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Preparation and Preformulation Study of *Tithonia Diversifolia* Dry Extract as a Potential Antimalarial Pharmaceutical Raw Material

Nuri[1,2], Endah Puspitasari[1,2], Siti Muslichah[1,2], Dewi Dianasari[1,2], Yudi Wicaksono[3]

[1]Department of Pharmaceutical Biology, Faculty of Pharmacy, University of Jember, Jember, Indonesia 68121

[2]Bio-Active Natural Product Development Research Group, Faculty of Pharmacy, University of Jember, Jember, Indonesia 68121

[3]Herbal Medicine Innovation Research Group, Faculty of Pharmacy, University of Jember, Jember, Indonesia 68121

ABSTRACT

Comprehensive physicochemical characterization is essential in the development of pharmaceutical dosage forms to ensure quality, stability, and performance. This study aimed to prepare and evaluate the preformulation characteristics of *Tithonia diversifolia* leaf dry extract as a candidate for antimalarial drug development. Extraction was performed by maceration using 96% ethanol, followed by vacuum drying with colloidal silicon dioxide (Cab-O-Sil) at concentrations of 10–40% w/w. The resulting dry extract exhibited a dark green color, characteristic odor, and bitter taste. The terpenoid content was determined to be 2.9720 ± 0.0551% w/w using TLC-densitometry. Scanning electron microscopy revealed irregular particle morphology with rough surfaces and particle size distribution of 10–50 µm. Flow properties showed an angle of repose of 12.68–22.45° and flow rate of 0.89–7.35 g/s, indicating good flowability. Moisture content ranged from 0.2–0.4% w/w, while maximum water uptake reached 9.47% at 21.5°C. Density analysis demonstrated true density of 1.3589 ± 0.0781 g/mL, bulk density of 0.4215 ± 0.0473 g/mL, and tapped density of 0.5093 ± 0.0334 g/mL. These findings indicate that the extract possesses suitable physicochemical properties for further development into solid dosage forms.

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I. INTRODUCTION

Preformulation studies are essential in pharmaceutical development, providing critical insights into physicochemical and mechanical properties that influence formulation performance. These studies enable rational selection of excipients and optimization of manufacturing processes (Gibson, 2004).

Tithonia diversifolia (Asteraceae) has been widely reported for its antimalarial activity. Previous studies identified sesquiterpene lactones, particularly tagitinin C, as major bioactive compounds with potent in vitro activity against *Plasmodium falciparum*. In vivo studies further confirmed its efficacy and safety profile (Nuri *et al*., 2011).

Despite promising pharmacological activity, limited data are available regarding its pharmaceutical properties, particularly in dry extract form. Therefore, this study focuses on the preparation and comprehensive preformulation evaluation of *T. diversifolia* dry extract to support its development into solid dosage forms.

II. MATERIALS AND METHODS

A. Materials

The materials used in this study include *Tithonia diversifolia* leaves, 96% ethanol, and Cab-o-sil. The equipment used includes a macerator, a Scanning Electron Microscope (Hitachi Tabletop Microscope TM3000), a PMB Moisture Analyzer (AE Adam), a Flowability Tester, and a Tap Density Tester (Logan TAP-2S).

B. Preparation of Plant Material

Leaves were washed, air-dried at ambient temperature (25–30°C) to constant weight, and milled into coarse powder. The powder was sieved to obtain uniform particle size.

C. Extraction

Approximately 4.47 kg of powdered plant material was subjected to maceration using 96% ethanol (solid–solvent ratio 1:10 w/v) for 24 h at room temperature with intermittent stirring. The extract was filtered using a Büchner funnel. The residue was re-macerated four times under identical conditions to ensure exhaustive extraction. Combined filtrates were concentrated under reduced pressure using a rotary evaporator at 40–50°C to obtain a viscous extract.

D. Preparation of Dry Extract

The concentrated extract was mixed with Cab-O-Sil at concentrations of 10%, 20%, 30%, and 40% (w/w). The mixture was homogenized and dried using a vacuum oven at 60°C for 2 h. The resulting dry extract was stored in airtight containers under desiccated conditions until further analysis.

E. Determination of Terpenoid Content (TLC-Densitometry)

Approximately 250 mg of extract was dissolved in methanol and adjusted to 25 mL. Samples and standard terpenoid solutions (2.8–11.4 µg) were spotted on TLC plates. The mobile phase consisted of toluene:ethyl acetate (3:1 v/v).

After development, plates were scanned using a densitometer, and quantification was performed based on calibration curve.

F. Particle Morphology (SEM)

Particle morphology was examined using Scanning Electron Microscopy (SEM) at 1000× magnification to assess shape, surface characteristics, and particle distribution.

G. Flow Properties

Flowability was evaluated by Angle of repose (fixed funnel method) and Flow rate (mass per unit time). Each measurement was conducted in triplicate.

H. Moisture Content (Loss on Drying)

Moisture content was determined using a moisture analyzer at 60°C for 15 min. Results were expressed as % w/w.

I. Density Measurements

True density determined using a pycnometer, bulk density measured before tapping, tapped density measured after 2000 taps. Compressibility index and Hausner ratio can be derived to evaluate flow characteristics.

III. RESULTS AND DISCUSSION

A. Extraction Yield and Efficiency

The extraction process yielded 0.675 kg of dry extract (15.09% w/w), indicating efficient recovery of ethanol-soluble phytoconstituents. Ethanol is known to effectively extract semi-polar compounds such as terpenoids and flavonoids, supporting the observed yield (Lee *et al*., 2024).

B. Terpenoid Content

The terpenoid content was quantified at 2.9720 ± 0.0551% w/w with a low coefficient of variation (1.85%), indicating high analytical precision. This result confirms the presence of bioactive constituents potentially responsible for antimalarial activity. Terpenoids, particularly sesquiterpene lactones, are known to interfere with parasite metabolism, including inhibition of heme detoxification pathways (Ivanescu *et al*., 2015).

C. Particle Morphology and Surface Characteristics

SEM analysis revealed irregularly shaped particles with rough surfaces and size distribution of 10–50 µm (Figure 1).

The rough surface morphology is advantageous for increasing surface area, enhancing wettability, and potentially improving dissolution rate (Zeng *et al*., 2025). The homogeneous distribution of Cab-O-Sil indicates effective adsorption of liquid extract onto the carrier matrix (Iranvandi *et al*., 2023).

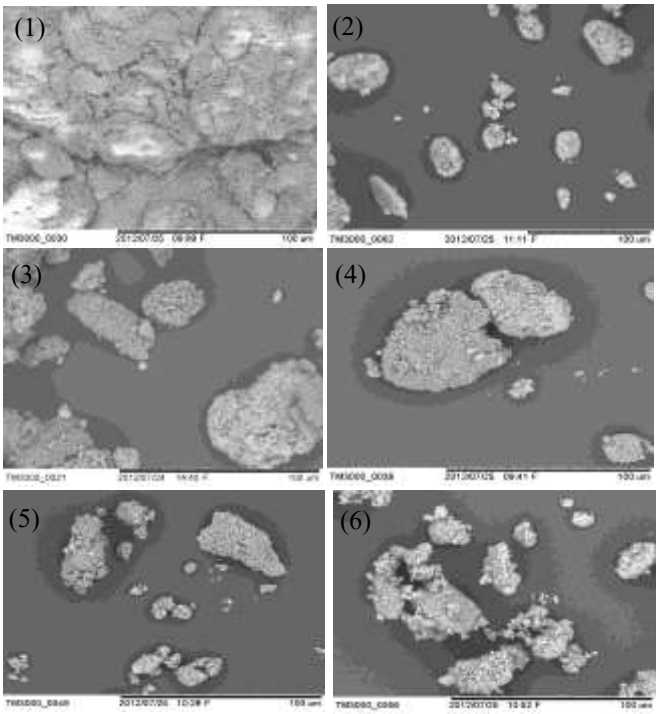

Figure 1. Morphology of dry extract particles of *Tithonia diversifolia* leaves as observed using SEM at 1000x magnification (1), Cab-o-sil (2), (3), (4), (5), and (6) are each dry extract, dry extract with the addition of Cab-o-sil 10, 20, 30 and 40% w/w

D. Flow Properties

The angle of repose ranged from 12.68° to 22.45°, indicating excellent to good flowability (<30°) (Table 1). However, flow rate decreased with increasing Cab-O-Sil concentration. Cab-O-Sil improves powder dispersion and reduces cohesion. However, its low density increases interparticle friction and reduces gravitational flow (Zheng *et al.*, 2024).

Table 1. Flow properties of *T. diversifolia* leaves dry extract

Cab-O-Sil (% w/w)	Angle of Repose (°)	Flow Rate (g/s)
10	12.68 ± 0.00	7.35 ± 0.41
20	21.14 ± 0.57	3.86 ± 0.63
30	21.64 ± 1.21	2.07 ± 0.31
40	22.45 ± 0.56	0.89 ± 0.63

This indicates a flowability–density trade-off, which is critical in selecting optimal excipient concentration during formulation.

E. Moisture Content

The moisture content ranged from 0.2–0.4% w/w (Table 2), indicating effective drying and low residual solvent/moisture content. Low moisture is essential to prevent microbial growth (Tapia *et al*., 2020), reduce hydrolytic degradation, and enhance shelf-life stability.

Table 2. Moisture content of *T. diversifolia* leaves dry extract

Cab-O-Sil (% w/w)	Moisture content (%)
10	0.200
20	0.401
30	0.266
40	0.200

F. Water Uptake Behavior

Maximum water uptake reached 9.47% at 21.5°C, indicating moderate hygroscopicity (Allada *et al*., 2016). This suggests that the extract requires moisture-protective packaging, inclusion of desiccants may be necessary. Cab-O-Sil likely contributes to moisture adsorption due to its high surface area.

G. Density and Compressibility

The true density (1.3589 g/mL) was significantly higher than bulk density (0.4215 g/mL), indicating high porosity. The tapped density (0.5093 g/mL) suggests moderate compressibility. The flowability and compressibility were evaluate based on Carr's Compressibility Index (CI) and Hausner ratio (H). Using these data, the CI and H values were 17.24% and 1.208, respectively. These values indicate that the extract is suitable for direct compression or wet granulation processes (Wakchaware *et al*., 2024.

H. Implications for Dosage Form Development

Based on the preformulation data good flowability supports manufacturability, moderate compressibility suggests need for binder optimization, hygroscopic nature requires controlled storage. Thus, the extract is a promising candidate for solid dosage forms, particularly tablets or capsules for antimalarial therapy.

CONCLUSION

The dry extract of *Tithonia diversifolia* demonstrates favorable physicochemical and micromeritic properties, supporting its suitability as a pharmaceutical raw material for solid dosage form development. These findings provide a critical foundation for further formulation and pharmacological optimization. bered.

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