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# Phytochemical Profile of *Calophyllum inophyllum L.* Leaf Extracts Using Different Solvents

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## ABSTRACT

The potential of plants as sources of medicine has long been utilized by traditional communities in Indonesia. *Calophyllum inophyllum* leaves are known to possess rich phytochemical reserves, yet the impact of solvent selection on metabolite recovery remains to be fully clarified. This study objective was to identify the phytochemical constituents of *C. inophyllum* leaf extracts obtained with different solvents and to evaluate their potential therapeutic applications based on solvent extraction efficiency. The dried *C. inophyllum* leaves were extracted via maceration using ethanol, ethyl acetate, as well as n-hexane. Qualitative phytochemical screening and quantitative assays for total phenols, tannins, flavonoids, and alkaloids were conducted in triplicate using colorimetric spectrophotometry. Statistical differences were investigated using one-way ANOVA followed by Duncan's test. The results show that ethanol extracts contained the highest concentrations of bioactive compounds. They include phenols (36.440 ± 2.479 mg GAE/g), tannins (50.928 ± 0.567 mg TAE/g), flavonoids (22.779 ± 0.765 mg QE/g), and alkaloids (14.173 ± 0.050 mg/g). As a polar solvent, ethanol was more effective at extracting phytochemicals compared to non-polar solvents. This study concludes that ethanol is the most effective solvent for maximizing bioactive recovery compounds from *C. inophyllum* leaves.

Keyword : *Calophyllum inophyllum L.* leaf; ethanol; ethyl acetate; hexane; phytochemical extraction

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## INTRODUCTION

Globally, periodontal diseases remain a major health concern. The WHO documented that periodontal disease was suffered by 10-15% of people worldwide; 80% of children and adolescents experience gingivitis, and nearly all adults have suffered from gingivitis, periodontitis, or both [1]. Gingivitis is an inflammatory condition of the gingiva, clinically characterized by swollen gums, redness, exudate formation, and alterations in gingival contour [2]. Bacterial accumulation within dental plaque causes it

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to mineralize and form calculus [2]. The biological potential of plants as sources of food and medicine has long been recognized and utilized by traditional communities in Indonesia [3]. In Indonesia, 48% of the population reported using ready-made traditional herbal preparations, 31.8% used traditional medicines for treatment, and 31.4% accessed traditional health services [4]. In Bali, medicinal plants are traditionally utilized in diverse forms, predominantly leaves (30.09%) prepared as *loloh* (33.8%) or *boreh* (23.61%) for a wide range of therapeutic purposes [5].

The most common management of gingivitis is dental scaling. Following scaling, mouth rinses are generally recommended [6]. Studies have demonstrated that mouth rinses hamper formation of plaque and reduce the severity of gingivitis [6], [7], [8]. Their mechanisms of action typically include bacterial cell disruption, degradation of plaque matrix enzymes, inhibition of bacterial aggregation, or prevention of bacterial adherence to tooth surfaces. *Calophyllum inophyllum L.* , belonging to the family *Clusiaceae*, is classified within a family comprising 20 genera and approximately 1,200 species. In Indonesia, this plant is widely distributed, especially in coastal areas, and produces a sticky resin that is either white or yellow [9]. *Calophyllum inophyllum L.* , or locally known as *nyamplung,* is a plant with multiple benefits for human health and daily life. It has traditionally been used as a source of fuel as well as in traditional medicine [10]. Among the diseases for which it is used are eye diseases, rheumatism, inflammation, and wounds [11].

*Calophyllum inophyllum L.* has attracted increasing attention for its rich content of secondary metabolites and broad pharmacological potential [12]. Previous studies have demonstrated that solvent selection significantly affects the solubility of the bioactive component [13]. For instance, a study evaluated the solvent-dependent phytochemical profile and activity of antibacterial of *Calophyllum inophyllum L.* flowers, highlighting the critical role of solvent polarity in extracting specific bioactive components [13]. This is due to compounds with different polarities exhibiting different solubility behaviors. However, the research focuses on the part of the flower. Another study on *Calophyllum inophyllum L.* reported the phytochemical compounds in it. Using the spectrophotometric method, the results revealed that the leaves contained 2.37% flavonoid, 7.68% tannin, and 2.53% polyphenol [14]. However, the study focused on a general phytochemical screening and identification of *Calophyllum inophyllum L.* leaves. Meanwhile, a study on *Calophyllum inophyllum L.* leaves investigated extraction of phenol and flavonoid from the leaves using acetone, ethanol, and methanol. Total phenolic content was acquired using 80% methanol in water [15]. However, this study focuses specifically on total phenolic and flavonoid contents. Meanwhile, a comprehensive profile using different solvents remains important to understand how varying solvent polarities influence the broader spectrum of secondary metabolites comprising saponins, alkaloids, tannins, and triterpenoids, which are equally crucial for therapeutic efficacy. Another study revealed the screening of *Calophyllum inophyllum L.* for its external bioactivity as an insect repellent and for antimicrobial activities, such as controlling mosquito larvae, aphids, fungi, and bacteria [16]. However, this study focuses on the antimicrobial activity against

pathogenic bacteria especially for insect. Study about the phytoconstituents of *Calophyllum inophyllum L.* using methanol as solvent found that it founds linoleic acid and methyl oleate at 32.25%, and at least of aminomethyl-dibenzosuberane at 0.28% [17]. These phytochemicals are expected to heal incurable diseases. However, the diversity and abundance of these phytochemicals are strongly influenced by extraction conditions, particularly solvent polarity and extraction strategy, and no mouth rinse to date has proven effective as a sole therapy [18]. A study has also revealed that *Calophyllum inophyllum L*. leaves have been identified the presence of flavonoids, tannins, saponins, phenols, alkaloids, and triterpenoids, which suggests *Calophyllum inophyllum L*. leaves as a promising bioactive compound [14], [15]. Nevertheless, the existing studies focus either on a single solvent extraction approach or target limited metabolite classes to obtain a comprehensive phytochemical profile of the leaves, especially for therapeutic applications based on solvent extraction efficiency.

Phytochemical screening is a preliminary test to identify the secondary metabolites present in natural products. This study performed *Calophyllum inophyllum L*. leaf extraction using three solvents of different polarities ethanol as polar, ethyl acetate as semi-polar, and n-hexane which is non-polar. This study aimed to identify the phytochemical constituents of *Calophyllum inophyllum L*. leaf extracts obtained with different solvents and to evaluate their potential as botanical therapeutic applications based on solvent extraction efficiency.

## METHODS

This study was conducted at the Agricultural Laboratory, Warmadewa University, from March 2025 to August 2025. Mature *Calophyllum inophyllum L.* leaves were collected as plant material. The leaves were gathered from Canggu Village, Badung, Bali, Indonesia, in March 2025. The plant was authenticated by a plant taxonomist, and the collected leaves were thoroughly washed. Extraction was carried out using analytical-grade ethanol, ethyl acetate, and n-hexane, while qualitative screening and quantitative assays (total phenolics, flavonoids, and tannins) were performed using standard phytochemical reagents, quercetin, and gallic acid standards [19], [20]. Essential equipment included standard laboratory glassware, an oven, a rotary evaporator, and a UV–Vis spectrophotometer (Libra S-60). The procedure after the leaves were collected, subsequently the leaves were washed thoroughly, sliced thinly, and subsequently at 50°C oven-dried in 48 hours. Fine powder were then grounded and saved in airtight glass containers. Maceration of 480 g of leaf powder was performed in 96% ethanol, ethyl acetate, and n-hexane (using a solvent volume sufficient to completely submerge the sample) at room temperature as long as 24 hours, protected from sunlight. Following filtration, the residues were re-macerated with fresh solvent for a total of two maceration cycles. Concentration of the combined filtrates was achieved via a vacuum rotary evaporator set at 45 °C under reduced pressure.

The *Calophyllum inophyllum L.* leaf extracts phytochemical screening was conducted using alkaloid, flavonoid, steroid, terpenoid, saponin, and tannin tests. Testing for alkaloid was executed by

mixing the extract with 3 drops of hydrochloric acid (HCl, 2 N), followed by 3 drops of Dragendorff's reagent. The presence of alkaloids was acknowledged when red or orange precipitates formed. The extract was treated with 3 drops of sodium hydroxide (NaOH). The appearance of an dense yellow color that disappeared upon adding 3 drops of sulfuric acid ($H_2SO_4$) indicated flavonoids. The steroid and terpenoid extracts were performed by mixing with 3 drops of chloroform, followed by 3 drops of Liebermann–Burchard reagent. Steroids were recognized by a bluish-green color, while terpenoids is known for a reddish-brown color. Briefly, 0.5 g of the extract was solubilized in 10 mL of heated water, allowed to cool, and thoroughly agitated for 10 seconds. Saponin was identified from the 1-10 cm height of stable foam for at least 10 min. The foam remained stable after the addition of hydrochloric acid (HCl, 2 N). Three drops of ferric chloride ($FeCl_3$, 1%) were used for the extract. A dark blue, bluish-black, or greenish-black coloration confirmed polyphenols and tannins. Quantitative determination of phytochemical constituents was conducted by laboratory staff at the Faculty of Agriculture, Warmadewa University. The analyses included total phenolic, flavonoid, tannin, and alkaloid contents. Folin–Ciocalteu method was used for detecting total phenolic content. Briefly, 0.01 g of extract was dissolved in 5 mL of citrate-phosphate buffer according to the respective treatment. The subsequent step was to pipette a 0.1 mL aliquot and mix it with 0.3 mL of 70% ethanol. 0.4 mL of Folin–Ciocalteu reagent was added. Incubation lasted for 6 minutes. Later, 4.2 mL of 5% $Na_2CO_3$ was added, vortexed, and incubated for 90 minutes. Measurement of absorbance was done using spectrophotometer at 760 nm wavelength. The readings were compared with a standard calibration curve prepared using gallic acid. Equation (1) was employed to calculate total phenolic content.

$$TPC = \frac{C \; x \; V \; x \; FP}{W} \tag{1}$$

Total phenolic content (TPC) was measured in mg GAE/ g extract, sample concentration was portrayed by C in mg/L, FP is the dilution factor, V is the sample volume in litres, and W means the sample weight (g). Figure 1 shows the standard curve for total phenolic content.

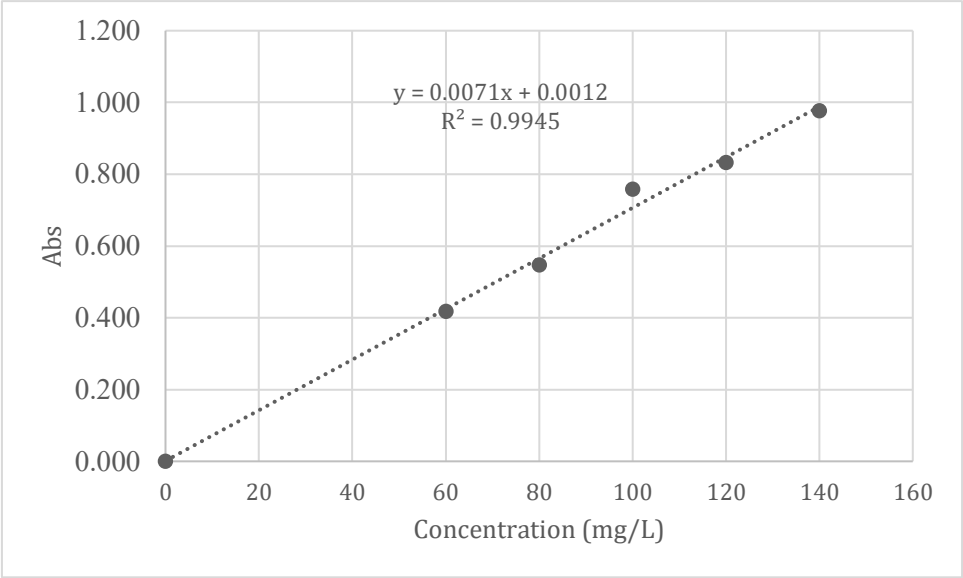



Figure 1. Gallic acid standard calibration curve for total phenolic quantification

Next, the total flavonoid content was determined spectrophotometrically using the $AlCl_3$ method. Briefly, a 0.01 g sample of extract was solubilized in 5 mL of citrate-phosphate buffer according to each experimental treatment. Subsequently, 4 mL of aquadest was mixed with 1 mL of sample and 0.3 mL of 10% $NaNO_2$. The incubation lasted for 5 minutes, followed by the addition of 0.3 mL of 10% $AlCl_3$ solution and 2 mL of 1% NaOH solution. The mixture was immediately analyzed using a spectrophotometer at a wavelength of 510 nm. A standard calibration curve was prepared using quercetin, stated in milligrams of quercetin equivalents per gram of extract (mg QE/g extract), calculated using Equation (1). Figure 2 shows the standard curve for flavonoids.

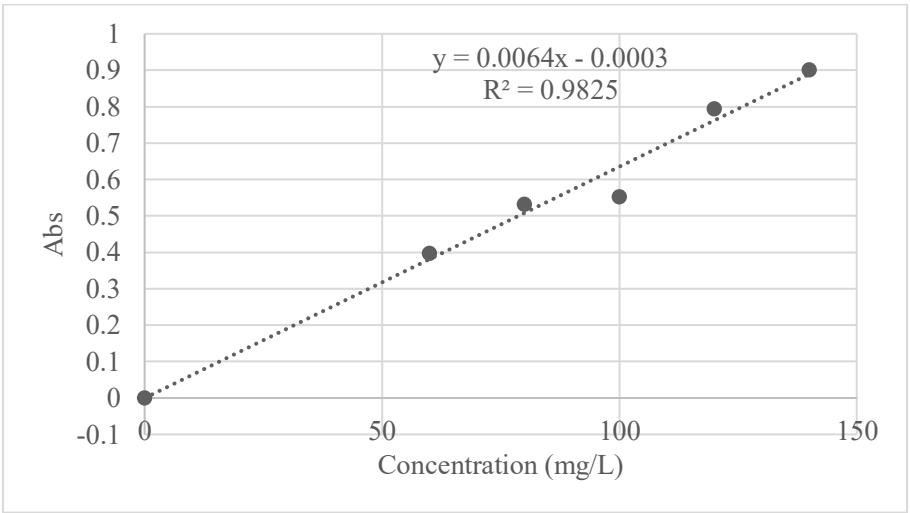



Figure 2. Quercetin standard calibration curve for total flavonoid content

The total tannin content used the Folin–Denis method. Briefly, 0.01 g of extract was dissolved in 5 mL of citrate-phosphate buffer. A 0.25 mL aliquot of the diluted sample was pipetted and mixed with 0.25 mL of Folin–Denis reagent. The mixture was vortexed, followed by the addition of 2 mL of

5% $Na_2CO_3$ solution. The mixture incubation run for 30 minutes after vortexed. The measurement of absorbance was performed at a wavelength of 725 nm. The total tannin content was expressed in mg TAE/g extract, using Equation (1) to calculate. Figure 3 shows the standard curve for total tannin content.

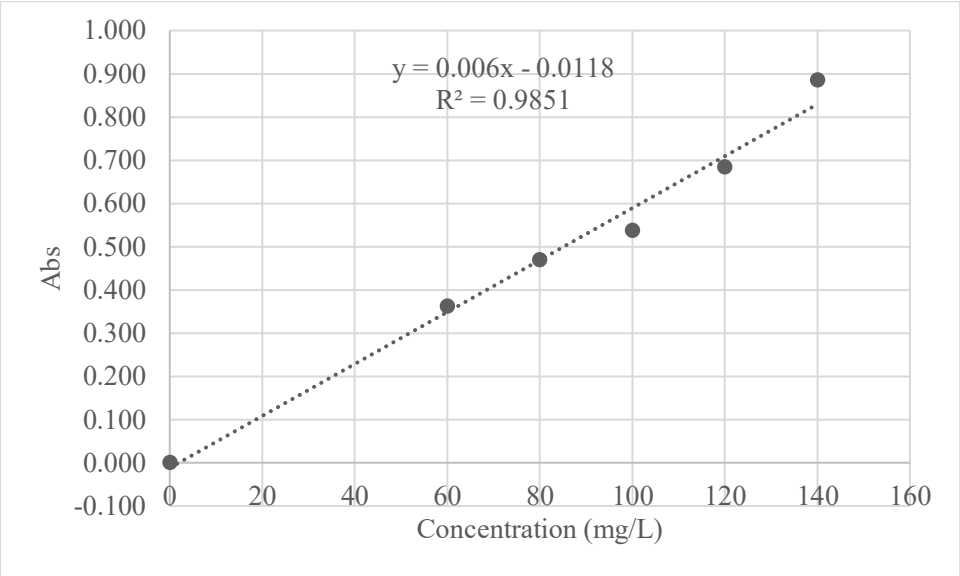



Figure 3. Tannic acid standard calibration curve for total tannin content

The determination of total alkaloid content was performed by concentrating the filtered extract using a hot plate under constant stirring at 50 °C. 25 mL of 2% HCl was added with concentrated extract as well as a 25 mL of n-hexane, followed by extraction using a 250 mL separatory funnel. The hydrochloric acid fraction was collected and adjusted to pH 9 by adding 35% (w/w) ammonium hydroxide. Subsequently, 25 mL of chloroform was added, and the mixture was extracted using a 250 mL separatory funnel. The chloroform extraction was repeated twice. The combined chloroform fractions were then evaporated to dryness to obtain the total crude alkaloid residue from the *Calophyllum inophyllum L.* leaves. The total alkaloid content was calculated using a gravimetric method according to the weight of the crude alkaloid residue obtained with Equation (2).

$$Total\ alkaloid\ content\ (\%) = \frac{W_1}{W_0} x100\% \quad (2)$$

where $W_1$ is the weight of crude alkaloids obtained in grams, and $W_0$ is the initial weight of the extract used in grams. Data obtained from qualitative and quantitative analyses were processed descriptively. Data are expressed as mean ±standard deviation (SD). Prior to one-way analysis of variance (ANOVA), the data were checked using the Shapiro-Wilk test and Levene's test for homogeneity to ensure

assumptions were met. Differences were considered statistically significant at $p < 0.05$, then by Duncan's multiple range test for post-hoc comparisons using SPSS version 24.

## RESULT

The extraction of *Calophyllum inophyllum* was performed as a single preparative batch for each solvent. The extraction yields are displayed in Table 1.

Table 1. *Calophyllum inophyllum* leaf extracts

| No | Extract Type | Yields (%) |
|---|---|---|
| 1 | Ethanolic extract | 13.88 |
| 2 | Ethyl acetate extract | 6.47 |
| 3 | N-hexane extract | 2.35 |

The ethanolic extract showed the highest yield at 13.88%, followed by the ethyl acetate extract at 6.47%, and the n-hexane extract at 2.35%.

Table 2. Phytochemicals of *Calophyllum inophyllum L.* leaf extracts

| Phytochemicals | Extracts | | |
|---|---|---|---|
| | Ethanol extract | Ethyl acetate extract | *n*-hexane extract |
| Alkaloids | Positive | Positive | Negative |
| Phenolics | Positive | Positive | Positive |
| Tannins | Positive | Positive | Positive |
| Flavonoids | Positive | Positive | Negative |
| Steroids | Negative | Negative | Negative |
| Triterpenoids | Negative | Negative | Negative |
| Saponins | Negative | Negative | Negative |

Table 2 shows results that demonstrate ethanolic and ethyl acetate extracts tested positive for alkaloids, phenolics, tannins, and flavonoids, while the n-hexane extract was positive only for phenolics and tannins. Meanwhile the steroid, triterpenoid, and saponin resulted in negative. Regarding the negative results for steroids, triterpenoids, and saponins across all extracts, this outcome is attributed to the specific phytochemical profile and biosynthetic pathways of *Calophyllum inophyllum L.* leaves, which are predominantly rich in phenolic compounds, flavonoids, tannins, and specialized lipids or coumarins rather than triterpenoids or saponins.

The phytochemical compounds identified as positive in the preliminary screening of *Calophyllum inophyllum L.* leaf extracts using different solvents were further analyzed quantitatively. The compounds assessed included phenols, tannins, flavonoids, and alkaloids.

Table 3. Analysis of variance (ANOVA) of *Calophyllum inophyllum L.* leaf extracts

| Phytochemical compound | $F_{(2,6)}$ | p-value |
|---|---|---|
| Phenolics | 559.46 | <0.001 |
| Tannins | 13,443.14 | <0.001 |
| Flavonoids | 2,335.34 | <0.001 |
| Alkaloids | 105,560.67 | <0.001 |

Table 3 reveals that the ANOVA results indicated that solvent type significantly influenced the concentrations of phenols, tannins, flavonoids, and alkaloids in the extracts ($p < 0.05$).

Table 4. Quantitative analysis of phenols, tannins, flavonoids, and alkaloids in *Calophyllum inophyllum L.* leaf extracts obtained with ethanol, ethyl acetate, and hexane

| Extracts | Phytochemicals | | | |
|---|---|---|---|---|
| | Phenols (mg GAE/g) | Tannins (mg TAE/g) | Flavonoids (mg QE/g) | Alkaloids (mg/g) |
| Ethanol extract | 36.440±2.479[a] | 50.928±0.567[a] | 22.779±0.765[a] | 14.173±0.050[a] |
| Ethyl acetate extract | 3.538±0.491[b] | 6.226±0.428[b] | 1.591±0.191[b] | 1.507±0.051[b] |
| n-hexane extract | 0.425±0.130[b] | 0.361±0.083[c] | not detected | not detected |

**Note:** Means in different superscript letters (a, b, c) in same column shows significantly different $p<0.05$, whereas values sharing the same superscript letter (ethyl acetate and n-hexane for phenols) are not significantly different based on Duncan's multiple range test

Table 4 shows that the ethanol extract consistently demonstrated the highest concentration across all tested phytochemicals, yielding 36.440 ± 2.479 mg GAE/g of phenols, 50.928 ± 0.567a mg TAE/g of tannins, 22.779 ± 0.765a mg QE/g of flavonoids, and 14.173 ± 0.050a mg/g of alkaloids. Meanwhile, the ethyl acetate extract yielded significantly lower amounts of these compounds, while the n-hexane extract was the least effective, showing negligible to undetectable levels of all phytochemicals, particularly flavonoids and alkaloids, which were not detected.

Table 5. Phytochemical content expressed per gram of dry leaf *C. inophyllum* powder

| Extract | Phenols(mg GAE/g dry leaf) | Tannins(mg TAE/g dry leaf) | Flavonoids(mg QE/g dry leaf) | Alkaloids(mg/g dry leaf) |
|---|---|---|---|---|
| Ethanol extract | 5.060 | 7.069 | 3.162 | 1.967 |
| Ethyl acetate extract | 0.229 | 0.403 | 0.103 | 0.098 |
| n-hexane extract | 0.010 | 0.008 | not detected | not detected |

To provide a fair comparison of extraction efficiency relative to the raw plant material, phytochemical contents were also evaluated per gram of dry leaf powder (calculated by multiplying extract content by extraction yield). The results in Table 5 confirmed that the ethanol extract yielded significantly higher quantities of all active constituents per gram of dry leaf compared to ethyl acetate and $n$-hexane extracts, reinforcing ethanol as the superior solvent for recovering bioactive compounds from *C. inophyllum* leaves

## DISCUSSION

The extraction and phytochemical profile of *Calophyllum inophyllum L.* leaves were heavily dependent on the polarity of the extraction solvents. Across all evaluated phytochemical groups containing comprising phenolics, tannins, flavonoids, and alkaloids, polar extraction using ethanol consistently achieved the highest recovery, followed by the ethyl acetate, while the non-polar n-hexane extract exhibited the lowest or non-detectable concentrations. Ethanol, being a polar solvent, is highly effective in dissolving phenolic compounds, which are generally polar due to the presence of hydroxyl groups which forms hydrogen bonds to polar solvents [21]. Consequently, ethanol extracted a significantly higher phenolic content compared with ethyl acetate and hexane. In addition, ethanol is often used in aqueous mixtures, which enhances the solubility of polar compounds such as phenolics and improves extraction efficiency. Besides polarity, viscosity and surface tension matters. Viscosity and surface tension are among the important factors because values which is lower, can enhance the plant matrix penetration. Even so, the performance depends strongly on the temperature that require optimization for efficiency [22]. Ethanol exhibits favorable transport properties and optimal diffusion coefficients, facilitating rapid cellular diffusion and the release of intracellular solutes.

The highest tannin content was also detected in the ethanol extract while the lowest was identified in hexane extract. The ethyl acetate extract yielded a tannin concentration higher than hexane but lower than ethanol. Ethyl acetate, being semi-polar, can dissolve certain semi-polar compounds, including some tannins. However, ethanol, with its higher polarity, is more effective in extracting polar tannins compared with ethyl acetate or hexane, the latter being non-polar and generally ineffective for tannin extraction [23].

For flavonoids, the ethanol extract again yielded the highest content. No flavonoids were detected in the hexane extract. Flavonoids are polyphenolic compounds that are typically polar due to their hydroxyl (-OH) groups, which readily form hydrogen bonds with polar solvents [22]. Ethyl acetate, being semi-polar, can dissolve certain flavonoids, especially those with lower polarity or methoxyl substituents [24]. However, its efficiency is much lower than ethanol, as not all polar flavonoids are soluble in semi-polar solvents [25]. Hexane is unable to dissolve flavonoids, which explains their absence in the hexane extract.

The results demonstrate that the influences of solvents exist and bring differences in the phytochemical composition of *C. inophyllum* leaf extracts. No alkaloids were detected in the hexane extract. Alkaloids are generally polar to semi-polar compounds due to the presence of nitrogen groups, which enable hydrogen bonding or ionic interactions with polar solvents [26]. Ethanol, being polar, is highly effective at dissolving alkaloids, explaining the highest concentration in the ethanol extract.

The extraction trends observed are strongly coherent with previous investigations on *Calophyllum* species. The phytochemical profile and the dominant presence of polar active constituents in *C. inophyllum* leaves align with the foundational work that verified the presence of key secondary metabolites including phenolics, flavonoids, and tannins in the leaf [14]. Furthermore, the clear superiority of polar solvents in maximizing the recovery of polyphenolic compounds, where the optimization study on *C. inophyllum* leaves demonstrated that solvent polarity is the decisive factor in extraction yield of phenolic and flavonoid fractions [15]. Although previous research focused on *Calophyllum inophyllum L.* flowers rather than leaves using various organic solvents, their findings similarly highlighted that polar solvent systems yield significantly richer bioactive profiles, reinforcing the consistent phytochemical behavior across different plant parts and the broader *Calophyllum* genus [13].

The results suggest that the majority of the targeted phytochemicals in *C. inophyllum* leaves are polar in nature, making ethanol the most efficient solvent for their extraction among ethyl acetate and n-hexane. The overall trend across all phytochemical groups (phenols, tannins, flavonoids, and alkaloids) indicates that ethanol consistently extracted the highest concentrations, followed by ethyl acetate, with hexane yielding the lowest or non-detectable levels. This finding supports the principle that polarity has a pivotal role in the extraction of phytochemicals. Ethanol, as a polar solvent, has a strong affinity for phenolic compounds, tannins, flavonoids, and alkaloids, which generally contain polar functional groups such as hydroxyl (-OH) or nitrogen atoms [27].

This study provides valuable insights into the solvent-dependent phytochemical extraction of *Calophyllum inophyllum L.* leaves. Nevertheless, limitation should be acknowledged. The quantitative evaluation was limited to major phytochemical classes (phenolics, tannins, flavonoids, and alkaloids) using colorimetric spectrophotometric assays, which do not resolve individual molecular structures. Advanced chromatographic and mass spectrometric profiling (such as LC-MS or GC-MS) is required to identify specific monomeric constituents. Besides, direct *in vitro* or *in vivo* bioactivity evaluations were not conducted.

## CONCLUSION

This study concludes that solvent polarity plays a pivotal role in recovering bioactive constituents from *Calophyllum inophyllum L.* leaves. These findings highlight ethanol as the most effective solvent for maximizing the bioactive compounds recovery from *C. inophyllum* leaves. Due to

its high polarity and favorable physicochemical properties, ethanol successfully maximized the recovery of major phytochemical groups, whereas less polar solvents yielded minimal or non-detectable amounts. Future research should incorporate advanced chromatographic profiling, such as LC-MS or GC-MS, for precise individual compound identification, explore alternative green solvent systems, and conduct comprehensive bioactivity assays to establish the therapeutic potential of these extracts.

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