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Mangifera indica (Mango) Bark Therapy Potentiates Wound Healing in Diabetic Rats

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Authors' contributions

Both authors participated actively in the study. Author RSA conceptualized and designed the study, supervised the experiment, analyzed and interpreted the results and prepared the manuscript. Author OJO performed the experiment, collected the data and performed initial analysis of the data. Authors RSA and OJO did the literature search, read and approved the manuscript. Author RSA is the guarantor of the study. The final manuscript was read and approved by both of them.

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ABSTRACT

Objective: One of the debilitating complications of diabetes mellitus is chronic foot ulcer. *Mangifera indica* (Mango) is a naturally occurring and widely cultivated plant with many health benefits attributable to its parts. The wound healing potential of its bark in adult diabetic rats was investigated.

Methods: The excised wounds of diabetic adult female wistar rats in groups of six were dressed with mango bark powder (MPD), mango bark ethanolic extract (MED), sofratulle (SD) and normal saline (ND) daily till healed. The corresponding control groups were MPC, MEC, SC and NC respectively. Every three days, the mean wound contraction rates were calculated from the measured wound areas. Granulation tissue was biopsied from an animal per group on day 3, 6 and 9 for histopathological evaluation and after healing, the scars of the remaining animals were biopsied for histology.

Results: The *M. indica* bark powder contained greater quantity of coumarins than the ethanolic extract; with terpenoids and steroids detected only in the powder. The MPD group had the highest

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mean wound contraction rates for the specified period. The mean wound contraction rates for the MPC group were significantly higher than those of the MED. The granulation tissues of the MPD and MPC groups had similar microscopic features to those of MEC, MED, SC, SD, NC and ND. Microscopy of the wound scars showed stratified squamous epithelia with abundant collagen fibres and blood vessels with dermal appendages seen in some of the groups.
Conclusion: Findings from this study showed that the *M. indica* bark.

Keywords: Mangifera indica (Mango) bark; diabetes mellitus; wound healing.

1. INTRODUCTION

According to Year 2020 diabetes report by the Centre for Disease Control and Prevention (CDC), 10.5% of the American population are diabetic and this translates to 34.2 million people as of 2018 and majority (more than 90%) were of type II with adults accounting for 34.1 million. About 13% of all United States adults (18 years and above) were reported as being diabetic [1]. Although no concise data is available for Nigeria, a systematic review of literature done in 2018, put the prevalence of diabetes at 5.77% which translated to 1 in 17 Nigerians as of 2017 [2]. The International Diabetes Federation put the global prevalence of diabetes amongst people between the aged 20-79 years at 8.8% which translated to 429.9 million as of 2017 and accounted for about 4 million deaths world-wide. The total health care expenditures for diabetes for 2017 (20-79 years) was seven hundred and twenty seven billion United States Dollar (USD 727 billion) [3]. Cardiovascular and renal complications are responsible for most of the diabetes related deaths. Another complication of diabetes is chronic foot ulcer which usually results from peripheral vascular disease. A lower limb or part thereof is said to be lost to amputation every 30 seconds somewhere in the world sequel to diabetes [3].

Mangifera indica grows in the Tropical and subtropical regions and is widely distributed in Nigeria. A potent antioxidant drug (Vimang®) with numerous pharmacological activities has been developed from its stem bark [4-6]. Documented human ailments in which *M. indica* stem bark has been found to have an ameliorative role include toothache, gastrointestinal disorders, respiratory tract infections, urinary tract infections [7-9] and anemia [10,11]. Extract of *M. indica* stem was able to lower blood glucose levels in rats with induced diabetes mellitus [12,13].

To the best of our knowledge, available literature on the plausible role of *M. indica* as a topical wound dressing material in diabetic rats (induced) is extremely scarce hence the need for this study. Thus this study was designed to investigate the role of the crude powder and ethanolic extract of *M. indica* in the management of excisional wounds in rats with induced diabetes mellitus.

2. MATERIALS AND METHODS

2.1 Plant Materials

2.1.1 Collection and identification of plant materials

Fresh barks were removed from *Mangifera indica* trees located at Ajibode settlement, Akinyele Local Government Area of Oyo State Nigeria. Species identification and confirmation was done at the Herbarium Unit of the Botany Department, University of Ibadan, Nigeria. After initial thorough washing under continuously flowing water, the barks were then completely dehydrated by air drying at room temperature for five weeks. Thereafter, grounded into fine textured powder by an electric grinder yielding 1,500 grammes; a portion of which was subsequently used for ethanolic extraction and the second portion as wound dressing material.

2.1.2 Preparation of powders and extracts

2.1.2.1 Ethanolic extraction

Five hundred grammes of the crude powder was used for ethanolic extraction with 100% ethanol producing a 13.5% yield that was stored under optimal conditions till use.

2.1.2.2 Phytochemical analyses

Phytochemical analyses of the *M. indica* stem bark powder and ethanolic extract for tannins, saponins, alkaloids, steroids, flavonoids, terpenoids and anthraquinones were done with the describe methods of Santhi and Sengottuvel [14] and for coumarins by Yadav et al. [15].

2.2 Animals

Forty eight healthy inbred adult female wistar rats of 170 to 260 g weight sourced from the Central Animal House, College of Medicine, University of Ibadan were used for the study. They were initially acclimatized in a well ventilated and illuminated environment with conducive ambient temperature for three weeks. They had liberal standard rat diet and water for the entire period of the study and were also weighed periodically. The animals were closely monitored and those that developed features of sepsis were withdrawn from the study. Animal handling was in compliance with the guidelines prescribed by the ethical conduct of animal research of the University of Ibadan. Also, the principles of laboratory animal care as contained in the 8th edition (2011) of the Guide for the Care and Use of Laboratory Animals by the National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals were observed [16].

2.3 Design of the Experiment

The animals were initially divided into two equal groups of 24 each, a group subsequently had induced diabetes mellitus. Each of these two main groups was further divided into four groups of six animals each premised on the type of materials used to dress the excised skin wounds. The designations of the final eight groups were as stated below:

- 1 Mango bark powder control (MPC)
- 2 Mango bark powder diabetic (MPD)
- 3.Mango bark extract control (MEC)
- 4 Mango bark extract diabetic (MED)
- 5.Sofratulle control (SC)
- 6. Sofratulle diabetic (SD)
- 7. Normal saline control (NC)
- 8. Normal saline diabetic (ND)

2.4 Induction of Diabetes Mellitus

The pre induction fasting blood sugar levels were estimated with single touch glucometer (ACCUCHECK®, Roche Diagnostics, Germany) using the blood obtained from the tails of the rats. The baseline pre induction blood sugar level ranged from 55- 75/dl. Based on the outcome of previous studies by us, a single dose of 100 mg/kg body weight of alloxan monohydrate dissolved in normal saline and administered intraperitoneally was used to induce diabetes mellitus. A72 hour post induction fasting blood sugar level above 250 mg/dl was considered diabetic [17].

2.5 Wound Creation

After prior sedation with intramuscular ketamine hydrochloride (120 mg/kg); the dorsolateral skin of each rat was cleansed with savlon antiseptic liquid and a 2 cm by 2 cm full thickness skin about 1.5 cm from the vertebral column was excised thus establishing an excisional wound.

2.6 Wound Management and Data Collection

The mango bark powder, mango bark extract, sofratulle and normal saline was used as wound dressing material for the respective paired group- MPC, MPD; MEC, MED; SC, SD; and NC, ND.

The wounds were dressed daily and prior to dressing, wound size estimation were done by taking dimensions along two perpendicular plane. The values obtained were used to derive the contraction rates in percentages and this was repeated every 3 days.

Granulation tissue biopsy was taken from a member of each group on day 3, 6 and 9. These samples were processed for histological evaluation using Haematoxylin and Eosin stain.

These slides were used for evaluation of wound healing in terms of cellularity, angiogenesis, fibroplasia and collagen synthesis. The excision of granulation tissue served as the exit point for such animals and the wounds of remaining animals in all the groups were allowed to heal. The resultant scars were similarly processed for light microscopy. Falling off of the eschar without any residual wound indicated the endpoint of complete epithelization and the days required for this connoted the duration of healing.

2.7 Data Analysis and Processing

The numerical aspects of the results were analyzed with Statistical Package for the Social Sciences (SPSS) version 24 and expressed as percentages, means plus standard deviation of means (SD). The student t-test was used for inter group comparison and level of significance was set at $p<0.05$.

3. RESULTS

Mangifera indica powder contained greater quantity of coumarins than the ethanolic extract.

Table 1. Phytochemical analyses *Mangifera indica* powder and extract

Anthraquinones		Terpenoids		Alkaloids		Flavonoids		Tannins	Steroids	Saponins	Coumarins
Powder	Extract	Powder	Extract	Powder	Extract	Powder	Extract	Powder +	Powder +	Powder +	Powder ++-
---	---	+	---	+	+	+	+	Extract +	Extract --	Extract +	Extract +

+ (present) and – (absent)

Table 2. Mean fasting blood sugar levels and mean body weight

Parameter	MPC	MPD	MEC	MED	SC	SD	NC	ND
Pre induction glucose level (mg/dl)	N/A	65.70	N/A	64.80	N/A	70.00	N/A	71.00
Post induction glucose level (mg/dl)		309.30		296		311		356.8
Pre induction weight (g)	202.50±14.27	231.5±24.74	219.50±12.83	209.5±20.03	192.80±13.64	210.0±15.02	215.8±18.24	218.3±18.35
Post induction weight-day 6	201.30±18.87	231.0±42.90	219.30±13.30	218.5±28.46	195.0±4.69	226.0±22.20	189.8±19.26	251.5±25.49
Post induction weight-day 12	212.0±32.44	259.0±15.59	219.00±18.26	210.7±26.50	205.0±20.25	233.3±25.50	221.67±14.01	254.0±23.64

NA= Not applicable. The control groups were not induced; the weights were itemized just to show the trend. The blood glucose levels in all the diabetic groups were markedly elevated and significantly higher (P≥ 0.05) than the pre induction levels

Anthraquinones were not detected in both samples of *M. indica* while terpenoids and steroids were detected only in the powder. Other phytochemicals were detected in both the powder and extract in equal proportions (Table 1). In all the diabetic groups, then mean fasting blood glucose levels were well above 250 mg/dl and remained high throughout the duration of the experiment. Following induction of diabetes, only the mango bark ethanolic extract group recorded weight reduction while the remaining diabetic groups gained weight between day 6 and 12 (Table 2).

On day 3 of the study, it was observed that mean wound contraction rate of the diabetic group was greater than that of its respective control and the mango bark powder diabetic (MPD) had the highest rate of 57%. This trend was also noticed on day 6 with the gap closing up. Also on day 6, the mean wound contraction rate for the mango bark ethanolic extract control (MEC) was negative. This implied that the mean wound size increased rather than reduce. The trend in the mean wound contraction rates on day 9 was similar to the previous one but the margin between the experimental and respective control had reduced considerably except for the mango bark extract groups (MED vs MEC) that had very wide margin (48.74±20.16 vs 6.81±24.24%). By day 12, all the diabetic groups had mean rates above 65% and the controls were marginally higher than the respective experimental groups. Wound healing had progressed satisfactorily in all the groups (control and diabetics) by day 15 and the mango bark ethanolic extract (MED) had the least rate of 82% (Table 3).

3.1 Mean Wound Contraction Rates Comparisons

Comparisons between the MPD group and the other diabetic groups on day 3 revealed that the mean wound contraction rate of the former was significantly higher than those of the latter groups (MPD vs MED; MPD vs SD and MPD vs ND). Also, at the same day 3, we observed that the MPD mean rate was significantly higher than those of MPC and MEC (57.02±5.09 vs 20.83±8.00; 57.02±5.09 vs 8.25±20.48%). Other mean wound contractions with significant differences on day 3 were from: MEC vs MED (8.25±20.48:29.96±9.92); MEC vs SD (8.25±20.48:31.34±6.26) and SC vs SD (20.58±6.54:31.34±6.26). Amongst the diabetic groups on day 6, the MED rate was significantly lower than that of MPD and SD (14.24±9.36:55.40±9.96; 14.24±9.36:48.71±8.28). Also on day 6, the mean rate for MPC was significantly higher than that of the MED (47.63±32.41 vs 14.24±9.36), while MEC was significantly lower to all the diabetic groups. Among the control groups on day 6, the mean rate for MEC was significantly lower to others i.e. MPC, SC and NC.

On day 9, most of the rate comparisons were insignificant apart from MEC vs MPD, MEC vs SD, MEC vs MPC and MEC vs SC; in which the mean rate of MEC group was significantly lower. For day 12, the MPD mean rate was significantly higher than those of MED and SD (90.23±1.42:65.08±4.57, 90.23±1.42:77.23±3.15). For the same period, we observed that the mean rate for MPC was significantly higher than those of MED and SD (91.90±2.23:65.08±4.57 and 91.90±2.23:77.23±3.15). While the mean rate for MEC was significantly lower than those of MPD, MPC and NC groups (77.21±1.58:90.23±1.42, 77.21±1.58:91.90±2.23 and 77.21±1.58:88.06±1.51) (Table 4).

3.2 Histology of Granulation and Scar Tissues

We observed infiltration by inflammatory cells in all the sections prepared from granulation tissue biopsies obtained from a member of each group

Table 3. Interval mean values of wound contraction rates in percentages (%)

Group	Day 3	Day 6	Day 9	Day 12	Day 15	Day 18
MPC	20.83±8.00	47.63±32.41	69.37±14.70	91.90±2.23	98.64±1.03	**
MPD	57.02±5.09	55.40±9.96	69.53±5.19	90.23±1.42	96.19±1.05	97.82±1.02
MEC	8.25±20.48	-12.54±3.29	6.81±24.24	77.21±1.58	91.30±1.14	94.29±0.04
MED	29.96±9.92	14.24±9.36	48.74±20.16	65.08±4.57	82.29±1.44	89.92±0.20
SC	20.58±6.54	43.96±7.10	55.29±14.52	80.41±4.66	86.65±1.48	**
SD	31.34±6.26	48.71±8.28	67.42±4.70	77.23±3.15	90.49±1.16	93.48±0.08
NC	17.62±25.19	41.92±12.36	38.17±14.85	88.06±1.51	95.39±1.13	**
ND	25.19±11.49	42.87±22.26	57.12±22.22	82.07±8.45	87.20±1.31	**

*** Healed wound. –(minus) connotes that the wound increased in size rather than contracted*

Table 4. Intra and Inter group comparisons of wound mean contraction rates

Compared groups	Day 3 mean rates	Day 6 mean rates	Day 9 mean rates	Day 12 mean rates
MPD vs MED	57.02±5.09*	55.40±9.96*	69.53±5.19	90.23±1.42*
	29.96±9.92	14.24±9.36	48.74±20.16	65.08±4.57
MPD vs SD	57.02±5.09*	55.40±9.96	69.53±5.19	90.23±1.42*
	31.34±6.26	48.71±8.28	67.42±4.70	77.23±3.15
MPD vs ND	57.02±5.09*	55.40±9.96	69.53±5.19	90.23±1.42
	25.19±11.49	42.87±22.26	57.12±22.22	82.07±8.45
MED vs SD	29.96±9.92	14.24±9.36*	48.74±20.16	65.08±4.57
	31.34±6.26	48.71±8.28	67.42±4.70	77.23±3.15
MED vs ND	29.96±9.92	14.24±9.36	48.74±20.16	65.08±4.57
	25.19±11.49	42.87±22.26	57.12±22.22	82.07±8.45
SD vs ND	31.34±6.26	48.71±8.28	67.42±4.70	77.23±3.15
	25.19±11.49	42.87±22.26	57.12±22.22	82.07±8.45
MPC vs MPD	20.83±8.00*	47.63±32.41	69.37±14.70	91.90±2.23
	57.02±5.09	55.40±9.96	69.53±5.19	90.23±1.42
MPC vs MED	20.83±8.00	47.63±32.41*	69.37±14.70	91.90±2.23*
	29.96±9.92	14.24±9.36	48.74±20.16	65.08±4.57
MPC vs SD	20.83±8.00	47.63±32.41	69.37±14.70	91.90±2.23*
	31.34±6.26	48.71±8.28	67.42±4.70	77.23±3.15
MPC vs ND	20.83±8.00	47.63±32.41	69.37±14.70	91.90±2.23
	25.19±11.49	42.87±22.26	57.12±22.22	82.07±8.45
MEC vs MPD	8.25±20.48*	-12.54±3.29*	6.81±24.24*	77.21±1.58*
	57.02±5.09	55.40±9.96	69.53±5.19	90.23±1.42
MEC vs MED	8.25±20.48*	-12.54±3.29*	6.81±24.24	77.21±1.58
	29.96±9.92	14.24±9.36	48.74±20.16	65.08±4.57
MEC vs SD	8.25±20.48*	-12.54±3.29*	6.81±24.24*	77.21±1.58
	31.34±6.26	48.71±8.28	67.42±4.70	77.23±3.15
MEC vs ND	8.25±20.48	-12.54±3.29*	6.81±24.24	77.21±1.58
	25.19±11.49	42.87±22.26	57.12±22.22	82.07±8.45
MPC vs MEC	20.83±8.00	47.63±32.41*	69.37±14.70*	91.90±2.23*
	8.25±20.48	-12.54±3.29	6.81±24.24	77.21±1.58
MPC vs SC	20.83±8.00	47.63±32.41	69.37±14.70	91.90±2.23
	20.58±6.54	43.96±7.10	55.29±14.52	80.41±4.66
MPC vs NC	20.83±8.00	47.63±32.41	69.37±14.70	91.90±2.23
	17.62±25.19	41.92±12.36	38.17±14.85	88.06±1.51
MEC vs SC	8.25±20.48	-12.54±3.29*	6.81±24.24*	77.21±1.58
	20.58±6.54	43.96±7.10	55.29±14.52	80.41±4.66
MEC vs NC	8.25±20.48	-12.54±3.29*	6.81±24.24	77.21±1.58*
	17.62±25.19	41.92±12.36	38.17±14.85	88.06±1.51
SC vs SD	20.58±6.54*	43.96±7.10	55.29±14.52	80.41±4.66
	31.34±6.26	48.71±8.28	67.42±4.70	77.23±3.15
NC vs SD	17.62±25.19	41.92±12.36	38.17±14.85	88.06±1.51
	31.34±6.26	48.71±8.28	67.42±4.70	77.23±3.15
NC vs ND	17.62±25.19	41.92±12.36	38.17±14.85	88.06±1.51
	25.19±11.49	42.87±22.26	57.12±22.22	82.07±8.45
NC vs SC	17.62±25.19	41.92±12.36	38.17±14.85	88.06±1.51
	20.58±6.54	43.96±7.10	55.29±14.52	80.41±4.66

*The comparisons of mean group wound contraction rates revealed that some differences were of statistical significance (P≥0.05) such are indicated with asterisk**

on day 3. Other structures and cells seen in those sections included blood vessels (predominantly capillaries), fibrillary structures, fibroblasts and macrophages (Plate 1). Reduced inflammatory cellular infiltrates, increased angiogenesis, fibrillary structures and fibroblasts characterized the granulation tissue histology on day 6 (Plate 2). The day 9 granulation

tissue biopsies showed predominance of fibroblasts and collagen in all the groups with more prominence in groups MED and SD (Plate 3). Multilayered squamous cells suggestive of stratified squamous epithelium, collagen and dermal appendages were the main histologic features of the scars (Plate 4).

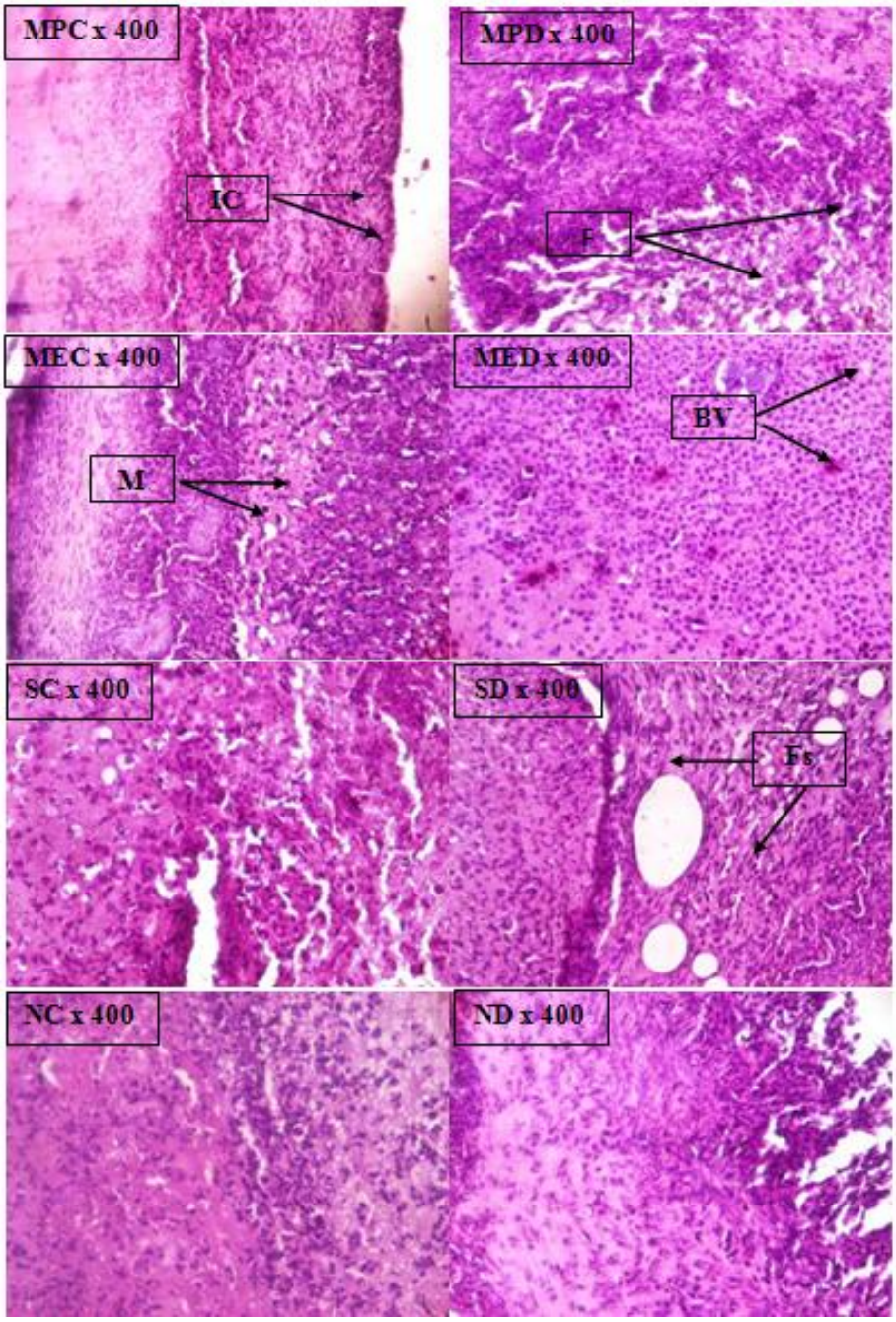

Plate 1. Granulation tissue at Day 3 (H & E)

MPC (Mango bark powder control), MPD (Mango bark powder diabetic), MEC (Mango bark extract control), MED (Mango bark extract diabetic), SC (Sofratulle control), SD (Sofratulle diabetic), NC (Normal Saline control), ND (Normal Saline diabetic), BV (Blood vessel), IC (Inflammatory cells), F (Fibroblast), Fs (Fibrillary structures) and M (macrophages)

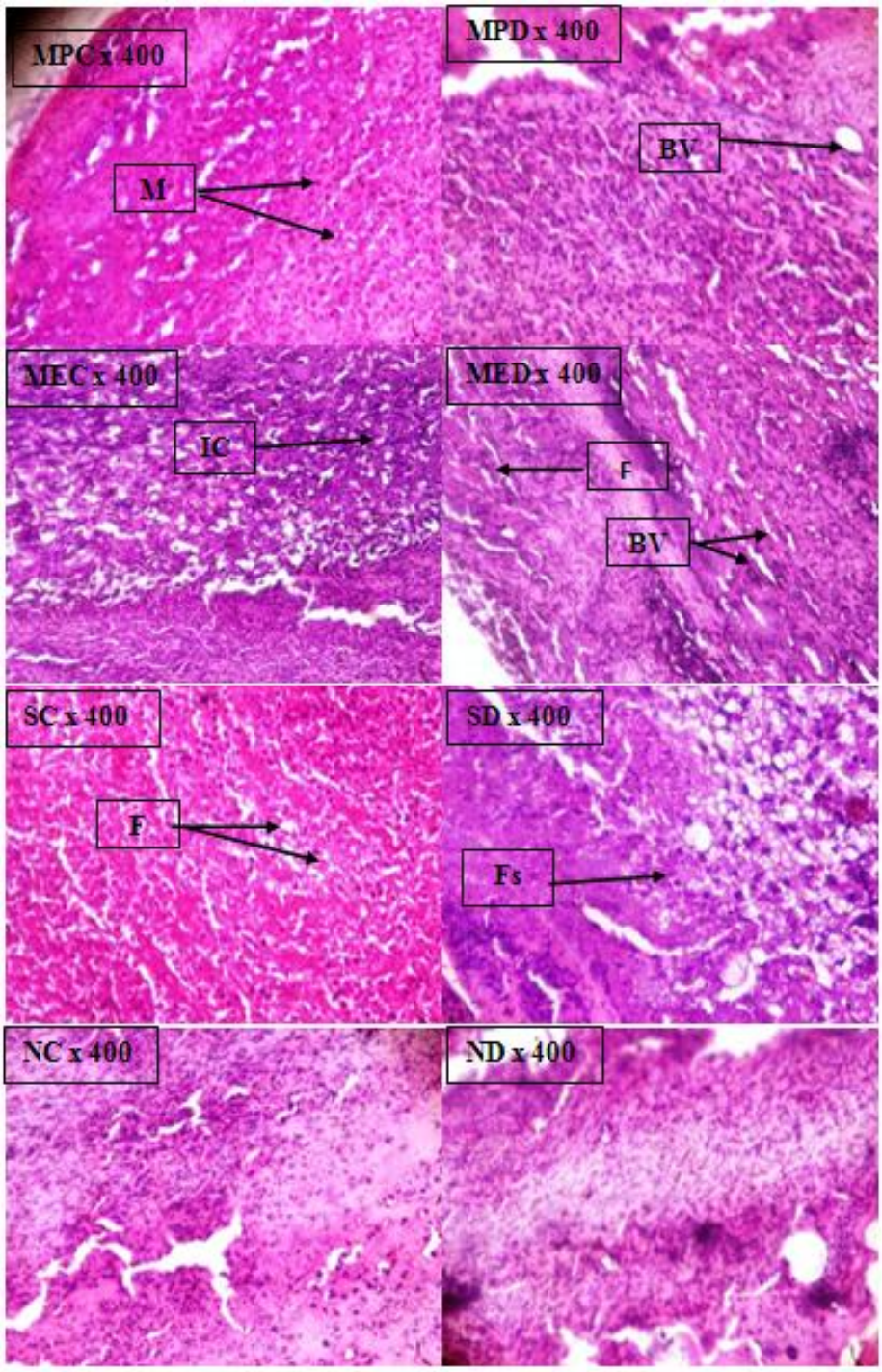

Plate 2. Granulation tissue at Day 6 (H & E)

MPC (Mango bark powder control), MPD (Mango bark powder diabetic), MEC (Mango bark extract control), MED (Mango bark extract diabetic), SC (Sofratulle control), SD (Sofratulle diabetic), NC (Normal Saline control), ND (Normal Saline diabetic), BV (Blood vessels), IC (Inflammatory cells), F (Fibroblast), Fs (Fibrillary structures) and M (macrophages)

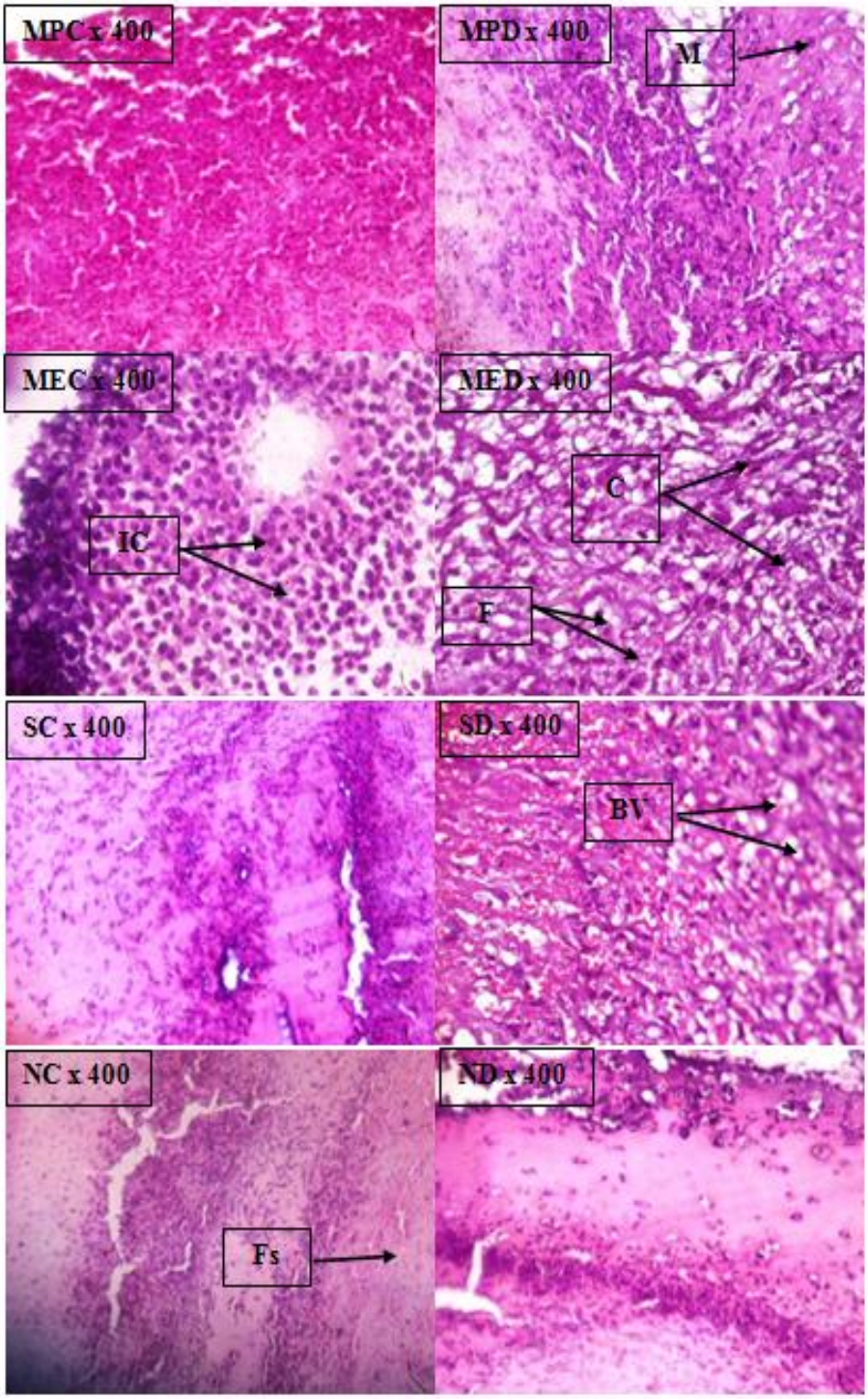

Plate 3. Granulation tissue at Day 9 (H & E)

MPC (Mango bark powder control), MPD (Mango bark powder diabetic), MEC (Mango bark extract control), MED (Mango bark extract diabetic), SC (Sofratulle control), SD (Sofratulle diabetic), NC (Normal Saline control), ND (Normal Saline diabetic), BV (Blood vessel), C (Collagen), IC (Inflammatory cells), F (Fibroblast), Fs (Fibrillary structures) and M (macrophages)

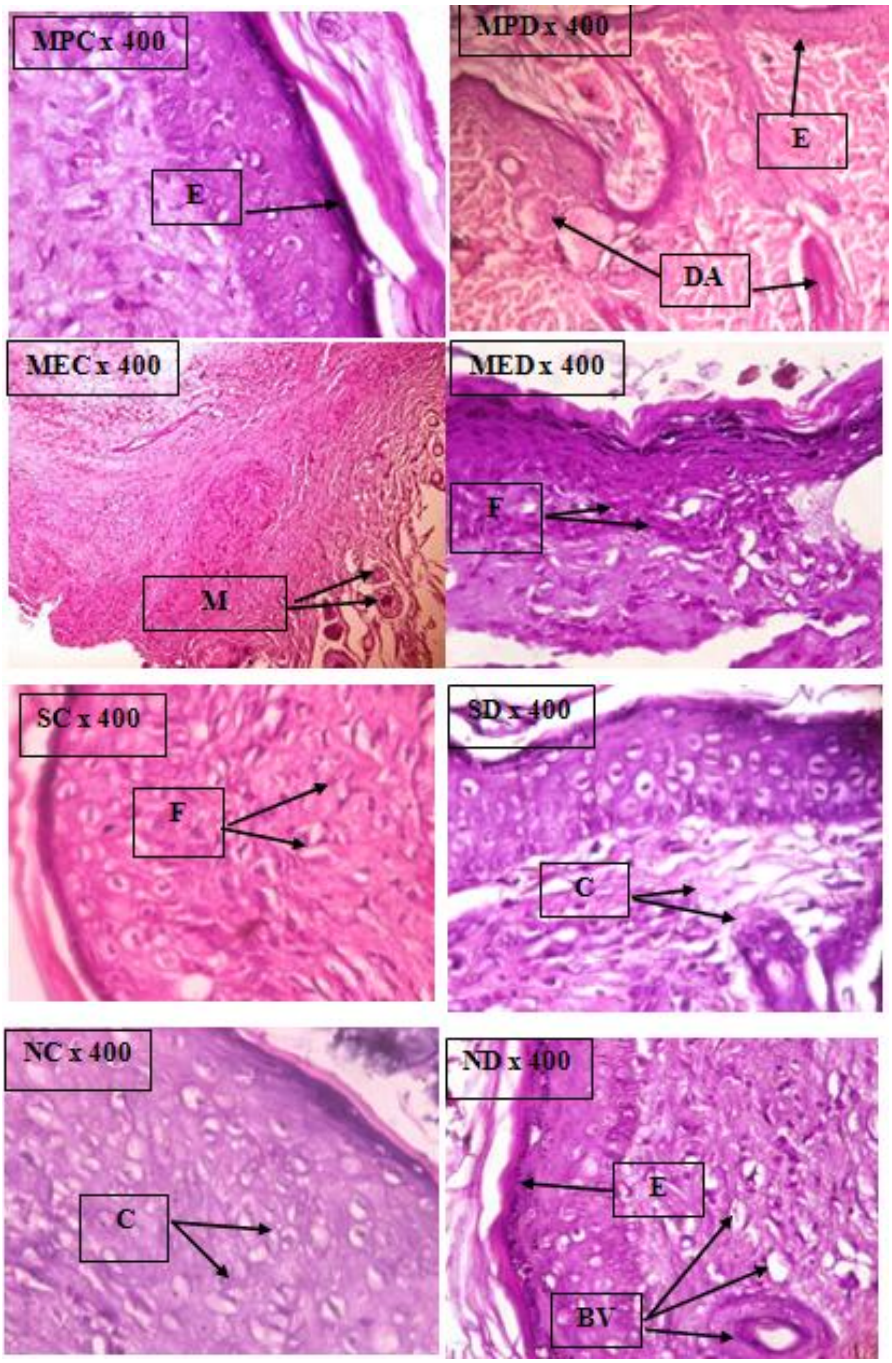

Plate 4. Sections from the wound scars (H & E)

MPC (Mango bark powder control), MPD (Mango bark powder diabetic), MEC (Mango bark extract control), MED (Mango bark extract diabetic), SC (Sofratulle control), SD (Sofratulle diabetic), NC (Normal Saline control), ND (Normal Saline diabetic), BV (Blood vessels), C (Collagen), DA (Dermal appendages), E (Stratified squamous epithelium), F (Fibroblasts) and M (macrophages)

4. DISCUSSION

Coumarins like other non-essential oil compounds such saponins, flavonoids and terpenoids have been demonstrated to exhibit anti-inflammatory, antibacterial and hypoglycaemic properties [18,19]. The powder formulation of *M. indica* used in this study had

greater quantity of coumarins while steroids and terpenoids were absent in the extract but present in the powder. The *M. indica* powder groups (control and diabetic) had the highest mean wound contraction rates next to them were the *M. indica* extract groups, these observations might be explained by the non-essential oil compounds of the mango bark. Since one of the evaluation parameters of wound healing in this study was wound contraction rate; drawing an inference that the bark of *M. indica* in both powder and ethanolic extract promote wound healing even in diabetic rat would not be inappropriate.

The mean contraction rates for the mango bark powder diabetic group were higher than those of the other diabetic groups (mango bark extract, sofratulle and normal saline) throughout the entire duration of the study. More importantly, these differences were significant at some timeline of the study this connoted that the powder formulation of *M. indica* bark accelerated the wound healing process in diabetic rats in this study.

The ethanolic extract of the bark demonstrated a lower wound healing potential than sofratulle and normal saline in diabetic rats as evidenced by a comparably lower mean wound contraction rates. While the converse was the case for the powder formulation of the bark as earlier as stated. Thus in our study, the powder of *M. indica* bark promoted wound healing faster and better than its ethanolic extract. This observation becomes very pertinent when the ease of preparation of the two formulations is considered as the preparation of the powder is less technically demanding and with reduced cost. Thus if this finding becomes translated to management of human diabetic foot ulcer, it is likely to be more receptive in terms of cost and application.

The powder formulation of *M. indica* bark in the control group (MPC) demonstrated greater wound healing ability than three diabetic groups of ethanolic bark extract, sofratulle and normal saline i.e MED, SD and ND. This conclusion was borne out of the fact that the mean contraction rates of the MPC group were higher and even of significance than those of the MED, SD and ND on some days of the study.

The ethanolic extract of the bark in non-diabetic rats demonstrated lower wound healing potential when compared with those of the four diabetic groups. The evidence of this was the significantly lower mean wound contraction rates of the MEC group to those of the MPD, MED, SD and ND. Also in non-diabetic milieu, the powder formulation of the bark proved to be better wound dressing material than the ethanolic extract as shown by the mean wound contraction rates of the MPC group being significantly higher than those of the MEC. Another major finding of this study was that the MPC demonstrated better wound healing than sofratulle and normal saline arising from the fact that the mean rates for MPC were greater than those of SC and NC. While the latter groups appeared to promoter wound healing better than MEC as evidenced by their significantly higher mean wound contraction rates.

Qualitative assessment of wound healing include inflammatory cellular infiltration, presence of fibroblasts which lay down collagen, neovascularization (angiogenesis) and re epithelialization. All these qualitative parameters were observed in both control and diabetic groups without any remarkable differences. The histology of the scars from the *M. indica* groups were similar to those of sofratulle and normal saline.

The phytochemistry of *M. indica* has been extensively studied with over 100 active constituents documented and diverse functions of the plant are being ascribed to these constituents [20].

The mangiferin and gallic acid components of a commercially available *M. indica* bark extract (Vimang) have been found to drastically reduced mitotic activity in advanced breast cancer [21].

Essential amino acids that are important for collagen synthesis such as alanine and glycine have been isolated from the bark of *M. indica* [22]. The immune status of any organism (animal or human) has a major impact on progression of wound healing and it can swing it either low or high. Reactive oxygen species (ROS) have diverse negative effects on biological molecules such as proteins, lipids and deoxyribonucleic acid with resultant structural and or functional alterations [23]. In non-pathological state, the intracellular ROS level is under tight control by various antioxidants, such as superoxide dismutase, catalase, glutathione peroxidase, peroxiredoxin, glutathione and thioredoxin. A delicately controlled ROS homeostasis is critical

for maintaining normal cell functions. Any disruption in the oxidation-antioxidation balance invariably leads to oxidative stress which is associated with a wide spectrum of human disorders such as delayed wound healing [24]. M.*indica bark* phytochemicals such as mangiferin, flavonoids, coumarins are potent antioxidants [25]; these substances will enhance the wound healing ability of the plant reducing the inflammatory phase of the healing process.

Both the quantitative and qualitative results of this study show that both the powder and ethanolic extract of *M. indica* bark promote wound healing in diabetic wistar rats. The mechanisms through which this is achieved could include the enhanced collagen synthesis (amino acids content), reduced inflammatory process (anti-inflammatory components) and reduced cellular oxidation (anti-oxidants constituents).

5. CONCLUSION

The powder formulation of *M. indica* bark has ability to promote wound healing in diabetic rats better than its ethanolic extract, sofratulle and normal saline. While its ethanoic extract was of lesser propensity. If further researches on diabetic human subjects are able to corroborate this finding, there will be significant reduction in the management of diabetic foot ulcers in terms of cost and manpower. This will translate to reduced morbidity and mortality from diabetic foot ulcers and consequently improve quality of life.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The animals were handled in accordance to the guidelines as prescribed by the ethical conduct of animal research of the University of Ibadan. Also, the principles of laboratory animal care as contained in the 8th edition (2011) of the Guide for the Care and Use of Laboratory Animals by the National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals were observed. (National Academies Press (US); 2011. Available from: https://www.ncbi.nlm.nih.gov/books/NBK54050/doi: 10.17226/12910).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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