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Unraveling the therapeutic potential of *Tephrosia linearis*: Anti-inflammatory, analgesic activity, and molecular docking approaches

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Highlights

- T. linearis ethanolic leaves contain flavonoids, tannins, alkaloids, and triterpenoids as major phytochemicals.
- The extract showed moderate safety in Wistar rats with an LD50 of 2692 mg/kg.
- It exhibited non-dose dependent analgesic and anti-inflammatory effects in CFA-induced arthritis model.
- Apigenin, luteolin, velutin bound strongly to COX2, PLA2, and TNFα in molecular docking assays.

Abstract

Background

Inflammatory diseases such as arthritis affect over 300 million people globally. The current treatment mainly involves the use of Non-Steroidal Anti-inflammatory drugs (NSAIDS) which

possess several adverse drug reactions that are sometimes life threatening. This has prompted many patients to gain interest in plant-based remedies. *Tephrosia linearis* (Willd.) Pers (Fabaceae) is widely used in Uganda to manage symptoms of inflammation. However, there was a paucity of information concerning its analgesic and anti-inflammatory activities. This study investigated the anti-inflammatory, analgesic, and acute toxicity effects of ethanolic extracts from the aerial parts of *Tephrosia linearis* in Wistar albino rats.

Methods

Plant samples were collected from Katakwi District, Eastern Uganda and extracted using 70 % ethanol. Quantitative phytochemical analysis was conducted using UV/Vis spectroscopy. Acute toxicity was assessed using Lorke's method, while analgesic and anti-inflammatory activities were evaluated through Complete Freud's Adjuvant-induced arthritis model. Three doses of *T. linearis* (200, 400, and 800 mg/kg) were compared with a control group receiving 20 mg/kg of diclofenac. Three marker compounds were assessed using *in silico* modeling to predict their pharmacokinetic properties, organ toxicity, and binding energy against selected protein targets involved in inflammation.

Results

The ethanolic extract contained significant concentrations of flavonoids (82.9 ± 0.1 mg/g), tannins (140.2 ± 0.9 mg/g), alkaloids (93.4 ± 1.0 mg/g), and triterpenoids (76.1 ± 1.5 mg/g). No toxic effects were observed at doses below 2000 mg/kg, with an estimated LD50 of 2692 mg/kg. The extract exhibited a non-dose dependent analgesic and anti-inflammatory activities that were significantly lower than that of diclofenac ($p < 0.05$). Molecular docking revealed strong binding affinities for apigenin, luteolin, and velutin with COX2, PLA2, and TNFα.

Conclusion

This study supports *T. linearis* as a safe herbal remedy for managing inflammation, suggesting further optimization through active ingredient isolation for enhanced therapeutic outcomes.

Introduction

Inflammation is a normal local tissue response to harmful stimuli, such as pathogens, damaged cells, toxic compounds or irradiation, aimed at mitigating injury and initiate healing [1]. Classic acute inflammation is marked by symptoms like redness, swelling, pain, and loss of function, resulting from increased vascular permeability and leukocyte recruitment [1]. This type typically resolves within hours to days. In contrast, chronic inflammation develops over longer periods due to persistent irritants or autoimmune conditions, leading to significant global health issues like arthritis and diabetes mellitus [2]. Arthritis affects over 300 million people globally and consists of more than 100 conditions characterized with joint pain and erosion [3]. Among the most common arthritis is osteoarthritis, which affects about 13 % of the global population and is linked to age, obesity, and past injuries [4]. Rheumatoid arthritis (RA), an autoimmune condition of unknown etiology, leads to systemic complications, including joint inflammation and destruction, impacting

approximately 1 % of the global population, with a higher prevalence in women [5], [6]. Although the burden of RA in Africa is poorly understood, it is reported that its incidence is about 40 new cases per 10,000 people [6].

Currently, there is no cure for arthritis; treatment primarily focuses on reducing inflammation and pain while maximizing joint function and preventing joint damage [7]. Commonly prescribed medications include non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin, diclofenac, and piroxicam, which inhibit cyclooxygenase activity there by inhibiting the synthesis of prostaglandins involved in the inflammatory cascade associated with arthritis [8]. Glucocorticoids such as prednisolone and hydrocortisone are also utilized because of their inhibitory effect on the Phospholipase A2 via lipocortins as well as inhibition of the release of inflammatory cytokines. Additionally, they reduce the expression of cyclooxygenase-2 (COX-2), yielding a net reduction in inflammatory responses [9]. However, the use of these medications can lead to various side effects, including osteoporosis, peptic ulcers, and hypertension, which depend on dosage and duration of treatment [10].

Tephrosia linearis (Willd.) Pers, a perennial shrub belonging to the Fabaceae family, grows up to about 130 centimeters in height [11]. This plant is widely distributed across tropical, sub-tropical, and arid regions and has been used traditionally for treating various ailments, including rheumatic pains, syphilis, edema, gastrointestinal disturbances, respiratory issues, and inflammatory conditions [12]. *In vitro* studies have validated the antibacterial, anti-cancer, and anti-inflammatory properties and have attributed the observed pharmacological properties to the abundant flavonoids such as apigenin, naringenin, and genistein present in this plant [13]. Several literature surveys have shown very little to no data that correlates the phytochemical, pharmacological and molecular mechanisms of *Tephrosia linearis* [14]. In this study, we aimed to investigate the *in vivo* anti-inflammatory effects, analgesic potential and acute toxicity of *T. linearis* extract using established animal models as well as predict the mechanism of action of slected marker compound using computational models [15], [16], [17].

Section snippets

Plant sample collection and identification

The leaves of *T. linearis* were harvested from their natural habitats from Aputon parish, Toroma Sub-County in Katakwi district, Teso region. Following good harvesting practices, samples were harvested with the help of a plant taxonomist (WHO, 2003). A Voucher specimen OSB/010/2023) was prepared and deposited at the Makerere University Herbarium for authentication and reference

purposes. Upon collection, the harvested samples were packed in zip lock bags and transported to the Busitema …

Experimental animals and dose determination

This study adhered strictly to the ARRIVE 2.0 guidelines to ensure ethical conduct, transparency, and reproducibility of animal research [23]. …

Animal model and housing conditions

A total of twenty (n = 20) healthy female Wistar albino rats aged 8–10 weeks, body weights (120–150 g), were obtained from the NaPRiC animal facility. Animals were housed in well-ventilated polypropylene cages (4 rats per cage) under standard laboratory conditions: temperature (22 ± 2°C), relative humidity (55 ± 10%), and a 12 h light/dark cycle. They …

Preliminary phytochemical screening of ethanolic extract of *T. linearis*

Qualitative phytochemical analysis of the ethanolic extract of *T. linearis* revealed the presence of several bioactive constituents with potential pharmacological significance (Table 1).The screening showed strong presence of saponins, flavonoids, tannins, alkaloids, and phenols, indicating a rich phytochemical profile. Glycosides were present, while steroids were not detected in the extract. …

Quantification of total phytochemicals present in *T. linearis*

The quantities of total crude phytochemicals in the ethanolic extract of *T. linearis*, in descending order …

Discussion

Herbal remedies are rich in bioactive phytochemicals compounds, hence serving as an alternative source of safe, cost-effective, and yet efficacious natural therapeutics for managing various ailments, including inflammatory condition [26]. Due to their potential for modulating inflammation with minimal side effects, plant-based compounds are increasingly explored as substitutes for conventional nonsteroidal anti-inflammatory drugs [27]. In this study, we investigated the analgesic, …

Conclusions

The findings from this study underscore the therapeutic potential of *Tephrosia linearis*, whose ethanolic crude extract demonstrated notable analgesic and anti-inflammatory activity, both in vivo and in silico. The mechanistic insights provided by molecular docking suggest that flavonoids such as apigenin, luteolin, and velutin exert their effects by targeting key inflammatory mediators—COX-2, PLA2, and TNF-α. While the extract appears relatively safe at low doses, the observed toxicity at …

CRediT authorship contribution statement

Sharon Tracy Edeya: Writing – review & editing, Formal analysis, Data curation. **Mercy Chebijira:** Writing – review & editing, Formal analysis, Data curation. **Moses Andima:** Writing – review & editing, Formal analysis, Data curation. **Tony Lukwago Wotoyitidde:** Writing – review & editing, Formal analysis, Data curation. **Samuel Baker Obakiro:** Writing – review & editing, Supervision, Resources, Project administration, Conceptualization. **Richard Maseruka:** Writing – review & editing, Formal analysis, …

Declaration of Competing Interest

The authors declare that there is no conflict of interest regarding the publication of this paper. …

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