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EVALUATION OF THE AQUEOUS EXTRACT OF THE TRUNK SCRAPS OF *TERMINALIA IVORENSIS* (COMBRETACEAE) ON THE CICATRISATION OF SKIN LEASES IN DIABETIC RATS (*RATTUS NORVENGICUS*)

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Keywords:

Diabetes, *Terminalia ivorensis*, Wound healing

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ABSTRACT: The complication most feared by diabetics remains the diabetic foot, due to the risk of amputation. *Terminalia ivorensis* belongs to the Combrétacée family and is rich in secondary metabolite products. Studies have shown that *Terminalia ivorensis* has antifungal potentiaĺ and is traditionally used to treat wounds . Topical application based on *Terminalia ivorensis* on wounds of rats rendered diabetic showed a rapprochement between the results given by this application and L-mesitran® used as a reference molecule. The aqueous extract at different concentrations (500, 1000 mg/ml) showed significant healing activitý after topical administration in rats.

INTRODUCTION: Diabetes mellitus is a chronic endocrine disease characterised by elevated blood sugar levels (hyperglycaemia) [1]. The disease is the source of many acute and chronic complications. Treatment requires numerous daily constraints, which can have serious repercussions on the quality of life of patients and their families. The seriousness of this disease is linked to its long-term complications, which are a source of disability and impairment of quality of life [2]. According to the WHO, diabetes mellitus is defined as permanent hyperglycaemia with a blood glucose level greater than or equal to 1.26g/l (7mmol/l) after two consecutive intakes or a postprandial blood glucose level greater than or equal to 2g/l (11mmol/l) [3].

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In 2015, the International Diabetes Federation (IDF) estimated that 415 million people worldwide had diabetes. If nothing is done by 2040, the number of diabetics is expected to rise to 642 million. Diabetes is responsible for one death every 7 seconds. In Côte d'Ivoire, diabetes is a major public health problem due to its high prevalence (6.2%), *i.e.* 700,000 people in the population [4]. Diabetes is a condition that predisposes patients to a number of complications. Among these, wounds play an important role, causing suffering, morbidity and mortality [5].

A diabetic wound is a group of mucocutaneous lesions that occur in a diabetic patient. Diabetic wounds are a scourge that frequently lead to work stoppage, professional reclassification and disability, as well as a deterioration in the patient's standard of living and social life. It therefore becomes a real public health problem. In fact, 15-20% of diabetics develop foot ulcers in the course of their lives, and 40% to 80% of these feet become

the breeding ground for various microbes and microscopic fungi. It is estimated that 5-10% of type 1 diabetics will have a toe, foot or leg amputated as a result of infection [6]. Studies carried out at the Treichville University Hospital in Abidjan (Côte d'Ivoire) in 1999 reported that 63.81% of patients hospitalised with limb injuries were diabetics. Of the 63.81% of diabetic patients, 91.43% were amputated for gangrene [7].

As a result, spending on diabetes is huge in Africa and is estimated to account for around 23% of the total health budget [8]. Nearly USD 9.5 billion was spent on diabetes on the African continent in 2019. In Africa, the use of traditional medicine is a common and ancestral practice. More than 75% of the African population have used traditional medicine at least once for healthcare [9]. Plants have been used successfully as wound healing agents [10]. Among the plants used in traditional medicine to treat wounds is *Terminalia ivorensis* (Combretaceae). However, there is no scientific data on its use in the treatment of diabetic wounds.

Terminalia ivorensis (Combrétacée) is a very large tree in the Ivorian forest, easily recognisable by its clearly stepped, horizontally spreading branches and its large cylindrical bole without buttresses at the base [11].

The general aim of this work is to enhance the value of African pharmacopoeia plants (medicinal plants) by studying the healing properties of the aqueous extract from the bark of the trunk of *T. ivorensis*.

MATERIALS:

Biological Material:

Plant Material: The biological material used in this work consisted of bark from *Terminalia ivorensis* (Combrétaceaes), A. Chev. Samples of bark were collected from the trunk of the *Terminalia ivorensis* tree in June 2022 in Abidjan (Côte d'Ivoire) at the Institut Pasteur. A branch of the tree was removed for identification at the Centre National de Floristique (CNF) at the Université Félix Houphouët Boigny in Côte d'Ivoire. The specimen was registered under the following herbarium number N° 4CJ003156.

Animal Material: The animal material used to study astringent activity consisted of wistar rats (*Rattus norvegicus*). A total of thirty-five (35) male and female rats with a body mass of between 137 and 250g were used for the various tests. Nine [9] of the female rats were nulliparous and non-pregnant. The animals were reared in the vivarium of the École Normale Supérieure (ENS). All animals were treated and handled according to the standards of the manuals on the care and use of experimental animals. Their diet consisted of pellets and dried bread. They had access to tap water served in bottles.

Study Methods:

Induction of Diabetes: Experimental induction of diabetes in animal models is essential for the advancement of knowledge and understanding of various aspects of its pathogenesis and ultimately the discovery of new therapies and cure. Animal models of diabetes are therefore very useful and advantageous in biomedical studies because they offer the promise of new insights into human diabetes [12].

After an overnight fast (food deprivation for 16 hours but not water), diabetes was induced in rats by intraperitoneal injection of a freshly prepared solution of Streptozotocin (Sigma ST Lowis, Mo) at a dose of 60 mg/kg body weight or a volume of 2 ml/kg (which destroys β-cells). Streptozotocin is dissolved in NaCl sodium chloride buffer. After 48 hours of injection (time for diabetes to develop), diabetes was confirmed in rats by measuring fasting blood glucose levels using a One call plus glucometer. Only rats with a blood glucose level greater than 2.5 g/l were considered diabetic and retained for this experiment.

Pharmacological Study of the Aqueous Extract of *Terminalia ivorensis* in Wound Healing:

Wound Induction Technique: The pharmacological test was evaluated on a total of 35 rats, divided into seven (07) batches of five (05) rats each.

1. Batch 1: non-diabetic control rats treated with distilled water.
2. Lot 2: diabetic control rats treated with distilled water.
3. Lot 3: diabetic negative control rats treated with L-Mesitran (reference molecule).

4. Batch 4: non-diabetic rats treated with EATi 500 mg/ml pc ointment.
5. Batch 5: non-diabetic rats treated with 1000 mg/ml bw EATi ointment.
6. Batch 6: diabetic rats treated with EATi 500 mg/ml bw ointment.
7. Batch 7: diabetic rats treated with EATi 1000 mg/ml bw ointment.

To create the wounds, the rats were anaesthetised using diethyl ether by inhalation. Once anaesthetised, the rats were placed prone on the bench. Their upper and lower limbs were held in place with transparent tape. The hair on their cervical regions was shaved, taking care to avoid skin lesions. The skin was then disinfected using 70° surgical spirit [1]3. Prior to excision, anaesthesia was assessed by the disappearance of various reflexes, the disappearance of voluntary movements, as well as the disappearance of responses to painful stimulation, such as pinching of the interdigital spaces or at the base of the tail. A template was used to mark the animal's back (made-up circle 2 cm in diameter). Then, on the marked excision site; a deep dermal excision of the skin flap was made [14].

Once the wounds had been made, they were treated according to the group to which each rat belonged. The rats were then placed in an individual cage in a quiet area and allowed to recover from anaesthesia. The wounds were not protected by a dressing on the first day.

Formulation of Ointments: The ointments are formulated from the dry extract of *Terminalia ivorensis* bark (obtained after drying the filtrate in an oven) and distilled water. This mixture was agitated using a shaker to obtain the ointments. Two different concentrations of ointment (500 and 1000 mg/ml) were formulated and selected per batch in order to monitor the progress of wound healing. The ointments were packaged in hermetically sealed 50ml sterile jars and stored in a cool place.

Study of the Curative Effects of Pasty Aqueous Extract on Wounds Induced in Wistar Rats: This study was carried out using the 500 mg/ml and 1000 mg/ml aqueous extracts, prepared under the previously mentioned conditions. The protocol described by [15] was used. A 2 cm diameter circular incision wound was made in the dorso-omoplate region of each ether anaesthetised rat. Four (04) batches (two (02) batches of diabetic rats and two other batches of non-diabetic rats) of five (05) rats each placed in individual cages were respectively treated, by direct topical application, with *Terminalia ivorensis* bark extract at 500mg/ml and 1000mg/ml. Wounds were dressed every two days and wound diameters were measured every four days for the 22 days of treatment using a graduated ruler. All animals were monitored regularly until complete wound healing and had free access to food and water. At 7 and 14 days post-operatively, one (01) rat per batch was randomly selected for macroscopic evaluation of the wound healing process; the criteria used were the presence of a scar or crust, granulation tissue development, progression of epithelialisation and the possible occurrence of infections.

Macroscopic Assessment of Scarring: Generally, wound healing involves a series of changes in the appearance of the wound. Observable changes in physical appearance or wound characteristics have been one of the methods used to assess the healing process [16]. These changes are often associated with wound severity and infection. Macroscopic assessment of wounds (e.g. swelling, redness and exudation from the wound surface), have become parameters in the process of assessing wound healing [17]. In addition to wound diameter, wound contraction is also considered to be part of the macroscopic assessment parameters. Wound contraction is part of the healing process, which ensures wound closure and occurs when the wound edges begin to move towards each other, reducing the size of the wound [16].

Planimetric Study: The planimetric study allows direct quantitative assessment by calculating the wound surface and the percentage of contraction over time [18]. The diameters of excision wounds from different batches are measured [19]. Measurements were taken periodically every four days for 18 days. The surface areas and standard deviations were then averaged and the percentages of contractions were calculated [14].

The surface area and percentage of wound shrinkage or contraction were calculated using the following formula:

$$S= D^2/2^2\times\pi$$

S = wound area; π = 3.14; D = wound diamete

Statistical Analysis: The means of the surface areas, the percentages of contractions and their standard deviations were calculated and analysed using one way ANOVA in GraphPad prism 8.4.3 software.

RESULTS:

Effect of *Terminalia Ivorensis* (Combretaceae) Ointment on Wound Healing:

Variation in Wound Surface Area: The figure shows the evolution of the surface area of the rat wounds over the 22 days of treatment. On the first day, the surface area of the rat wounds was 3.14 ± 0.00 cm² for all batches. However, on day 4, the wound surface areas of diabetic and non-diabetic treated rats decreased significantly ($p<0.01$) compared with control rats **Fig. 1.**

The wound areas of rats from the non-diabetic (ND) group treated with the extract at a concentration of 500 mg/ml were equal to 3.14 ± 0 cm² on day 1, with insignificant differences on day 4 ($p < 0.05$): 2.365 ± 0.177 cm². On days 8, 12 and 16, the differences were highly significant ($p < 0.001$) and were equivalent to 1.771 ± 0.136 cm², 0.9001 ± 0.1151 cm² and 0.2015 ± 0.0454 cm² respectively **Fig. 2.**

Wound surface areas in the non-diabetic (ND) group of rats treated with the 1000 mg/ml extract showed a non-significant decrease on day 4 ($p > 0.05$) to 2.559 ± 0.2905 cm², compared with 3.14 ± 0 cm² on day 1. On days 8, 12, 16 and 20, they were highly significant ($p < 0.0001$): 1.614 ± 0.075 cm², 0.5914 ± 0.0448 cm² and 0.0758 ± 0.0273 cm². The surface area of diabetic wounds treated with 500 mg/ml *T. ivorensis* was 2 ± 0.096 cm² on day 4, with a non-significant decrease ($p > 0.05$). They showed a highly significant decrease on days 8, 12 and 16 with ($p < 0.001$) equivalent to 2.214 ± 0.3749 cm² on day 8, 1.460 ± 0.433 cm² on day 12 and 1.2434 ± 0.138 cm². The surface areas of the diabetic wounds treated with the 1000mg/ml dose were 3.038±0.102 cm² on the first day, with no significant difference ($p > 0.05$) in the variation in wound surface areas. On days 8 and 12, there was a highly significant decrease ($P < 0.001$) of 1.833 ± 0.088 and 1.567 ± 0.133 cm² compared with day 1 (Figure 3). On day 16, the difference was significant ($p < 0.01$) at 0.871 ± 0.241 cm². Thus, the surface areas of the wounds all decreased over time. Finally, L-Mesitran used to treat a batch of rats showed a non-significant difference ($p < 0.05$) of 2.324 ± 0.054 cm² on day 8. On days 12 and 20, there was a significant reduction ($P < 0.01$), 1.628 ± 0.068 and 0.305 ± 0.020 cm², compared with day 1 **Fig. 3.** Finally, on day 16, the difference observed was highly significant ($p < 0.0001$) at 0.831 ± 0.015 cm². In other words, the surface areas of the wounds all decreased over time.

Variation in the Percentage of Contraction: For the control batch, the percentage of contraction evolved progressively in a non-significant manner significantly ($P > 0.05$) from day 4 to day 20. This percentage increased from 3.981 ± 2.094%. On day 4 to 67.29 ± 3.41% on day 20 **Fig. 3**.

In the group of non-diabetic rats treated with 500 mg/ml *T. ivorensis*, the percentage of contractions was highly significant on days 8 and 16. On day 8, this percentage was 43.58 ± 4.331% and on day 16, it was 93.58 ± 1.44%. However, on day 12 it was 71.33±3.66% with a non-significant contraction ($p > 0.05$). Finally, on day 20, there was a considerable increase in the percentage of wound contraction: 100.00± 0.00%.

In the batch of non-diabetic rats treated with a concentration of 1000 mg/ml of *T. ivorensis*, the percentage of contractions was highly significant ($p < 0.0001$) on days 8, 16 and 22. On day 8, this percentage was 48.58 ± 2.417% and 97.58% ± 0.87. On day 12, the percentage became significant ($p < 0.01$) and rose to 81.17 ± 1.417%. On days 16 and 20, there was a considerable increase in the percentage of wound contraction, which was 96.58 ± 0.87% on day 16 and 100.00 ± .00% on day 20 **Fig. 3**. The batch of diabetic rats treated with 500 mg/ml *T. ivorensis* showed a highly significant ($p < 0.0001$) percentage of wound contraction on days 4 and 8. On day 4, this percentage was 31.5±2.23% and on day 8 it was 42.57±2.75%. On day 12, the percentage of contractions was insignificant ($p<0.05$) at 66.23±5.63%.

Furthermore, on days 16 and 20 there was a non-significant ($p > 0.05$) but considerable increase in the percentage of wound contraction: 84.67± 4.66% on day 16 and 96.45± 3.13% on day 20. In the group of rats treated with L-Mesitran, the percentage of wound contraction increased non-significantly from day 4 to day 12 ($p > 0.05$), rising from 10.15 ± 1.35% on day 4 to 46.77 ± 3.39% on day 12. On day 16, the difference was not very significant ($p < 0.05$) and corresponded to 71.21 ± 4.08%. Finally, on day 20 there was no significant difference, except that the percentage of contraction was very high at 89.4 ± 3.87% **Fig. 3.** Thus, the percentage of contraction increased progressively until the wound was completely healed.

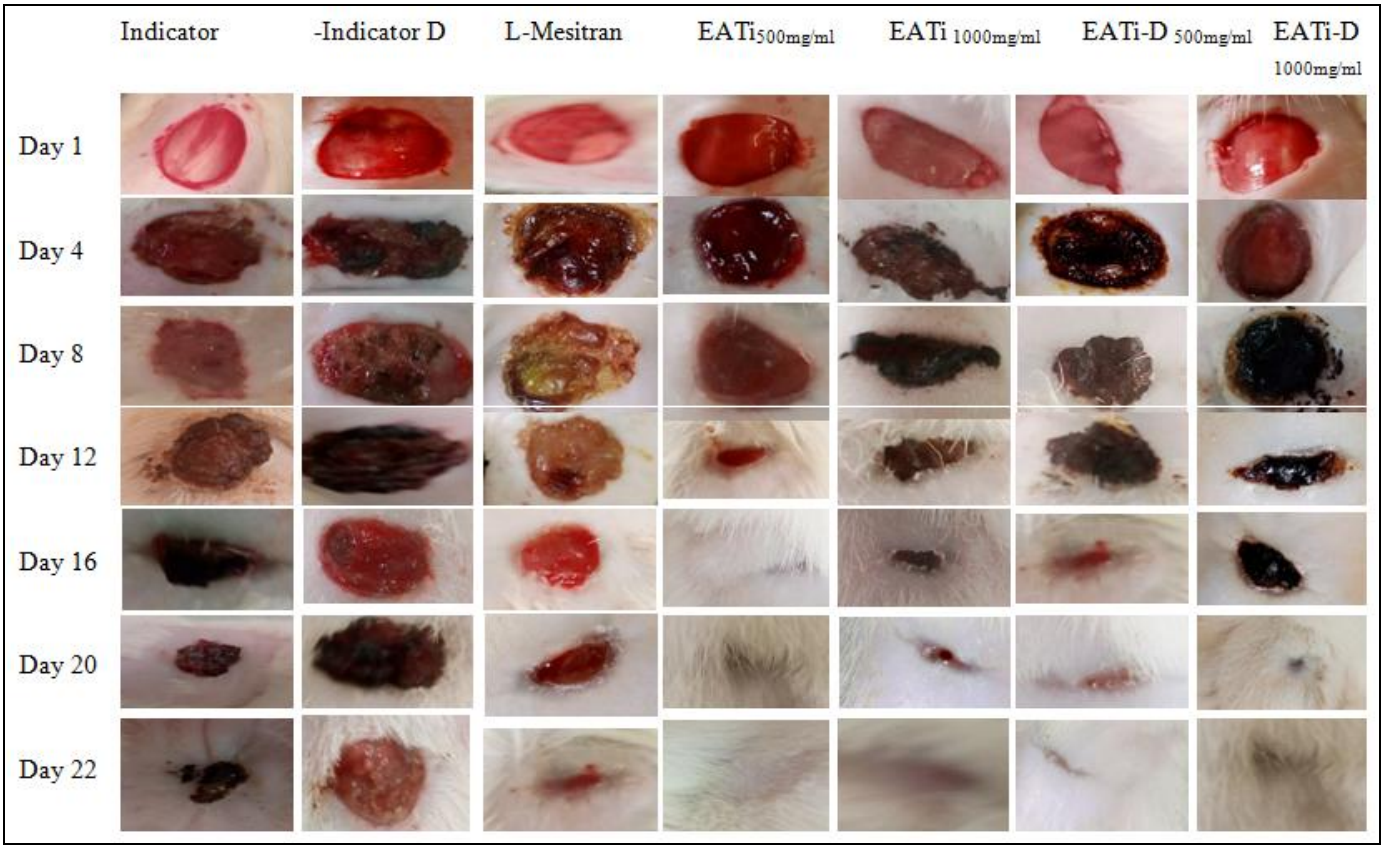

FIG. 1: PHOTOGRAPH SHOWING THE EVOLUTION OF RAT WOUND SURFACES AFTER TOPICAL APPLICATION OF THE AQUEOUS EXTRACT OF *TERMINALIA IVORENSIS* BARK FOR 22 DAYS

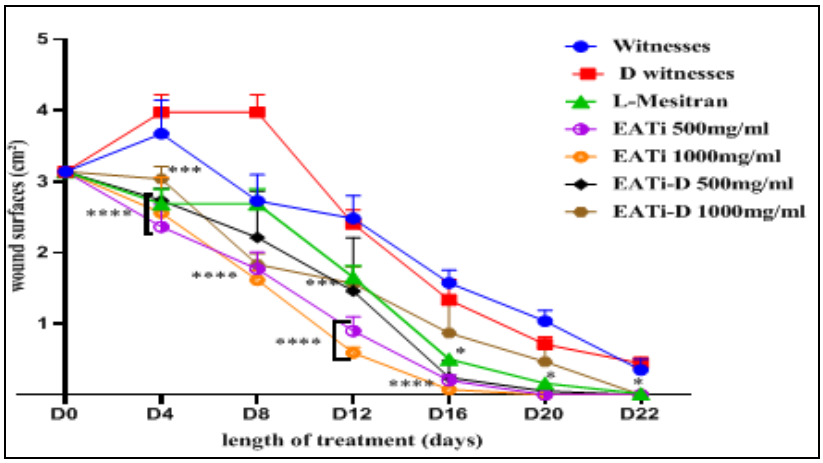

FIG. 2: CHANGES IN THE SURFACE AREA OF RAT WOUNDS AFTER TOPICAL APPLICATION OF THE AQUEOUS EXTRACT OF *TERMINALIA IVORENSIS* BARK FOR 22 DAYS AS A FUNCTION OF TREATMENT. Wound surface retraction was expressed in square centimetres. Results are expressed as mean ± MSE; n= 5 rats per batch. $p > 0.05$: Not significant, *: Indicates $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$; ****: $p < 0.0001$. Comparison between treated batches and controls.

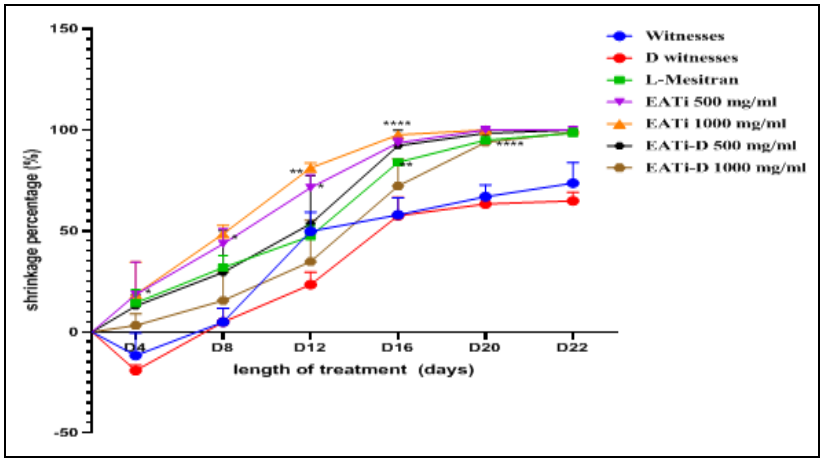

FIG. 3: PERCENTAGE CHANGES IN THE SHRINKAGE OF RAT WOUNDS AFTER TOPICAL APPLICATION OF THE AQUEOUS EXTRACT OF *TERMINALIA IVORENSIS* BARK FOR 22 DAYS. Results are expressed as mean ± MSE; n= 5 rats per batch; Not significant if p>0.05; *: Indicates p<0.05; **: p<0.01; ***: p<0.001; ****: p<0.0001. For treated batches compared with controls.

Assessment of Healing Parameters: The tumour is the first sign that healing has begun, which can be seen clinically in the swelling around the wound. The tumour shows the mobilisation of macrophages. On day 4, the two batches of non-diabetic wounds treated with EATi ointments 500 mg/ml and 1000 mg/ml developed moderate swelling with an average of 1.66±0.33 compared with the batches of negative control rats, both diabetic and non-diabetic, which showed significant swelling with an average of 2.66±0.33. The positive control rats treated with L-Mesitran also showed significant swelling with an average swelling of 2.33±0.33. On day 8, the results showed little swelling in the non-diabetic rats (1.00 ± 0.00) compared with the non-diabetic negative control group and the rats treated with L-Mesitran, which had moderate swelling, whereas the wounds of the diabetic negative control group still showed significant swelling.

There was little swelling in the non-diabetic batches of EATi 500 mg/ml (1.00 ± 0.00) and EATi 1000mg/kg (0.66 ± 0.33) on day 12 and no swelling on day 16. There was also little swelling in the wounds treated with L-Mesitran (1.00 ± 0.00) and in the two batches of diabetic wounds (1.00 ± 0.00) on days 12 and 16. Both diabetic and non-diabetic control wounds showed moderate swelling at days 12 and 16. For the rest of the experiment, swelling was absent in almost all batches except for the controls, which showed little swelling until day 22, with a value of 0.66±0.33 for diabetic wounds and 0.33±0.33 for non-diabetic controls **Table 1.** As for the exudate, there was a progressive evolution of the wounds in the seven (07) batches from day 4 to day 22 of treatment. On days 4 and 12, all batches showed significant exudation, with only the non-diabetic rats treated with EATi 500mg/ml and 1000mg/ml showing little exudation (1.00±0.00). On day 16, there was no exudation in the batches treated with EATi 500 mg/ml and 1000 mg/ml ointments, little exudation in the diabetic batches treated with EATi-D 500 mg/ml and EATi-D 1000 mg/ml and moderate exudation in the control and L-Mesitran batches. On the last day of the experiment, there was an absence of exudate in all batches except the controls, which showed little exudate **Table 2.**

Lastly, a high level of redness was observed in all the wounds of the seven (07) control and treated batches on days 4 and 8. On day 12, there was little redness in all the wounds except those of the control batches, which showed a moderate value (2.00±0.00). At the end of the experiment, there was an absence of redness on almost all the wounds except for the diabetic control wounds **Table 3.**

TABLE 1: ASSESSMENT OF WOUND SWELLING DURING TREATMENT

	Duration of treatment (days)					
Lots	**D4**	**D8**	**D12**	**D16**	**D2O**	**D22**
Witnesses	Important	Moderate	Moderate	Faible	Faible	Absente
D-witnesses	Important	Important	Moderate	Moderate	Low	Low

L-Mesitran	Important	Moderate	Low	Low	Absent	Absent
$EATi_{500mg/ml}$	Moderate	Low	Low\	Absent	Absent	Absent
$EATi_{1000mg/ml}$	Moderate	Low	Low	Absent	Absent	Absent
$D\text{-}EATi_{500mg/ml}$	Important	Moderate	Low	Low	Absent	Absent
$D\text{-}EATi_{1000mg/ml}$	Important	Moderate	Moderate	Low	Absent	Absent

TABLE 2: ASSESSMENT OF WOUND EXUDATION DURING TREATMENT

	Duration of treatment (days)					
Lots	**D4**	**D8**	**D12**	**D16**	**D20**	**D22**
Witnesses	Important	Important	Important	Low	Low	Low
D-witnesses	Important	Important	Important	Moderate	Moderate	Low
L-Mesitran	Important	Important	Moderate	Low	Absent	Absent
$EATi_{500mg/ml}$	Moderate	Moderate	Low	Absent	Absent	Absent
$EATi_{1000mg/ml}$	Important	Low	Low	Absent	Absent	Absent
$D\text{-}EATi_{500mg/ml}$	Important	Important	Low	Low	Absent	Absent
$D\text{-}EATi_{1000mg/ml}$	Important	Important	Moderate	Low	Absent	Absent

TABLE 3: ASSESSMENT OF WOUND REDNESS DURING TREATMENT

	Duration of treatment (days)					
Lots	**D4**	**D8**	**D12**	**D16**	**D20**	**D22**
Witnesses	Important	Important	Important	Low	Low	Absent
D-witnesses	Important	Important	Important	Moderate	Moderate	Low
L-Mesitran	Important	Important	Moderate	Absent	Low	Absent
$EATi_{500mg/ml}$	Important	Important	Low	Absent	Absent	Absent
$EATi_{1000mg/ml}$	Important	Important	Moderate	Absent	Absent	Absent
$D\text{-}EATi_{500mg/ml}$	Important	Important	Low	Low	Absent	Absent
$D\text{-}EATi_{1000mg/ml}$	Important	Important	Moderate	Low	Absent	Absent

Effect of *Terminalia ivorensis* ETA on Organ Weight: The results of relative organ weights are reported in **Table 4.** The results obtained revealed no significant changes in organ weights between the different batches of rats with a ($p > 0.05$). This table shows the effect of the aqueous extract of *Terminalia ivorensis* bark on the relative organ weights in percentages (%), namely heart, liver, lung, kidney and spleen, of rats exposed to the different doses compared with the control. The relative weights of the various organs were approximately equal in all batches.

TABLE 4: RELATIVE ORGAN WEIGHTS

	Relative weight of organs						
Lots	**Témoin**	**D-Témoin**	**L-Mésitran**	**$EATi_{500mg/ml}$**	**$EATi_{1000mg/ml}$**	**$D\text{-}EATi_{500mg/ml}$**	**$D\text{-}EATi_{1000mg/ml}$**
Heart	0,39±0,03	0,350,02	0,34±0,03	0,36±0,01	0,36±0,01	0,32±0,01	0,37±0,02
Liver	4,51±0,23	4,07±0,23	3,98±0,19	4,66±0,47	5,54±0,25	4,79±0,10	5,02±0,41
Lung	0,67±0,06	0,85±0,08	0,93±0,04	0,78±0,08	1,20±0,22	0,69±0,10	0,92±0,14
Spleen	0,42±0,02	0,48±0,05	0,59±0,13	0,37±0,03	0,45±0,16	0,53±0,16	0,45±0,12
Kidney	0,74±0,59	0,71±0,06	0,72±0,04	0,66±0,01	0,77±0,19	0,89±0,08	1,00±0,09
Thymus	0,14±0,66	0,13±0,01	0,12±0,01	0,17±0,02	0,16±0,03	0,14±0,01	0,13±0,03

DISCUSSION: Topical application of concentrations of *T. ivorensis* bark extract did not cause irritation of healthy skin. These topically applied ointments inhibited erythema, exudate and unpleasant odours fairly rapidly. Taken together, these phenomena explain the increase in the speed and time taken for healing to occur. The work of [20] also reports that the acceleration of the scarring process may be linked to the anti-inflammatory power through the formation of complexes that neutralise numerous irritating agents. As for the reduction in wound surface area, the batches that received the plant-based treatment, more specifically the batches with the concentrations (500 mg/ml and 1000 mg/ml) had smaller surface areas than the control batches and the L-Mesitrant batch. According to [21], the planimetric study therefore provides a direct quantitative assessment by calculating the surface area of the wound, its evolution over time and, by deduction, an assessment of the quality of the granulation tissue. Assessment of the macroscopic appearance of wounds, which appear less inflamed as the days progress, suggests that the plant is capable of

modulating the inflammatory response. As for the rate of wound contraction, the wounds treated with our plants showed a better evolution with significant values on day 16 with a $P<0.05$. By day 22, they had contracted by 64.88% for the control batches, 64.88% for the diabetic control, 98.03% for the batch treated with L-mesitran, 100% for the batches treated with 500 mg/ml aqueous extract for both diabetics and non-diabetics, 98.87% for the 1000 mg/ml diabetic batch and 100% for the non-diabetic batch treated with 1000 mg/ml *Terminalia ivorensis*.

This rate of contraction could be explained by the presence of myofibroblasts, of which the 500 mg/ml batch appears to be the most abundant, results which are in agreement with those of [22, 18] report that contraction is due to the transformation of certain fibroblasts into myofibroblasts capable of contracting. Visible wound contraction is evident 5 to 9 days after injury. The healing activity of our plant may also be linked to its antioxidant activity, which destroys free radicals in the wound. This high antioxidant activity is linked to the various components, mainly polyphenols and tannins. L-Mesitran, which is used to treat wounds, contains several components and bioactive substances, but this medicine is only effective on smaller wounds and may trigger local allergic reactions and contact eczema during treatment, due to certain components, which may disrupt the healing process. Wounds treated with the plant showed better healing than those treated with L-Mesitran and control wounds.

The results revealed significant differences between the wound healing parameters (tumour, exudate and redness) observed in the different batches of treated and control rats on days 4 and 8 of treatment. The presence of tumours was also non-significant, meaning that there was no excessive multiplication of benign or malignant tumour cells in the wounds. It was also found that the number of fibroblasts in the wounds of batches treated with the aqueous extract of *Terminalia ivorensis* bark was significantly higher than in the other two batches. This means that the plant promotes fibroblasty [23]. This increase in collagen-producing fibroblasts is thought to promote good quality scarring. This explains the high presence of exudate, redness and dead tissue in wounds. It should also be noted that the wounds of the diabetic rats treated with distilled water gave off a slight nauseating odour, due to the bacteria that reside in necrotic tissue, which means that the wounds of the control batches were infected. However, this was not the case for the batches of rats treated with L-Mesitran or *Terminalia ivorensis* ointment.

CONCLUSION: It emerges that the plants have an obvious healing activity completely in accordance with the effectivenesś which is recognized to them in traditional medicine and would act in synergy . This healing activitý can be explaine d by the presence of secondary metabolites such as polyphenols and sterols, which are rich in anti-inflammatory, antibacterial and antioxidant properties.

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CONFLICT OF INTEREST: Nil

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