journal of Pharmaceutics 2016(1): 9249040.

Vitale S, Colanero S, Placidi M, Di Emidio G, Tatone C, Amicarelli F, D'Alessandro AM (2022). Phytochemistry and Biological Activity of Medicinal Plants in Wound Healing: An Overview of Current Research. Molecules 27(11):3566.

Yadav JP, Panghal M (2010). *Balanites aegyptiaca* (L.) Del. A Review of Its Traditional Uses, Phytochemistry and Pharmacological Properties. International Journal of Green Pharmacology 4(3):140-146.