



Review Article

Anti-inflammatory and analgesic potential of *Tamarindus indica* Linn. (Fabaceae): a narrative reviewRichard Komakech ^{a,b,c}, Yong-goo Kim ^b, Gilbert Motlalepula Matsabisa ^d, Youngmin Kang ^{a,b,*}^a University of Science & Technology (UST), Korean Institute of Oriental Medicine, Korean Convergence Medicine Major, Daejeon, Republic of Korea^b Herbal Medicine Resources Research Center, Korea Institute of Oriental Medicine, Daejeon, Republic of Korea^c Natural Chemotherapeutics Research Institute (NCRI), Ministry of Health, Kampala, Uganda^d University of the Free State, Bloemfontein, South Africa

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ABSTRACT

Chronic inflammation is one of the causes of a number of non-infectious diseases in the world. Over the years, *Tamarindus indica* has played fundamental roles in traditional medicine as an anti-inflammatory and analgesic drug. It is a commercialized biocompatible medicinal plant species with a wide range of therapeutic window and with suggested LD50 greater than 5000 mg kg⁻¹ body weight when administered to the Wistar rats. This review examined the anti-inflammatory and analgesic potential and mechanism of various extracts from *T. indica* pulp, leaves, seeds, stem bark, and roots. The preclinical studies provided strong pharmacological evidence for the anti-inflammatory and analgesic activities of the different parts of *T. indica* and this may be attributed to the various bioactive compounds in it including alkaloids, flavonoids, tannins, phenols, saponins, and steroids. The anti-inflammatory and analgesic effects of the extracts from the different parts of *T. indica* may be due to its ability to inhibit a number of biological processes including cyclooxygenase-2 (COX-2) expression, inducible nitric oxide synthase (iNOS), 5-lipoxygenase biosynthesis, and tumor necrosis factor- α . The analgesic activity of *T. indica* may also be through the activation of the opioidergic mechanism at both the peripheral and central levels. Although further pre-clinical studies still need to be conducted, these results demonstrated that *T. indica* has potent anti-inflammatory and analgesic activities and hence provides justification for its use in traditional medicine to treat body pain and other inflammatory related diseases including arthritis and offers a basis for future clinical studies and possible drug development.

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1. Introduction

Inflammatory processes play a fundamental role in the initial defence of the body after infection or damage of a tissue, hence limiting further damage to the affected site.¹ However, although inflammation reaction in the early stages of infection play an important role in biological defence mechanisms,² chronic inflammation has long been linked to be the cause of a broad range of non-infectious diseases including arthritis.^{3,4} Despite the fact that inflammation can be treated by use of synthetic drugs, some of the anti-inflammatory drugs instead have the ability to block the activity of various kinase enzymes resulting in a significant decrease in host defence toward infections.⁴ As a result, the use of medicinal plants to treat and manage diseases including inflammatory and body pain which has been in existence since time immemorial is becoming more popular globally.^{4,5} Indeed, the importance of medicinal plants in treatment and prevention of the human inflammatory diseases cannot be underestimated.⁶ *Tamarindus indica*;

which is one of the highly commercialized medicinal plants is known for its potent anti-inflammatory activities.^{7,8} This tropical tree has been used to treat inflammation, stomach pain, throat pain, and rheumatism in traditional medicine.^{9–12} Additionally, the plant has also been used to manage myriad of other disease conditions including, wound healing, diarrhea, dysentery, parasitic, infestation, fever, malaria, respiratory conditions, helminthes infections, constipation, cell cytotoxicity, gonorrhoea, eye diseases, and as an aphrodisiac^{12–14} and also highly valued as a food supplement.¹⁵ Owing to the numerous economic and health benefits, *T. indica* has been traded widely throughout the world.^{7,16,17} In fact, the medicinal activities and use of *T. indica* in traditional folk medicine are attributed to the presence of phytochemicals in the different parts of the plant including flavonoids, alkaloids, tannins, phenols, triterpenoids, fatty acids, saponins, and steroids.^{18–21} Over the years, its medicinal use to treat and manage inflammation and body pain has been evaluated and published in a number of peer reviewed journal articles. This review therefore sought to examine the anti-inflammatory and analgesic potential and mechanism of *T. indica* phytochemicals and extracts as a basis for future drug development.

2. Methods

In this narrative review, we obtained information from original peer reviewed articles published in scientific journals, with a focus on the botany, traditional medicinal uses, toxicity, anti-inflammatory

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and analgesic potential with respect to *T. indica*. To obtain the relevant data, Google Scholar, PubMed, Scopus, AMED, Cochrane Library electronic literature databases were searched using the terms (“*Tamarindus indica*” AND “Botany” OR “Medicinal uses” OR “Toxicity” OR “Anti-inflammatory” OR “Analgesic” OR “Phytochemicals”) OR (“Phytochemicals in *Tamarindus indica*” AND “Anti-inflammatory” OR “Analgesic”) from 1980 to March, 2019. Only peer reviewed articles published in English language were considered in the study. Secondary data were collected, discussed, summarized, analyzed, results compared, and conclusions made accordingly.

3. Tamarindus indica Linn.

3.1. Botany and distribution of *T. indica* L.

T. indica belongs to the plant family Fabaceae¹¹ (older classification Leguminosae) and sub-family Caesalpinioideae.¹³ It is one of the few commercialized indigenous tropical medicinal plants in the global market.⁷ Tamarind is an evergreen tree that grows to a height of approximately 24 m and bole diameter at breast height of 1–2 m with a spreading crown (Fig. 1a). The stem bark is rough and greyish (Fig. 1b). The leaves are alternate and compound, with opposite leaflets that are narrowly oblong. The petiole and rachis are finely haired (Fig. 1c) with pale yellow or pink flowers (Fig. 1d). The fruit is a pod, indehiscent, sub-cylindrical and are straight or curved, velvety (Fig. 1e), with rusty-brown pulp (Fig. 1f). Seeds are 3–10 in number per pod, approximately 1.6 cm long and 0.6 cm in width, irregularly shaped, and testa is hard, shiny, and smooth (Fig. 1g).^{12,14}

This unique, rare, and highly valuable medicinal plant is widely distributed throughout the sub-Saharan Africa.⁷ *T. indica* also covers wide geographical ranges in Asia especially in the Indian subcontinent, Pakistan, and Bangladesh.¹²

3.2. Toxicology of *T. indica*

Pre-clinical acute, sub-chronic, and chronic acute toxicological tests using different parts of *T. indica* (Table 1) have been conducted over the years. In an acute toxicity study in which a single dose was used for the determination of the therapeutic index, it was observed that the aqueous pulp extract administered at a dose of 4500 mg/kg⁻¹ body weight using Wistar rats animal model was generally safe with no apparent congestion and hemorrhage in gastro intestinal track and no lesions observed on the liver and kidneys and 100% survival although the animals exhibited some behavioral changes such as aggressive scratching of the body, mouth part anorexia, and mild restlessness.²² In fact, the oral LD₅₀ of the ethanolic pulp extract on the Wistar rats was observed to be greater than 5000 mg/kg body weight with 100% survival of the experimental animals.^{23,24} Furthermore, the acute toxicity evaluation in Wistar rats of the leaves' 72% (v/v) ethanolic extracts at 5000 mg/kg body weight showed no observable changes on the skin, hair, behavior, and in vital organs including liver, kidneys, heart, spleen and lung.²⁵ Additionally, it was observed that the average water and food intake in the experimental group and that in the control group were not statistically different at *p* value = 0.898 and *p*-value = 0.0678 for water and food intake respectively. In an oral mucous irritability tests, the tamarind leaves' fluid extract exhibited mild irritant attributed to the numerous organic acids in it including citric acids, tartaric acids and malic acid.²⁶ As observed, although *T. indica* pulp and leaves have been observed to be generally safe, the ethanolic stem bark crude extract and fractions at 25% and 50% concentrations of pre-determined LD50 on chicken embryos resulted in increased level of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in the blood although not near the values that signify a disease state.²⁷ Similarly, ethanolic stem bark crude extract was observed to be toxic at a high dose of 200 µg/mL resulting in over 87% death of the test brine shrimp animal models.²⁷ In the sub-chronic toxicity test using rabbits model, it was observed that the pulp water extract is generally safe with 100% survival and enhanced high production of the white blood and red blood cells when the experimental animals were dosed daily with 100 mg/kg body weight *T. indica* pulp water extract for 35 days except for the mild pathologies on liver and kidneys.²⁸ However, although this sub-chronic toxicological study showed overall safety of *T. indica* pulp, the use of only 100 mg/kg body weight of *T. indica* pulp water extract is way below the previously suggested therapeutic index of 4500 mg/kg body weight for *T. indica* pulp

water extract in an acute toxicity study using Wistar rat model.²² In the chronic toxicity study to evaluate the long term use of *T. indica*, the pulp water extract was observed to be generally safe with 100% survival, no significant changes in body weight, hematologic, and clinical biochemistry profiles at doses up to 1 g/kg administered daily for six months.²⁹ However, there was a reduction (*p* < 0.05) in the spleen weight of female rats when administered at 200 mg/kg body weight per day for 6 months and also increased (*p* < 0.05) the relative kidney weight of the male rats when administered at 1000 mg/kg body weight per day for 6 months. However, despite these promising general safety of the different parts of *T. indica* especially the pulp and leaves with a wide therapeutic index, further sub-acute, sub-chronic, and chronic toxicological studies still ought to be conducted to further ascertain its safety in regards to the long term use and this will also set a firmer foundation for future clinical trials.

3.3. Anti-inflammatory and analgesic activities of *T. indica*

The processes of inflammation and body pain are interlinked and hence there are several drugs with both analgesic and anti-inflammatory activities.^{31,32} *T. indica* is widely regarded in traditional medicine as one of the most important plants for treatment of body pain related to the musculoskeletal system and other anti-inflammatory related illnesses.^{8,13,33,34} In fact, *T. indica* is known to exert anti-inflammatory and analgesic effects probably by down regulating the nuclear factor-kappa B (NF-κB) and the p38 mitogen-activated protein kinase pathway.³⁵ As summarized (Table 2), all main parts including stem bark, roots, leaves, and seeds of this tree species have been observed to have significant anti-inflammatory and analgesic effects.

Petroleum ether stem bark extract at 50 mg/kg intraperitoneal injection was observed to show significant (*p* < 0.05) potent antinociceptive activity in animal models through the inhibition of the of the writhing response induced by acetic acid when compared to the control group.¹⁴ Additionally, the hexane, ethyl acetate, methanol, and water fractions of *T. indica* stem bark dose of 200 mg/kg was observed to significantly (*p* < 0.001) inhibit the writhing response in albino rats; an analgesic activity mediated via peripheral and central mechanisms of pain generation.³⁶ Similarly, an *in vivo* study in albino mice model showed that the antinociceptive activity of the aqueous extracts of *T. indica* fruits may be through the activation of the opioidergic mechanism at both the peripheral and central levels at a dose range of 60–600 mg/L with the percentage of analgesia recorded to be between 51.8 and 74.1%. In addition,⁹ Pulp extracts has also been observed to effect metabolism and inflammation.⁴³

T. indica seed extract is known to exhibit strong anti-inflammatory, anti-nociceptive, and anti-arthritis effects in an animal models.⁴⁴ A serine proteinase inhibitor, known to provide anti-inflammatory activity against human neutrophil elastase, was identified, isolated, and purified from *T. indica* seeds.⁴⁵ In fact, 95% ethanolic seed extract of *T. indica* was observed to be a potent agent for reducing levels of pro-inflammatory mediators and arthritis-mediated cartilage and bone degradation in adult Wistar rats at a dosage range of 25–50 mg/kg per day after 15 days of treatment.³⁴ In another *in vivo* study, the petroleum ether seed extracts and the ethyl acetate fraction of *T. indica* seeds significantly (*p* < 0.01) increased latency to tail flick in the tail immersion method in Wistar rats, and elevated the mean basal reaction time in the hot plate method at a dose of 50 mg/kg and 100 mg/kg body weight.³⁷ Similarly, the methanolic seed extract of *T. indica* significantly (*p* < 0.01) reduced carrageenan induced paw edema in Wistar albino rats at doses of 100 mg/kg, 200 mg/kg and 400 mg/kg body weight³⁷ and also showed a significant anti-inflammatory and central analgesic activity (*p* < 0.05) in a dose-dependent manner in rat models.³⁹ In an *in vivo* study using albino wistar rats based on the hot plate method and acetic acid induced writhing test, the aqueous root extract of *T. indica* exhibited 74.83% pain inhibition and 54.33% percent protection from pain caused by acetic acid respectively at 200 mg/kg body weight compared to the analgesic standard drugs (pentazocine and Aspirin) with percentage of 89.82% and 68.50% respectively at same concentration; an indication of *T. indica* potent analgesic principles acting within the prostaglandin pathways.⁴⁰ Furthermore, the anti-inflammatory effect of *T. indica* aqueous root extract on the carrageenan induced rat paw oedema in Wistar rats was observed to be significant at percentage inhibition of 37.83% at a dose of 200 mg/kg compared to that of the standard drug Aspirin at percentage inhibition of 59.45% at same dose.⁴⁰

The oral administration of hydroethanolic extracts of *T. indica* leaves to Wistar rats at doses of 500, 750, and 1000 mg/kg body weight produced

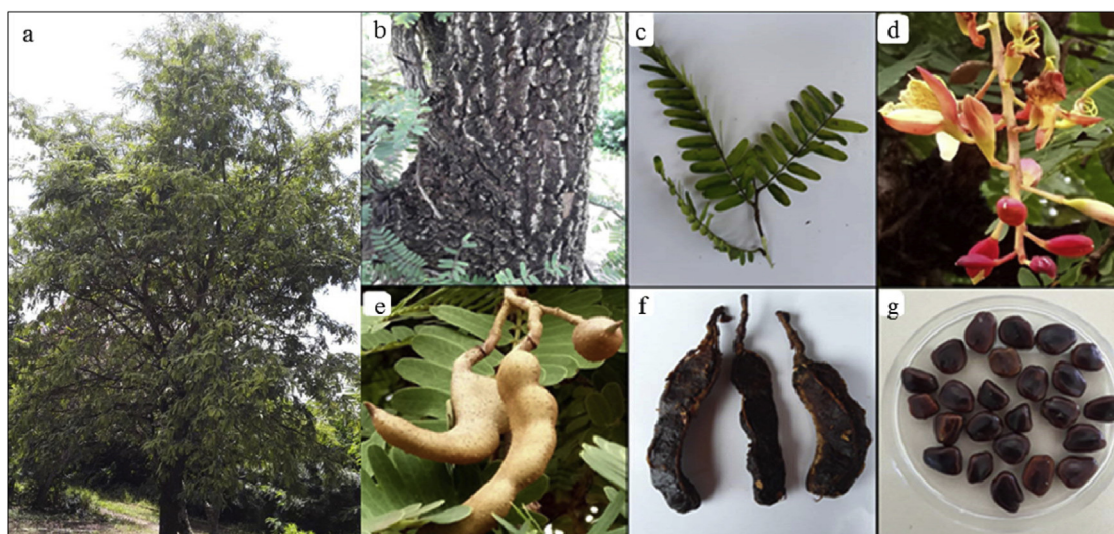


Fig. 1. The botanical morphology of the main features of *Tamarindus indica*. (a) *Tamarindus indica* tree growing in Eastern Uganda. (b) Greyish stem bark of *T. indica*. (c) Alternate, compound, opposite leaflets leaf of *T. indica*. (d) *T. indica* flowers. (e) *T. indica* fruits. (f) Rusty-brown pulp of *T. indica*. (g) Irregularly shaped, shiny, and smooth seeds of *T. indica* with very hard testa.

Table 1
Pre-clinical Toxicological Study on the Various Parts of *Tamarindus indica*

Plant part used	Extract used	Animal model	Dosage used	Type of study	Percentage survival	Overall conclusion	Reference
Pulp	Ethanoliceextract	Wistar rats	5000 mg/kg body weight	Acute toxicity	100	Non-toxic and considered safe	22
Pulp	Aqueous extract	Wistar rats	4500 mg/kg body weight	Acute toxicity	100	No apparent congestion and hemorrhage in gastro intestinal track and no lesions observed on the liver and kidney.	23
Leaves	72% (v/v) ethanolic extract	Wistar rats	5000 mg/kg body weight	Acute toxicity	100	No changes in skin or pelage were observed and mucous membranes and eyes showed normal appearance and colour.	25
Leaves	Fluid extract	Wistar rats	2000 mg/mL body weight	Acute toxicity	100	No observable change in the animal's hair and skin. Normal behavior and mucous or eye coloration	30
Stem bark	Ethanolice extract	Brine shrimp	200 µg/mL	Acute toxicity	13	<i>Tamarindus indica</i> stem bark extract toxic at higher dose	27
Pulp	Water extract	Rabbits	100 mg/kg body weight	Sub-chronic toxicity	100	Enhanced performance of the liver and kidneys and increased white blood cells and red blood cells counts	28
Pulp	Water extract	Wistar rats	1000 mg/kg body weight	Chronic toxicity test	100	No abnormalities in hematology and blood biochemistry parameters.	29

Table 2
The Anti-inflammatory and Analgesic Activities of the Extracts from Different Parts of *T. indica*

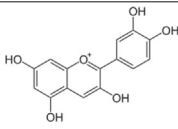
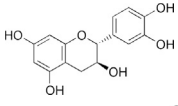
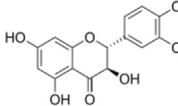
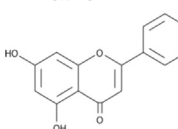
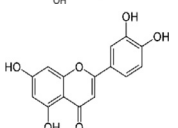
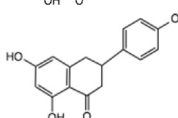
Plant part used	Extract and dosage administered	Animal model used	Pharmacological effects and conclusion	Reference
Stem bark	Hexane, ethyl acetate, and methanol fractions administered at 200 mg/kg body weight	Wistar rats	Inhibited the writhing response an indication of potent antinociceptive activity	36
Pulp	Aqueous extract administered at a dose of 60, 100, 300 and 600 mg/kg	Albino mice	Exhibited an antinociceptive activity through activation of the opioidergic mechanism at both the peripheral and central levels.	9
Seeds	Ethanolice extract administered at 25–50 mg/kg body weight	Wistar rats	Reduced the levels of pro-inflammatory mediators and arthritis-mediated cartilage and bone degradation.	34
	Petroleum Ether fraction and Ethyl acetate fractions administered at 50 and 100 mg/kg body weight	Wistar rats	Increased latency to tail flick in the tail immersion method.	37
	Methanolice extract administered at doses of 100 mg/kg, 200 mg/kg and 400 mg/kg body weight	Wistar rats	Reduced carrageenan induced paw edema in rats an indication of potent antinociceptive activity.	38
Roots	Methanolice extract administered at 200 mg/kg body weight	Wistar rats	Exhibited anti-inflammatory and central analgesic activity.	39
	Aqueous extract administered at 300 and 600 mg/kg body weight	wistar rats	Enhanced pain inhibition.	40
Leaves	Hydro-ethanolice extract administered at 500, 750, and 1000 mg/kg body weight	Wistar rats	Enhanced anti-inflammatory and anti-nociceptive actions.	41
	Aqueous extract administered at 400 mg/kg body	wistar rats	Enhanced anti-inflammatory and anti-nociceptive activities.	33
	Ethanolice extract administered at 400 mg/kg body	Swiss albino mice	Enhanced analgesic activity.	42

significant ($p < 0.01$) anti-inflammatory and anti-nociceptive actions in a dose-dependent manner.⁴¹ Similar study in albino rats showed that an aqueous extracts of *T. indica* leaves exhibited significant ($p < 0.05$) dose-dependent anti-inflammatory and anti-nociceptive activities at a concentration of 400 mg/kg body weight.³³ In fact, a greater analgesic activity was observed in a tail immersion study using adult Swiss albino mice, when a concentration of 400 mg/kg ethanolic extracts of *T. indica* leaves was administered compared to a 25 mg dose of Diclofenac sodium.⁴² As observed, various doses have been used to evaluate the pre-clinical anti-inflammatory and analgesic potential for the different parts of *T. indica*. Therefore, there is need for further preclinical studies to harmonization of these dosages to enhance effective and safe clinical studies to further confirm the anti-inflammatory and analgesic potential of the pulp, leaves, stem bark, and roots of *T. indica*.

The presence of myriad of the principle bioactive compounds in different parts of *T. indica* including flavonoids, alkaloids, tannins, phenols,

triterpenoids, fatty acids, saponins, and steroids,^{19,40} may explain the unique anti-inflammatory and analgesic nature of all the parts of this plant species. However, despite the fact that these classes of secondary metabolites have been confirmed in *T. indica*, only specific flavonoids have been isolated and identified (Table 3) including procyanidins, catechin, taxifolin, apigenin, luteolin, and naringenin.^{46,47} Flavonoids' ability to inhibit 5-lipoxygenase enzyme plays a key role in the suppression of leukotriene biosynthesis and hence reducing the body inflammatory reactions.⁴⁸ Procyanidins; an oligomeric flavonoids found in large quantity and makes over 60% of the phytochemicals in the *T. indica* seeds and fruit pulp,⁴⁶ are known to possess potent anti-inflammatory and analgesic activities.⁴⁹ Procyanidins exerts its anti-inflammatory and analgesic activities by inhibiting the inflammatory cytokine production, suppressing the nucleotide-binding oligomerization domain-like receptors, inhibiting inflammasome activation,⁵⁰ and via the inhibition of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2).³⁵

Table 3
The Anti-Inflammatory and Analgesic Activities of Isolated Flavonoids from *Tamarindus indica*

Phytochemicals	Compound structure	Pharmacological target(s)	Overall effect (s)	Study conducted	Reference
Procyanidins		NF-κB pathways; inhibiting iNOS and COX-2 expressions.	Down regulation of inflammation and body pain	<i>In vivo</i>	35
Catechin		NF-κB mitogen activated protein kinases.	Down regulation of inflammation and body pain.	<i>In vivo</i>	52
Taxifolin		Inhibition of LPS-induced tumor necrosis factor-α.	Down regulation of inflammation and body pain.	<i>In vivo</i>	58,59
Apigenin		Inhibition of NO production and iNOS, and COX-2 expression	Down regulation of inflammation and body pain.	<i>In vivo</i>	63,65
Luteolin		Down regulation of inflammatory mediators and cytokines	Down regulation of inflammation and body pain.	<i>In vivo</i>	67
Naringenin		Inhibition of the pro-inflammatory cytokines. Modulate transient receptor potential channels	Down regulation of inflammation and body pain.	<i>In vivo</i>	71,72

In fact, both COX-2 and iNOS have been implicated in osteoarthritis conditions and hence their inhibition is of significance in the therapeutic intervention of osteoarthritis.⁵¹

Catechin's potent anti-inflammatory and analgesic activities is attributed to its ability to modulate inflammation and oxidative stress related to cell signaling pathways including NF-κB and mitogen activated protein kinases.⁵² Furthermore, catechin is one of the bioactive compounds with potent ability to suppress the pro-inflammatory signaling pathways,⁵³ and also reduces visceral pain induced by acetic acid through gamma-aminobutyric acid receptors.⁵⁴

Taxifolin has great therapeutic potential for many major inflammatory diseases^{55,56} and showed significant ($p < 0.05$) reduction in pain when applied topically to painful knee joint, shoulder, calf, hip, lower and upper back.⁵⁷ It inhibits Lipopolysaccharide (LPS)-induced tumor necrosis factor-α and interleukin-6 production⁵⁸; an indication that taxifolin has a significant anti-inflammatory effect. Similarly, taxifolin is also known to enhance its anti-inflammatory effects by inhibiting LPS-induced production of nitrite oxide.⁵⁹ In type II diabetes, taxifolin inhibits pro-inflammatory neutrophils and hence protects the vascular systems from damage and as well as preventing the inflammatory white blood cells from attacking and adhering to the brain thereby giving protection to the brain.⁶⁰

Apigenin is a monomeric dietary flavonoid with potent analgesic and anti-inflammatory activities due to inhibition of Prostaglandin E2 and pro-inflammatory cytokines including interleukin-1β, and tumor necrosis factor-α.⁶¹ In an *in vivo* study, apigenin inhibited the collagenase activity associated with rheumatoid arthritis, and suppressed LPS-induced nitric oxide production in a dose dependent manner in RAW 264.7 macrophage cells and also exhibited significant anti-inflammatory activity by blocking nitric oxide-mediated COX-2 expression and monocyte adherence.⁶² In the tail immersion test, administration of 10 mg/kg of apigenin produced dose dependent analgesia, with maximum activity recorded after 30 minutes.⁶³ In addition to having an effective anti-inflammatory and pharmacological activities on both diabetes and Alzheimer's diseases,⁶⁴ apigenin has also been used to treat acute lung injury through inhibition of COX-2 and NF-κB gene expression in lung.⁶⁵

Luteolin is a monomeric flavone, is a strong neuroprotective agent capable of suppressing inflammation within brain tissues.⁶⁶ Luteolin's anti-inflammatory activity is due to the inhibition of nitric oxide production, down-regulation of inflammatory mediators and cytokines,⁶⁷ reactive oxygen species production, and tumor necrosis factor-α.⁶⁸ In addition to its anti-inflammatory effects, luteolin is known to possess

potent analgesic activity as evidenced in acetic acid-induced writhing, formalin, and hot plate tests.⁶⁹

Naringenin is a bitter and colorless monomeric flavanone belonging to a class of flavonoids contained in *T. indica*⁴⁶ with potent anti-inflammatory activity due to its ability to reduce cytokine production.⁷⁰ It reduces pain induced by inflammatory stimuli by modulating transient receptor potential channels, and activating the nitric oxide signaling pathway to induce nociceptor neuron hyperpolarization.⁷¹ It potentially inhibits the pro-inflammatory cytokine response induced by LPS in both macrophages and in whole blood⁷²; an anti-inflammatory mechanism exhibited by naringenin which can be exploited for treating inflammatory diseases such as periodontitis. Naringenin is also known to possess analgesic potential due to its ability to modulate transient receptor potential channels⁷¹ and inhibit superoxide anion-induced inflammation related pain.⁷³ Its repeated administration was observed to be effective in relieving the neuropathic pain.⁷⁴

Alkaloids are major bioactive secondary metabolites contained in *T. indica*^{20,21,40} with significant anti-inflammatory potential.^{75,76} In fact, over 80% of alkaloids evaluated are known to possess anti-inflammatory activity⁷⁷ with some of the alkaloids having greater anti-inflammatory potency than aspirin.⁷⁸ Alkaloids have also been showed to inhibit writhing response in model animals and increase tail flick latency in the radiant heat tail-flick method; an indication that this class of compound has significant analgesic potential.⁷⁹

Tannins are bitter-tasting, polyphenolic biomolecules and represents one of the major bioactive secondary metabolites contained in *T. indica*^{20,21} with strong anti-inflammatory activity.^{80,81} Its anti-inflammatory activity has been shown by its ability to prevented rat paw edema induced by carrageenan and dextran.^{82,83} Phenolic compounds are potent anti-inflammatory agents⁸⁴ due to its ability to inhibit either the production or action of pro-inflammatory mediators⁸⁵ and inhibit the leukocyte chemotaxis.⁸⁶ In fact, phenol has been used for local analgesic therapy since time immemorial.⁸⁷ The anti-inflammatory and analgesic activities of a number of plants have been attributed to the presence of saponins.^{88,89} It exhibits the anti-inflammatory activity through suppression of NF-κB, phosphoinositide 3-kinase, and mitogen-activated protein kinase signaling pathways.⁹⁰ Furthermore, an *in vivo* study showed that saponins can significantly inhibit paw edema, algisia, and nitrite production without affecting cell viability;⁹¹ an indication of its potent analgesic activity.

Therefore, the presence of all these bioactive compounds in *T. indica* somewhat justifies the use of this plant in traditional medicine for the

treatment and management of inflammation and related disease conditions including body pain.

4. Conclusion

Throughout the world, diseases caused by inflammation are a significant health burden and hence all possible measures have to be explored to tackle it. *T. indica* has a rich history of use as anti-inflammatory and analgesic medicinal plant in traditional medicine. In fact, the anti-inflammatory effects of *T. indica* may be due to its ability to inhibit a number of biological pathways including NF- κ B activation pathways, and leukotriene biosynthesis while its analgesic activity may be via the activation of the opioidergic mechanism at both the peripheral and central mechanisms of pain generation and inhibition of the prostaglandin pathways. And as observed in this study, although the anti-inflammatory and analgesic activities of the classes of bioactive compounds flavonoids, alkaloids, tannins, phenols, and saponins discussed in this study were from different sources and not directly isolated from *T. indica* and experimented, their presence in *T. indica* gives an insight into the anti-inflammatory and analgesic potential of *T. indica*. We therefore recommend that future study may focus on the evaluation of the anti-inflammatory and analgesic activities of the bioactive compounds isolated from *T. indica* pulps, leaves, and stem bark. Furthermore, although several animal based *in vivo* studies have shown promising evidence for *T. indica* efficacy as an anti-inflammatory and analgesic plant species, there is need for clinical trials which is still lacking to enhance future drug development for the treatment and management of inflammatory diseases and body pain. And prior to the clinical studies that may focus on the use of *T. indica* pulp, leaves or stem bark for treatment and management of arthritis including osteoarthritis and body pain, further pre-clinical sub-chronic and chronic toxicity studies still ought to be done to evaluate the safety associated with its long term use.

Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical statement

No ethical approval was required for this manuscript as this study did not involve human subjects or laboratory animals.

Data availability

The data supporting the findings of this study are available within the article.

Authors' contribution

KR carried out the data search and was the major contributor in writing the manuscript. YK carried out part of the secondary data search and contributed in manuscript writing. MGM and YK technically designed and helped in writing the manuscript. All the authors read and approved the final manuscript.

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