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EXPLORING THE ANTI-ARTHRITIC PROPERTIES OF ALKALOID-RICH EXTRACT FROM *T. UMBELLIFERUM*: IMPLICATIONS FOR GOUT-INDUCED ARTHRITIS MANAGEMENT

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Abstract:
This study explores the anti-arthritic properties of the alkaloid-rich extract from *Tanacteum umbelliferum* in gout, a form of arthritis characterized by urate crystal accumulation in joints. Chronic hyperuricemia and gout can lead to severe joint pain, swelling, and damage. Through meticulous investigation using the protein denaturation method, the study evaluates the influence of *T. umbelliferum* alkaloid-rich extract on preventing protein denaturation, a key factor in arthritis development. The extract shows notable efficacy in countering protein denaturation, with lower IC_{50} values indicating heightened anti-arthritic activity. The findings suggest that *T. umbelliferum* extract may serve as an optimistic anti-arthritic agent, potentially mitigating the progression and symptoms of gout-induced arthritis. These results contribute to understanding the mechanisms underlying arthritis pathogenesis and offer insights into the therapeutic potential of natural alkaloid-rich extracts in arthritis management.

Keywords: *Tanacteum umbelliferum,* Alkaloid, Arthritis, Denaturation, Hyperuricemia

1. Introduction:

Gout is a rheumatic inflammatory disorder distinguished by the deposition of uric acid crystals, particularly monosodium urate, within the joints (Manjuladevi, Krishnan, & Rahini, 2019). Hyperuricemia, a significant metabolic issue, occurs when UA levels in the blood surpass 6.8 milligram/dl, often remaining asymptomatic. Elevated uric acid levels can impact both gender, with a rising prevalence, especially among the elderly, according to epidemiological studies (Chalès, 2019).

Elevated levels of uric acid can result in the development of urate crystals not only in the joints, causing gout, but also in the renal system, raising the risk of urate nephrolithiasis (Anaizi, 2023). Uricase depletion, arising from the breakdown of nucleic acids either internally or through the decomposition of food, leads to the production of uric acid as a byproduct of nucleic acid metabolism in humans (Rodríguez et al., 2023). The concentration of urate in the bloodstream is affected by

various factors, including dietary intake, such as the consumption of purines from food, the activity of urate synthase, and the rate of urate excretion (Zou, Zhao, & Wang, 2021).
Hyperuricemia may result from either an overproduction of uric acid or insufficient elimination from the bloodstream. Uric acid crystals, such as monosodium urate crystals, can deposit in synovial fluids in joints, affecting the articulating tissues of various joints and other body tissues (Zhang et al., 2019). The continual elevation of uric acid concentration in extracellular fluids promotes the crystallization process within the joints. Persistent hyperuricemia often triggers acute gout flare-ups, typically presenting as a mono-articular attack, initially affecting the first metatarsophalangeal joint (Brovold et al., 2019).
The aim of current study was to explore the untapped potential and protective effects of *Tanacetum umbelliferum* alkaloid rich extract against arthritic condition related to hyperuricemia. The study was helpful in exploring the new management options to prevent arthritic condition.

2. Methodology:

2.1 Anti-arthritic activity:

The alkaloid-rich extract was used to evaluate its potential protective effects against arthritis. The assessment of anti-arthritic activity was carried out using the protein denaturation (thermal) method, employing fresh egg albumin and following the procedure outlined by Rajpoot et al. (2023) with slight modifications. Initially, 5 ml of reaction mixtures were prepared by combining 0.2 ml of egg albumin, 2.8 ml of phosphate-buffered saline (PBS), and 2 ml of various concentrations (125, 250, and 500 µg/ml) of the samples in a test tube. The control mixture comprised 0.2 ml of egg albumin, 2.8 ml of PBS, and 2 ml of distilled water. Diclofenac sodium, at the same concentration as the extract, was used as a positive control (2 ml). These mixtures were then incubated at 37 °C for 15 minutes, followed by heating at 70 °C for 5 minutes. After cooling to room temperature, absorbance was measured at 660 nm using a UV-visible spectrophotometer (Rajpoot et al., 2023). The percentage inhibition and percentage denaturation of egg albumin protein was calculated using the provided formulas below;

$$\%\ Inhibition = \frac{Abs.\ of\ control - Abs.of\ Sample}{Abs.of\ Control} \times 100$$

3. Results and Discussion:

3.1 Anti-arthritic activity:

Table 3.1: Anti-arthritic activity by protein denaturation method

Test Sample	**Conc. µg/ml**	**Percentage Inhibition ± SEM**	**IC_{50} µg/ml**
Alkaloid Extract	500	70.3± 0.8	84.90
	250	65.2± 0.4	
	125	48± 0.3	
Diclofenac sodium	500	81.4 ± 0.7	40.53
	250	70.4 ± 0.4	
	125	60 ± 0.6	
	62.5	48 ± 0.6	
Negative Control	5ml		

Values are presented as mean ± SEM

Table 3.2: ANOVA table of anti-arthritic activity

Anti-arthritic					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	13394.248	7	1913.464	2.038E3	.000
Within Groups	15.022	16	.939		
Total	13409.270	23			

P < 0.001, represent the significant value as compared to control group

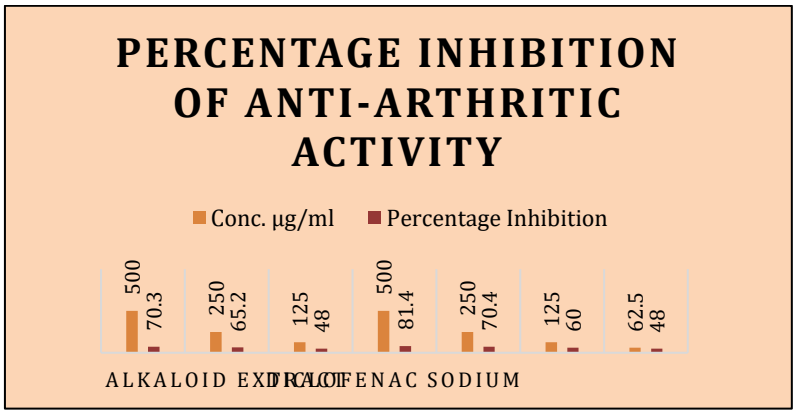

Figure 3.1: Percentage inhibition of anti-arthritic activity

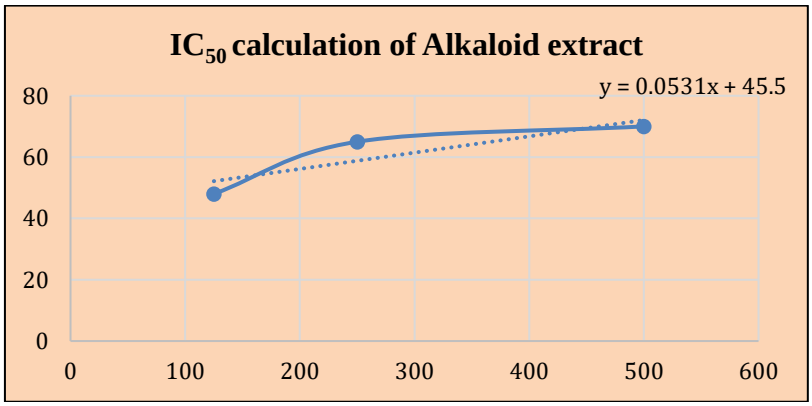

Figure 3.2: IC_{50} of alkaloid extract for anti-arthritic activity

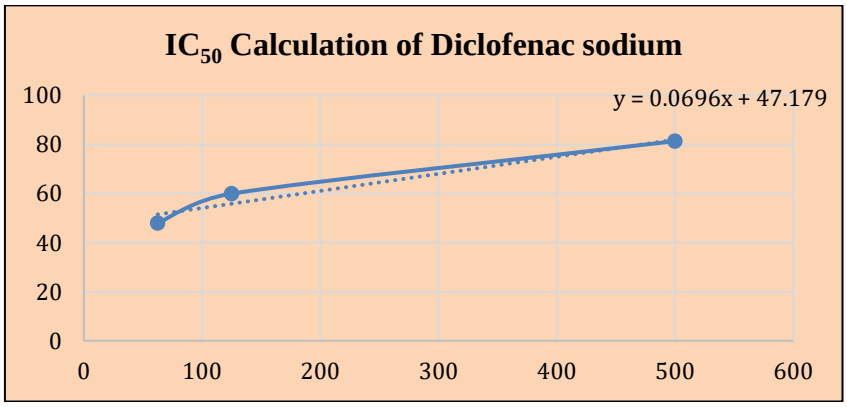

Figure 3.3: IC_{50} of positive control for anti-arthritic activity

The investigation into the anti-arthritic properties of the alkaloid-rich extract from T. *umbelliferum* was conducted meticulously through the protein denaturation method. The study explored into the

influence of *T. umbelliferum* alkaloid-rich extract and its constituents on preventing protein denaturation. Three distinct dose levels 500, 250 and 125µg/ml of the alkaloid extract exhibited notable efficacy in countering protein denaturation with the percentage inhibition of 70%, 65% and 48% as outlined in table 3.1, figure 3.1. As lower IC_{50} value is indicative of heightened anti-arthritic activity shown in figure 3.2, 3.3 with significance level 0.000 shown in table 3.2. Numerous researchers hypothesized that protein denaturation stands as a key factor in the etiology of arthritis. *In vivo*, the process of protein denaturation may trigger the generation of auto-antigens in different rheumatic conditions. Changes in electrostatic, hydrogen, hydrophobic, and disulfide bonding are likely to reinforce the mechanism of denaturation (Ahmad, Abuzinadah, Alkreathy, Banaganapalli, & Mujeeb, 2018). From the compiled findings, it becomes apparent that the alkaloid-rich extract derived from *T. umbelliferum* demonstrates notable efficacy as an anti-arthritic agent.

4. Conclusion:

The study underscores the debilitating impact of gout-induced arthritis and the importance of exploring effective treatments. Through meticulous investigation, the alkaloid-rich extract from *T. umbelliferum* demonstrates notable efficacy in countering protein denaturation, indicating its potential as a promising anti-arthritic agent with significant therapeutic implications.

5. Acknowledgment:

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6. Conflict of interest:

Authors declare that there is no conflict of interest among authors

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