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ANTINOCICEPTIVE EFFECTS OF *TRECULIA AFRICANA* DECNE (AFRICAN BREADFRUIT) SEED LECTIN IN WISTAR RATS

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The aim. *The use of synthetic compounds to treat many diseases must be strictly controlled due to their potential health hazards. Hence, there is a need to search for natural products to serve as safe alternatives to synthetic products. This study investigated the antinociceptive effects and anti-inflammatory activities of Treculia africana seed lectin.*
Materials and methods. *Lectins were purified from Treculia africana seeds using ion exchange and size-exclusion chromatography. The antinociceptive activity of the lectin was assessed in Wistar rats using abdominal writhing and paw-licking tests induced by acetic acid and formalin, respectively. Anti-inflammatory activity was assessed using carrageenan-induced paw oedema.*
Results*. Treculia africana seed lectins at 10 mg/kg (p.o.) produced sedation, reduced ambulation, reduced response to touch, analgesia, and decreased defecation in experimental animals. Administration of Treculia africana seed lectin (1 mg/kg and 10 mg/kg) in experimental animals significantly reduced (P<0.05) acetic acid-induced muscular writhing in a dose-dependent manner with 23.88 and 36.80 per cent inhibition, respectively. Both early and late phases of formalin-induced nociception were significantly inhibited (P<0.001) by the lectin at all doses (0.1, 1.0 and 10.0 mg/kg), comparably with the standard drug, diclofenac sodium. At 10 mg/kg, T. africana lectin caused a 69.12 % and 65.55 % reduction in both early and late phases of formalin-induced paw licking. Treculia africana lectin also significantly brought about a reduction (P<0.05) in inflammation induced by sub-plantar injection of carrageenan as measured by a decrease in paw swollenness.*
Conclusion. *The study showed that Treculia africana lectin possesses antinociceptive and anti-inflammatory properties and can potentially be employed therapeutics to ameliorate pain and inflammation.*
Keywords*: hemagglutinin, agglutinin, analgesic activity, pain-relieving lectin, inflammation, Moraceae*

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1. Introduction

Lectins are a heterogeneous group of (glyco)proteins that bind reversibly and specifically to glyco-moieties with several biological properties such as insecticidal [1, 2], antinociceptive, anti-inflammatory [3], antiviral [4], antifungal, antibacterial, antiproliferative [5, 6], anthelmintic [7, 8], and mitogenic [9] activities. The stability or biological activities of most of these proteins remain stable, even when subjected to harsh conditions, and are therefore considered strong candidates for therapeutic use [10].

Pain serves physiological functions, including notification of hazardous stimuli [11]. Pain response is necessary for tissue healing and regeneration [11]. In his hypothesis, Omoigui [12] summarised that all pain originates from inflammation and associated response. Inflammation is a defensive process in animal cells that usually occurs in response to injuries or pathogenic infections [13]. Inflammatory response usually results in tissue repair; however, a prolonged inflammatory process may result in chronic diseases and organ damage [13, 14].

Anti-inflammatory agents are essential in controlling inflammation and limiting its course. These agents work by inhibiting the overproduction of mediators of inflammation, especially pro-inflammatory cytokines, inducible nitric acid synthase (NOS) activity and cyclooxygenase (COX)-2. Anti-inflammatory drugs also act by inhibiting protein kinase C and mitogen-activated protein kinase by altering the DNA-binding capacities of transcription factors [15]. Due to the adverse effects of synthetic anti-inflammatory drugs caused by prolonged usage, the search for anti-inflammatory agents from natural sources is of paramount interest. Plant lectins are recently being explored in the study of inflammation, and they have been discovered to act either as an anti-inflammatory or pro-inflammatory agent [14].

Treculia africana Decne, commonly known as African breadfruit, wild jackfruit and African boxwood, belong to Moraceae. It is commonly consumed as food and used for ethnomedicinal purposes in many countries in the tropics, such as West African countries, West Indies and Jamaica [16, 17]. In folk medicine, different parts of the *T. africana* plant are used to treat/manage various ailments such as diabetes, fever, helminth infections, indigestion, rheumatism, leprosy, whopping cough and malaria and swellings [18, 19].

Earlier, Adeniran et al. [17] and Adeniran [20] purified the lectin from the seeds of the *T. africana* plant

and investigated its physicochemical properties and toxicity in experimental rats. Shimokawa et al. [21] also described the purification of two jacalin-related lectins from the seeds. In 2010, Aderibigbe and Agboola [22] reported that the ethanolic extracts of *T. africana* stem bark had analgesic properties.

It is important to study and investigate the therapeutic properties of some of the active components of this plant in order to understand which ones the identified properties could be attributed to. This would aid future research into drug development and formulations. Thus, the present study aims to evaluate the unexplored antinociceptive and anti-inflammatory properties of *T. africana* seed lectin in experimental Wistar rat models of nociception and inflammation.

2. Planning (methodology) of research

The studied plant is highly regarded in traditional medicine due to its many health benefits, amongst which is to manage persons with pain and inflammation. Research has shown that different *T. africana* extracts are associated with various therapeutic properties. The protein lectin has been shown to possess many bioactivities. This study is intended to establish that the lectin isolated from this plant has analgesic properties.

Fig. 1 shows the graphical methodology followed for the research.

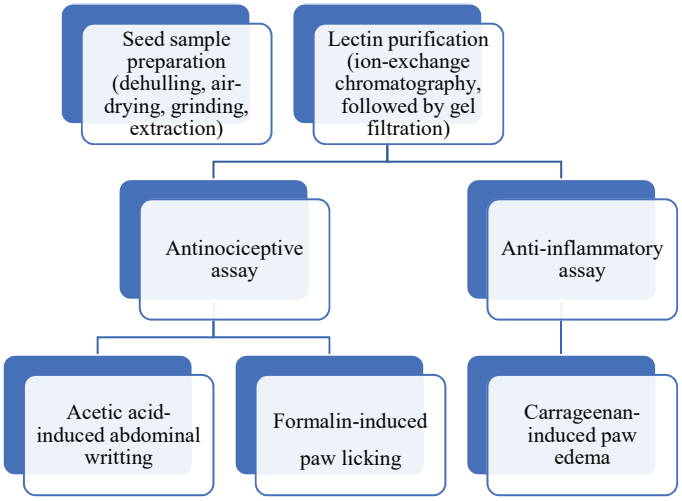

Fig. 1. General approaches in the planning of the research

3. Materials and Methods

3. 1. Materials

Bovine serum albumin (BSA), Sephadex G-100, DEAE-cellulose, and Folin-Ciocalteu's phenol reagent and the enzymes used for hydrolysis were obtained from Sigma Aldrich (St. Louis, MO, USA). All other reagents, which were of analytical grade, were purchased from Loba Chemie (Mumbai, India).

3. 2. Sample collection and preparation

Treculia africana fruits were purchased from Oja-Oba Market, Ado-Ekiti, Nigeria. The plant was identified and authenticated by a taxonomist at the Department of Plant Science, Ekiti-State University. A copy of the plant sample was deposited in the departmental herbarium, and a voucher number UHAE2018076 was obtained. The seeds were removed, air-dried, ground to a fine powder and kept at four degrees Celsius until further use.

3. 3. Experimental animals

Healthy adult Wistar rats of both genders weighing between 50–70 g were used for this study. The animals were procured from the animal house of Afe Babalola University, Ado-Ekiti and acclimatized for 14 days in a laboratory environment of 12 h light/dark phase. The rats were allowed free access to standard rat pellets and water *ad libitum.* They were grouped into five of five animals each and maintained at room temperature. Animals were subjected to an overnight fast before each experiment. This research was approved by Afe Babalola University's Animal Ethical Committee, Ado-Ekiti, Nigeria and assigned approval number: 17SCI031002. The ethical standards of experiments were in accordance with ARRIVE guidelines and conducted in accordance with the EU Directive 2010/63/EU on protecting laboratory animals.

The study was carried out between 2018 and 2019.

3. 4. Lectin purification

Ground *Treculia africana* seeds were defatted with petroleum ether. The crude extract was obtained by suspending defatted *T. africana* seed powder in phosphate-buffered saline (PBS) (10 %, w/v) and stirring for three hours. The mixture was kept overnight at four degrees Celsius and centrifuged at 4000 rpm for 20 min. The lectin was obtained by purifying the crude extract on a DEAE-cellulose column, followed by purification on a Sephadex G-100 column, as earlier described by Adeniran et al. [17], followed by lyophilization. Protein concentration was determined using the Lowry method described by Olson and Markwell [23] with 1 mg/ml bovine serum albumin (BSA) as standard.

3. 5. Behavioural screening

This was used to detect the possible effects of *T. africana* lectin on the central nervous system of the study animals. Specific behaviours (sedation, ambulation, response to touch, analgesia, and defecation) were observed. Rats were treated with a single dose of saline (10 mL/kg, *p.o*) or the lectin isolated from *T. africana* seeds at doses (*p.o*) of 0.1, 1.0 and 10 mg/kg (normal saline was used as a vehicle for the animal study). Animals were observed for 4 h, and their behaviour was recorded at 30, 60, 120, 180, and 240 min after treatment.

3. 6. Antinociceptive activity

Acetic acid-induced writhing test

The acetic acid-induced abdominal writhing test was done according to the method described by Fonsêca et al. [24] and Ajayi et al. [25] with slight modifications. Experimental rats were pretreated orally (p.o) with normal saline (0.9 %), graded doses of *T. africana* lectin (0.1, 1.0 and 10 mg/kg) or diclofenac sodium (10 mg/kg). This was followed by the administration of acetic acid (0.85 %, 0.25 ml) by intraperitoneal (*i.p.*) route to induce abdominal constrictions 60 min after. The number of

writhing/muscular contractions (which includes the extension of lower limbs and elongation of the body) was counted for 15 min after injection.

Formalin-induced paw-licking test.

Formalin-induced paw-licking test in rats was done using a slightly modified method of Hunskaar and Hole [26]. Experimental Wistar rats were pretreated with *T. africana* seed lectin (0.1, 1.0 and 10 mg/kg, *p.o*), diclofenac sodium or vehicle (normal saline). The pain was induced in the rats after 30 min by administering formalin (2.5 %, 20 µL) under the skin of the dorsal surface of the right hind paw. Paw licking frequency was counted 0–5 min after administration of formalin (neurogenic phase) and 15–30 min after formalin (inflammatory phase) administration.

3. 7. Anti-inflammatory activity

The anti-inflammatory activity of *T. africana* lectin was assessed using the carrageenan-induced paw oedema model, which was determined by injecting 0.1 mL of 1 % carrageenan suspension into the sub-plantar region of the left hind paw of the rats to induce oedema 60 min after pre-treatment with varying concentrations of *T. africana* lectin (0.1 mg/kg, 1.0 mg/kg and 10 mg/kg, *p.o*), vehicle (3 mL/kg), or diclofenac sodium (10 mg/kg) as described by Oladokun et al. [27]. The sub-plantar region of the paw was measured before and at 2 and 5 h after induction of oedema using a micrometre screw gauge. An increase in paw thickness was measured by taking the difference in paw before induction of inflammation and at the respective experimental hours. Percentage inhibition of inflammation was calculated as (1)

$$\text{Percentage inhibition (\%)} = \frac{\left(V_f - V_i\right)\text{control group mean} - \left(V_f - V_i\right)\text{test group mean}}{\left(V_f - V_i\right)\text{control group mean}} \times 100, \quad (1)$$

where V_i and V_f represent initial and final paw thickness, respectively.

3. 8. Statistical analysis

Results were expressed as mean ± standard deviation. Statistical significance of differences (set at $P<0.05$) among groups were analyzed using one-way analysis of variance (ANOVA) followed by Tukey post-hoc test. Data analysis was done using Graph pad statistical package (Prism 5).

4. Results

4. 1. Purification of *Treculia africana* lectin

A mannose-binding lectin, which agglutinated human blood groups A, B and O non-specifically, was purified from *Treculia africana* seeds by ion-exchange chromatography followed by gel filtration chromatography (Fig. 2, a, b).

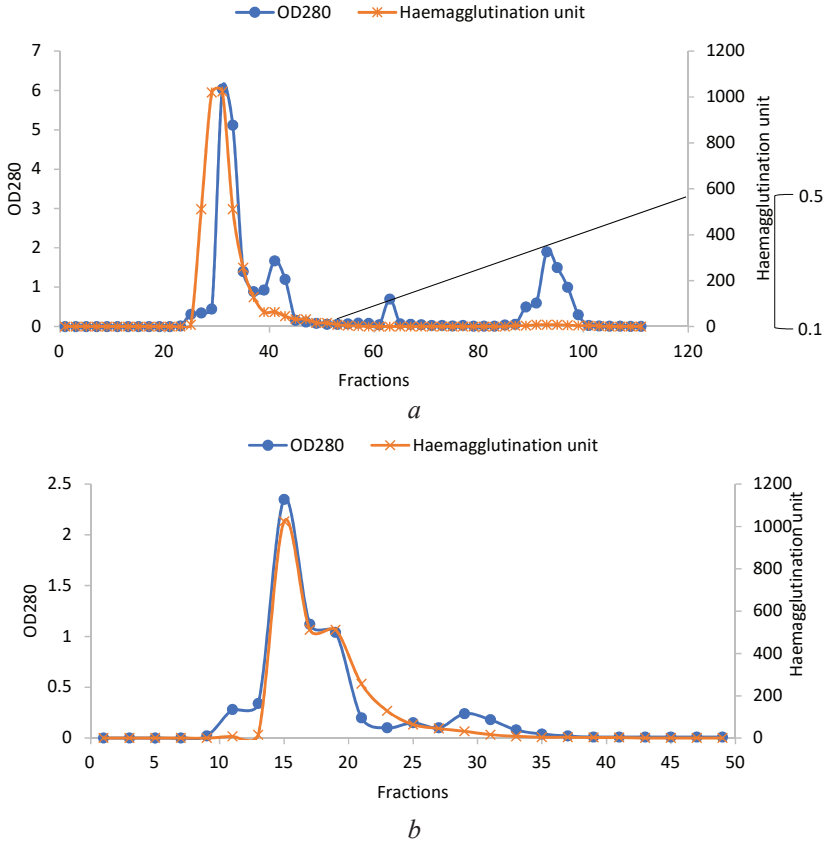

Fig. 2. Column chromatography profile of *Treculia africana* seed lectin: *a* – Ion-exchange chromatography of *T. africana* seed crude extract on DEAE-cellulose column (elution buffer: 0.025 PBS, pH 7.2. Adsorbed protein was eluted with a linear gradient of 0.1 – 0.5 M NaCl in phosphate-buffered saline; column size: 1.6×40 cm; flow rate: 24 ml/h; fraction volume: 2 ml); *b* – Gel filtration of pooled fractions from ion-exchange on Sephadex G-100 (elution buffer: 0.025 PBS; column size: 1.5×63 cm; flow rate: 20 ml/h; fraction volume: 4 ml)

4. 2. Behavioural results on oral administration of *Treculia africana* seed lectin

Lectin isolated from *Treculia africana* seeds at a dose of 10 mg/kg (p.o.) produced sedation, reduced ambulation, reduced response to touch, analgesia, and a decrease in defecation. However, at doses of 0.1 mg/kg and 1.0 mg/kg, no observable effects on motor coordination were recorded. Thus, the highest dose of *Treculia africana* seed lectin indicated depressive activity in the central nervous system.

4. 3. Acetic acid-induced muscular writhing

Treculia africana seed lectin (0.1, 1.0 and 10.0 mg/kg) administration (*p.o*) produced a significant and dose-dependent inhibition of acetic acid-induced muscular writhing compared to rats in the control group (5.66 %, 23.38 % and 36.80 %, respectively). However, inhibition of writhing response in experimental rats by the standard drug diclofenac sodium at 10 mg/kg was significantly higher (P<0.05) than those produced by *T. africana* lectin at 0.1 and 1.0 mg/kg but not significantly different from the response elicited at 10 mg/kg of lectin (Table 1).

Table 1

Antinociceptive activity of *Treculia Africana* seed lectin as evaluated by acetic acid-induced writhing test

Group	Number of muscular contractions	% inhibition
Negative control (10 ml/kg normal saline)+0.25 ml of 0.85 % acetic acid	35.33±2.08	–
Diclofenac sodium (10 mg/kg)+0.25 ml of 0.85 % acetic acid	15.45±1.53***	56.26
Lectin (0.1 mg/kg)+0.25 ml of 0.85 % acetic acid	33.33±5.49	5.66
Lectin (1 mg/kg)+0.25 ml of 0.85 % acetic acid	27.07±3.27*	23.38
Lectin (10 mg/kg)+0.25 ml of 0.85 % acetic acid	22.33±4.53***	36.80

*Note: values are expressed as mean ± standard deviation (SD), n=5. A significant difference in comparison to the negative control group: ***p < 0.0001, *p < 0.05*

4. 4. Formalin–induced paw licking

Injection of formalin into the paw of rats caused an increase in the number of times spent paw licking in the two phases of formalin-induced nociception (early phase: 22.67±2.52 and late phase: 80.33±5.01). However, administration of *T. africana* seed lectin caused a significant reduction in time spent licking formalin-injected paw in both phases (Table 2) (P<0.0001). At 10 mg/kg, *T. africana* lectin caused a reduction in paw licking by 69.12 % and 65.55 % in the early and late phases, respectively which was not significantly different from the response elicited by diclofenac sodium.

Table 2

Antinociceptive activity of the lectin isolated from *Treculia Africana* seeds evaluated by formalin – induced paw licking test in rats

Group	Early phase (0–5 min)		Late phase (15–45 mins)	
	No of paw licking	% Inhibition	No of paw licking	% Inhibition
Negative control (10 ml normal saline/kg)+20 µl of 25 % formalin	22.67±2.52	–	80.33±5.01	–
Diclofeanac sodium (10 mg/kg)+20 µl of 25 % formalin	7.00±1.00***	69.12	23.00±1.31***	71.37
Lectin (0.1 mg/kg)+20 µl of 25 % formalin	15.67±1.53***	30.88	49.67±2.08***	38.17
Lectin (1.0 mg/kg)+20 µl of 25 % formalin	17.00±2.00***	25.01	37.33±5.03***	53.53
Lectin (10 mg/kg)+20 µl of 25 % formalin	7.00±0.58***	69.12	27.67±2.08***	65.55

*Note: Values are expressed as mean ± standard deviation (SD), n=5. A significant difference in comparison to the negative control group: ***p<0.0001*

4. 5. Anti-inflammatory activity of *Treculia africana* seed lectin

Carrageenan-induced rat paw oedema was markedly inhibited by oral pre-treatment with *T. africana* seed lectin or diclofenac sodium (P<0.0001). At 3 h after induction of paw oedema and treatment, *T. africana* lectin (10 mg/kg) significantly inhibited paw swollenness, even higher than diclofenac sodium (77.53 %) (Fig. 3). At the later phase of response, i.e., at 5 h, inhibition caused by diclofenac sodium was significantly higher than all doses of *T. africana* lectin (64.91–70.13 %).

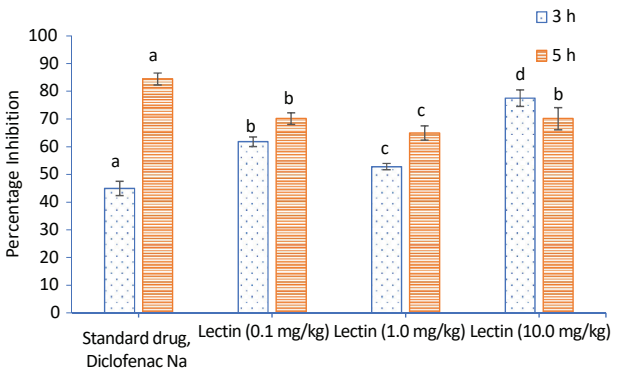

Fig. 3. Anti-inflammatory activity of *Treculia africana* seed lectin in carrageenan-induced paw oedema test. Percentage inhibition was calculated in reference to the control group (treated with normal saline). Values are expressed as mean±standard deviation (SD), n=5. Values with different superscripts along the column are significantly different (p<0.05)

5. Discussion

Pain can be said to be an uncomfortable feeling triggered by disease or injury. Pain has three elements:

1. Nociception, that is, activation of heat, pressure or chemical stimuli (all termed noxious stimuli) receptors, which in turn initiate a signal that is transmitted to the brain.

2. The feeling of the pain.

3. Behavioural changes in response to the pain.

The primary goal of pain management is blockage of the inbound signals before they can elicit their effects [28]. Even though conventional pharmacological therapies for pain are generally effective, they produce intolerable side effects such as gastrointestinal effects, kidney dysfunction, hypertension aggravation and deterioration of joints, and unwanted interactions with other drugs, hence the search for alternative approaches [29, 30]. Pain control hinders detrimental outcomes such as muscular, gastrointestinal and cardiovascular alterations [31, 32]. The abilities of any pain relieving agent to express their activities depend on the type of noxious stimuli used to elicit pain [33].

Naturally occurring bioactive agents, such as lectins, are reliable and have been an abundant resource for drug development. Lectins are ubiquitous and information mediators. Several lectins have been shown to play an essential role in pain and inflammation [30]; thus, the isolation, purification and exploration of medicinal properties of lectins from various sources, particularly plants, cannot be overemphasized.

Induction of abdominal writhing by acetic acid is a standard and simple test for assessing anti-nociception, particularly the nonspecific pain-relieving activity of a product [3, 34]. Acetic acid stimulates visceral and somatic nociceptive neurons by releasing endogenous chemo-sensitive inflammatory mediators such as prostaglandins and cytokines, causing an increase in peritoneal fluid, thereby contributing to the occurrence of nociception of inflammatory origin [3, 34–36]. The antinociceptive activity shown by *T. africana* seed lectin may be due to the inhibition of these endogenous mediators in a similar manner to *Canavalia grandiflora* seed lectin [37] and *Bauhinia monandra* leaf lectin [3], which brought about a significant reduction in acetic acid-induced writhing. The neurotransmitter glutamate level is increased in the spine, and the antinociceptive effect of *Treculia africana* lectin could be possibly due to a reduc-tion in the level of this excitatory amino acid in the cere-brospinal fluid [38].

Formalin-induced paw licking test, because of the two phases involved (neurogenic and inflammatory phase), is usually performed to differentiate between central and peripheral actions [24, 26]. Formalin acts by directly exciting sensory neurons, resulting in the opening of TRPA1 (transient receptor potential ion channel-1), a mediator of inflammatory pain [39]. The first phase of inhibition indicates the blocking of direct nerve stimulation. In contrast, second-phase inhibition, dependent on the release of mediators from damaged cells that stimulate peripheral nociceptors, indicates anti-inflammatory activity [25]. It has been reported that drugs/compounds that inhibit nociception in both phases of formalin-induced test act on the central and peripheral nervous system, while drugs that act only in the second phase are peripherally acting drugs [26, 40]. *Treculia africana* seed lectin, as revealed in the study, reduced the paw-licking time at both phases. This shows that *T. africana* seed lectin can act on and alleviate both neuropathic pain and inflammatory processes and thus possess both antinociceptive and anti-inflammatory properties.

Due to the carbohydrate-binding affinities of lectins, they can exert their medicinal applications through lectin domain interaction [41]. Lectins could bind and block carbohydrate moieties on leukocytes, cause a reduction in intercellular adhesion molecule-1 expression, and prevent leukocytes from rolling and binding to the surface of endothelial cells, thus inhibiting the inflammatory process [30]. Lectins can also act by inhibiting pro-inflammatory cytokines. Since there is a direct relationship between inflammation and pain development, the antinociceptive effects of *T. africana* lectin may be directly linked to the reduction of inflammation.

Carrageenan-induced paw oedema is a standard model for investigating the anti-inflammatory properties of pharmaceutical products. The extent of inflammation and pain in this model is majorly contributed by an increase in prostaglandin-E2 production, mediated by COX-2 in the central nervous system [3]. The anti-inflammatory potential of *T. africana* seed lectin may be a result of the inhibitory effect of the lectin on the release of inflammatory mediators. Several lectins have shown similar anti-inflammatory properties as *T. africana* seed lectin on carrageenan-induced paw oedema, such as *Bauhinia monandra* leaf lectin (60 mg/kg, 60.5 % inhibition) [3], *Tetracarpidium conophorum* seed lectin (12 mg/kg, 62–79 % inhibition) [27], and *Bryothamnion triquetrum* lectin (10 mg/kg, 73.52–96.51 %) [42].

To establish the underlying mechanism of the anti-inflammatory effects of *Treculia africana* lectin, there is a need for further investigations using several models of inflammation, immunohistology and gene expression.

Limitations of the study. Even though the molecular weight of *Treculia africana* lectin has been determined in earlier studies, it would have been appropriate to compare the molecular weight of the lectin purified in this study with the earlier one.

Prospects for further research This study established that *Treculia africana* lectin has analgesic (in formalin-induced paw licking and acetic acid-induced muscular writhing models of nociception) and anti-inflammatory (in carrageenan-induced paw oedema model) potentials. However, there is a need to investigate the interaction of *Treculia africana* seed lectin in several other models of nociception and inflammation and establish its mechanism of action.

6. Conclusion

From the results of this study, *Treculia africana* lectin is shown to be an effective protein in inhibiting/

reducing nociception both centrally and peripherally and inflammation in acetic acid-induced muscular writhing, formalin-induced paw licking and carrageenan-induced paw oedema models of nociception and inflammation. The inhibition of nociception and inflammation by the lectin compared favourably with the standard drug, diclofenac sodium. This could explain the use of *T. africana* in folk medicine. This study presented experimental corroboration for the efficacy of the use of the plant in managing diseases linked with pain and inflammation traditionally. *T. africana* lectin could thus be used as potential therapeutics in the management of nociception and inflammation.

Conflict of interest

The authors declare that they have no conflict of interest in relation to this research, whether financial, personal, authorship or otherwise, that could affect the research and its results presented in this paper.

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References

1. Pohleven, J., Brzin, J., Vrabec, L., Leonardi, A., Čokl, A., Štrukelj, B. et al. (2011). Basidiomycete Clitocybe nebularis is rich in lectins with insecticidal activities. Applied Microbiology and Biotechnology, 91 (4), 1141–1148. doi: https://doi.org/10.1007/s00253-011-3236-0

2. Kehinde, A. A., Oludele, O. O., Adenike, K., Mosudi, B. S. (2016). Anti-insect potential of a lectin from the tuber, Dioscorea mangenotiana towards Eldana saccharina (Lepidoptera: Pyralidae). Journal of Agricultural Biotechnology and Sustainable Development, 8 (3), 16–26. doi: https://doi.org/10.5897/jabsd2015.0249

3. Campos, J. K. L., Araújo, C. S. F., Araújo, T. F. S., Santos, A. F. S., Teixeira, J. A., Lima, V. L. M., Coelho, L. C. B. B. (2016). Anti-inflammatory and antinociceptive activities of Bauhinia monandra leaf lectin. Biochimie Open, 2, 62–68. doi: https://doi.org/10.1016/j.biopen.2016.03.001

4. Gondim, A. C. S., Roberta da Silva, S., Mathys, L., Noppen, S., Liekens, S., Holanda Sampaio, A. et al. (2019). Potent antiviral activity of carbohydrate-specific algal and leguminous lectins from the Brazilian biodiversity. MedChemComm, 10 (3), 390–398. doi: https://doi.org/10.1039/c8md00508g

5. Liao, W.-R., Lin, J.-Y., Shieh, W.-Y., Jeng, W.-L., Huang, R. (2003). Antibiotic activity of lectins from marine algae against marine vibrios. Journal of Industrial Microbiology and Biotechnology, 30 (7), 433–439. doi: https://doi.org/10.1007/s10295-003-0068-7

6. Gautam, A. K., Gupta, N., Narvekar, D. T., Bhadkariya, R., Bhagyawant, S. S. (2018). Characterization of chickpea (Cicer arietinum L.) lectin for biological activity. Physiology and Molecular Biology of Plants, 24 (3), 389–397. doi: https://doi.org/10.1007/s12298-018-0508-5

7. de Medeiros, M. L. S., de Moura, M. C., Napoleão, T. H., Paiva, P. M. G., Coelho, L. C. B. B., Bezerra, A. C. D. S., da Silva, M. D. C. (2018). Nematicidal activity of a water soluble lectin from seeds of Moringa oleifera. International Journal of Biological Macromolecules, 108, 782–789. doi: https://doi.org/10.1016/j.ijbiomac.2017.10.167

8. Batista, K. L. R., Silva, C. R., Santos, V. F., Silva, R. C., Roma, R. R., Santos, A. L. E. et al. (2018). Structural analysis and anthelmintic activity of Canavalia brasiliensis lectin reveal molecular correlation between the carbohydrate recognition domain and glycans of Haemonchus contortus. Molecular and Biochemical Parasitology, 225, 67–72. doi: https://doi.org/10.1016/j.molbiopara.2018.09.002

9. Singh, R. S., Walia, A. K., Kennedy, J. F. (2019). Purification and characterization of a heterodimeric mycelial lectin from Penicillium proteolyticum with potent mitogenic activity. International Journal of Biological Macromolecules, 128, 124–131. doi: https://doi.org/10.1016/j.ijbiomac.2019.01.103

10. Coelho, L. C. B. B., Silva, P. M. dos S., Lima, V. L. de M., Pontual, E. V., Paiva, P. M. G. et al. (2017). Lectins, Interconnecting Proteins with Biotechnological/Pharmacological and Therapeutic Applications. Evidence-Based Complementary and Alternative Medicine, 2017, 1–22. doi: https://doi.org/10.1155/2017/1594074

11. White, F. A., Bhangoo, S. K., Miller, R. J. (2005). Chemokines: Integrators of Pain and Inflammation. Nature Reviews Drug Discovery, 4 (10), 834–844. doi: https://doi.org/10.1038/nrd1852

12. Omoigui, S. (2007). The biochemical origin of pain: The origin of all pain is inflammation and the inflammatory response. Part 2 of 3 – Inflammatory profile of pain syndromes. Medical Hypotheses, 69 (6), 1169–1178. doi: https://doi.org/10.1016/j.mehy.2007.06.033

13. Abdulkhaleq, L. A., Assi, M. A., Abdullah, R., Zamri-Saad, M., Taufiq-Yap, Y. H., Hezmee, M. N. M. (2018). The crucial roles of inflammatory mediators in inflammation: A review. Veterinary World, 11 (5), 627–635. doi: https://doi.org/10.14202/vetworld.2018.627-635

14. Santos, A. L. E., Júnior, C. P. S., Neto, R. N. M., Santos, Maria. H. C., Santos, V. F., Rocha, B. A. M. et al. (2020). Machaerium acutifolium lectin inhibits inflammatory responses through cytokine modulation. Process Biochemistry, 97, 149–157. doi: https://doi.org/10.1016/j.procbio.2020.06.012

15. Zhu, F., Du, B., Xu, B. (2017). Anti-inflammatory effects of phytochemicals from fruits, vegetables, and food legumes: A review. Critical Reviews in Food Science and Nutrition, 58 (8), 1260–1270. doi: https://doi.org/10.1080/10408398.2016.1251390

16. Osukoya, O., Nwoye-Ossy, M., Olayide, I., Ojo, O., Adewale, O., Kuku, A. (2020). Antioxidant activities of peptide hydrolysates obtained from the seeds ofTreculia africanaDecne (African breadfruit). Preparative Biochemistry & Biotechnology, 50 (5), 504–510. doi: https://doi.org/10.1080/10826068.2019.1709980

17. Adeniran, O. A., Kuku, A., Obuotor, M. E., Agboola, F. K., Famurewa, A. J., Osasan, S. (2009). Purification, characterization and toxicity of a mannose-binding lectin from the seeds ofTreculia africanaplant. Toxicological & Environmental Chemistry, 91 (7), 1361–1374. doi: https://doi.org/10.1080/02772240902732357

18. Ajayi, O. S., Aderogba, M. A., Obuotor, E. M., Majinda, R. R. T. (2017). Antioxidant activities of the extracts and isolated compounds from Treculia africana (Decne) leaf. Nigerian Journal of Natural Products and Medicine, 21, 32–38.

19. Chukwuma, P. C., Nwabueze, T. U., Ogbonnaya, M., Onumadu, K. S., Irondi, A. E. (2018). Effect of traditional processing methods on the proximate composition and carbohydrate components of African breadfruits (Treculia africana) seeds. Research Journal of Food Science and Quality Control, 4 (2), 1–8.

20. Adeniran, O. A. (2015). Purification and Physicochemical Characterization of Lectin from the Seeds of Treculia Africana Decne. Ile-Ife.

21. Shimokawa, M., Nsimba-Lubaki, S. M., Hayashi, N., Minami, Y., Yagi, F., Hiemori, K. et al. (2014). Two jacalin-related lectins from seeds of the African breadfruit (Treculia africana L.). Bioscience, Biotechnology, and Biochemistry, 78 (12), 2036–2044. doi: https://doi.org/10.1080/09168451.2014.948376

22. Aderibigbe, A., Agboola, O. (2010). Studies of behavioural and analgesic properties of Treculia africana in mice. International Journal of Biological and Chemical Sciences, 4 (2), 338–346. doi: https://doi.org/10.4314/ijbcs.v4i2.58120

23. Olson, B. J. S. C., Markwell, J. (2007). Assays for Determination of Protein Concentration. Current Protocols in Protein Science, 48 (1). doi: https://doi.org/10.1002/0471140864.ps0304s48

24. Fonsêca, D. V., Salgado, P. R. R., de Carvalho, F. L., Salvadori, M. G. S. S., Penha, A. R. S., Leite, F. C. et al. (2015). Nerolidol exhibits antinociceptive and anti-inflammatory activity: involvement of the GABAergic system and proinflammatory cytokines. Fundamental & Clinical Pharmacology, 30 (1), 14–22. doi: https://doi.org/10.1111/fcp.12166

25. Ajayi, A. M., Badaki, V. B., Ariyo, O. O., Ben-Azu, B., Asejeje, F. O., Adedapo, A. D. A. (2020). Chrysophyllum albidum fruit peel attenuates nociceptive pain and inflammatory response in rodents by inhibition of pro-inflammatory cytokines and COX-2 expression through suppression of NF-κB activation. Nutrition Research, 77, 73–84. doi: https://doi.org/10.1016/j.nutres.2020.03.004

26. Hunskaar, S., Hole, K. (1987). The formalin test in mice: dissociation between inflammatory and non-inflammatory pain. Pain, 30 (1), 103–114. doi: https://doi.org/10.1016/0304-3959(87)90088-1

27. Oladokun, B. O., Omisore, O. N., Osukoya, O. A., Kuku, A. (2019). Anti-nociceptive and anti-inflammatory activities of Tetracarpidium conophorum seed lectin. Scientific African, 3, e00073. doi: https://doi.org/10.1016/j.sciaf.2019.e00073

28. Robertson, S. A. (2002). What is pain? Journal of the American Veterinary Medical Association, 221 (2), 202–205. doi: https://doi.org/10.2460/javma.2002.221.202

29. Wirth, J. H., Hudgins, J. C., Paice, J. A. (2005). Use of Herbal Therapies to Relieve Pain: A Review of Efficacy and Adverse Effects. Pain Management Nursing, 6 (4), 145–167. doi: https://doi.org/10.1016/j.pmn.2005.08.003

30. Wu, M., Cai, J., Yu, Y., Hu, S., Wang, Y., Wu, M. (2021). Therapeutic Agents for the Treatment of Temporomandibular Joint Disorders: Progress and Perspective. Frontiers in Pharmacology, 11. doi: https://doi.org/10.3389/fphar.2020.596099

31. Ramos, D. de B. M., Araújo, M. T. de M. F., Araújo, T. C. de L., Silva, Y. A., dos Santos, A. C. L. A., e Silva, M. G. et al. (2020). Antinociceptive activity of Schinus terebinthifolia leaf lectin (SteLL) in sarcoma 180-bearing mice. Journal of Ethnopharmacology, 259, 112952. doi: https://doi.org/10.1016/j.jep.2020.112952

32. Yaksh, T. L., Woller, S. A., Ramachandran, R., Sorkin, L. S. (2015). The search for novel analgesics: targets and mechanisms. F1000Prime Reports, 7. doi: https://doi.org/10.12703/p7-56

33. Aoki, M., Tsuji, M., Takeda, H., Harada, Y., Nohara, J., Matsumiya, T., Chiba, H. (2006). Antidepressants enhance the antinociceptive effects of carbamazepine in the acetic acid-induced writhing test in mice. European Journal of Pharmacology, 550 (1-3), 78–83. doi: https://doi.org/10.1016/j.ejphar.2006.08.049

34. Dannerman, P. J. K. D., Sally, K., Wixson, B., White, W. J., John, G. (Eds.) (1977). Monitoring of Analgesia en. Anesthesia and Analgesia in Laboratory Animals, 83–99.

35. Liu, Z., Gao, W., Zhang, J., Hu, J. (2012). Antinociceptive and smooth muscle relaxant activity of Croton tiglium L seed: an in-vitro and in-vivo study. Iranian Journal of Pharmaceutical Research, 11 (2), 611–620.

36. Bari, A. U., Santiago, M. Q., Osterne, V. J. S., Pinto-Junior, V. R., Pereira, L. P., Silva-Filho, J. C. et al. (2016). Lectins from Parkia biglobosa and Parkia platycephala: A comparative study of structure and biological effects. International Journal of Biological Macromolecules, 92, 194–201. doi: https://doi.org/10.1016/j.ijbiomac.2016.07.032

37. Holanda, F., Coelho-de-Sousa, A., Assreuy, A., Leal-Cardoso, J., Pires, A., do Nascimento, K., Teixeira, C. et al. (2009). Antinociceptive Activity of Lectins from Diocleinae Seeds on Acetic Acid-Induced Writhing Test in Mice. Protein & Peptide Letters, 16 (9), 1088–1092. doi: https://doi.org/10.2174/092986609789055304

38. Shamsi Meymandi, M., Keyhanfar, F. (2013). Assessment of the antinociceptive effects of pregabalin alone or in combination with morphine during acetic acid-induced writhing in mice. Pharmacology Biochemistry and Behavior, 110, 249–254. doi: https://doi.org/10.1016/j.pbb.2013.07.021

39. McNamara, C. R., Mandel-Brehm, J., Bautista, D. M., Siemens, J., Deranian, K. L., Zhao, M. et al. (2007). TRPA1 mediates formalin-induced pain. Proceedings of the National Academy of Sciences, 104 (33), 13525–13530. doi: https://doi.org/10.1073/pnas.0705924104

40. Park, S.-H., Sim, Y.-B., Lee, J.-K., Kim, S.-M., Kang, Y.-J., Jung, J.-S., Suh, H.-W. (2011). The analgesic effects and mechanisms of orally administered eugenol. Archives of Pharmacal Research, 34 (3), 501–507. doi: https://doi.org/10.1007/s12272-011-0320-z

41. Leite, J. F. M., Assreuy, A. M. S., Mota, M. R. L., Bringel, P. H. de S. F., e Lacerda, R. R., Gomes, V. de M. et al. (2012). Antinociceptive and Anti-inflammatory Effects of a Lectin-Like Substance from Clitoria fairchildiana R. Howard Seeds. Molecules, 17 (3), 3277–3290. doi: https://doi.org/10.3390/molecules17033277

42. Fontenelle, T. P. C., Lima, G. C., Mesquita, J. X., Lopes, J. L. de S., de Brito, T. V., Vieira Júnior, F. das C. et al. (2018). Lectin obtained from the red seaweed Bryothamnion triquetrum: Secondary structure and anti-inflammatory activity in mice. International Journal of Biological Macromolecules, 112, 1122–1130. doi: https://doi.org/10.1016/j.ijbiomac.2018.02.058

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