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Variation of morphological characteristics, total phenolic, and total flavonoid in *Adenostemma lavenia*, *A. madurense,* and *A. platyphyllum*

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Abstract. *Nurlela, Nurfalah R, Ananda F, Ridwan T, Ilmiawati A, Nurcholis W, Takemori H, Batubara I. 2022. Variation of morphological characteristics, total phenolic, and total flavonoid in* Adenostemma lavenia, A. madurense, *and* A. platyphyllum. *Biodiversitas 23: 3999-4005. Adenostemma* has long been used as a herbal medication. Despite some studies regarding the morphology and potency of *Adenostemma* carried out, the variation of morphological traits, total phenolic content (TPC), and total flavonoid content (TFC) on different species of *Adenostemma* has been poorly investigated. This study was designed to observe the morphological characteristics, TPC, and TFC of *Adenostemma lavenia*, *A. madurense*, and *A. platyphyllum*. Morphological characteristics were observed using qualitative and quantitative parameters. The colorimetric method determined TPC and TFC in plant leaf ethanol extracts. The plants were morphologically diverse, which significant variation among the three species in plant height, length and width of leaf, and internodes distance. Morphological traits such as leaf length and width, plant height, and internodes distance significantly correlate with phenolic and flavonoid content in *Adenostemma*. These may be used as important selection criteria in *Adenostemma* for obtaining high phenolic and flavonoid content. The study revealed that different species of these plants with varying morphological traits substantially impact the content of their chemical compounds. The highest TPC and TFC were found in *A. lavenia*, suggesting that it is potentially an alternative source of bioactive compounds as herbal medicine.

Keywords: *Adenostemma*, bioactive, correlation, herbal medicine, qualitative, quantitative

INTRODUCTION

Herbal medicines have been defined by the World Health Organization (WHO) as finished, labeled pharmaceutical products containing an active substance, aerial or underground of the plant, or other plant material or mixtures (Parveen et al. 2015). To produce herbal medicine, the bioactive extract should be standardized based on the active compound and subjected to restricted safety testing. The active compound is directly tied to the bioactivities or efficacy of herbal medicine (Khan and Ahmad 2019). If it is consumed properly, herbal medicine has a high efficacy with low side effects (Ocktarini et al. 2011).

Asteraceae Bercht. & J. Presl is the second largest family in the world, with around 1623 genera and 24,700 species (Wu et al. 1994; Funk 2009; Christenhusz and Byng 2016). Asteraceae have been used for a long time for traditional medicine and food (Valentin-Silva et al. 2016; Sabir et al. 2017; Laldingliani et al. 2022). More than 30 species of *Adenostemma* J. R. et G. Forst (tribe Eupatorie) are found in Asia, Africa, Australia, America, and numerous oceanic islands (Koyama et al. 2016). *Adenostemma lavenia* (L.) O. Kuntze usually grows wild, even considered a weed. *A. lavenia*, also known as sticky daisy, grows widely in tropical Asia. *A. lavenia* can be found in almost every province in Indonesia, but it is not widely cultivated. In Java, it is known as legetan warak (Batubara and Prastya 2020a). Backer and Bakhuizen van den Brink (1965) were successful in identifying Java's plant species and recognized *A. lavenia*. They described *A. lavenia* as a glandular-hairy or subglabrous stem; ovate, obtuse or acute apex, dentate or serrate leaves; grows in humid environments, areas with some shade, woodlands, brushwood, ditches, and along the roadside. The other species of *Adenostemma* are *A. madurense* and *A. platyphyllum*. *Adenostemma madurense* in Korea, as reported by Koyama (2001), has leaves that range in shape from oblong-ovate to lanceolate and have dentate-serrate margins. Its achenes are also robustly tuberculate or muricate. According to Blair and Madrigal (2005), *A. platyphyllum* that grows in Colombia has an erect stem, broadly ovate leaves with a rough leaf surface, and white flowers. Meanwhile *A. madurense* and *A. platyphyllum* in Indonesia have not been well characterized.

Adenostemma lavenia is widely used as a medicinal herb to treat pneumonia, fever, hepatitis, inflammation, and skin wounds (Chen et al. 2019). Because *A. lavenia* leaves

contain various secondary metabolites such as terpenoids, flavonoids, alkaloids, polyphenols, and essential oils, they are frequently utilized (Batubara and Prastya 2020b). Different species of *Adenostemma*, which have morphological traits similar to *A. lavenia*, such as *Adenostemma madurense* and *Adenostemma platyphyllum*, have been found to possess bioactive chemicals with antibacterial, anti-inflammatory, and antioxidant properties (Prasad et al. 2013; Maeda et al. 2022).

Plant phenolic compounds, including flavonoids, are the secondary metabolites that contribute the most to antioxidant, antibacterial, anti-inflammatory, and anticancer activities (Kaur and Mondal 2014; Elisha et al. 2016; Teixeira et al. 2017; Akhtar et al. 2018). The concentration of the active compound in a plant varies based on the species, growing region, harvest time, and plant sections used (Khumaida et al. 2019; Ren et al. 2020; Suryani et al. 2022). Konieczynski et al. (2016) found that medicinal plants differed in their chemical composition, enormously depending on plant species, regardless of the origin. Eight species of *Tulbaghia* exhibited diverse phenolic and flavonoid content, resulting in different antioxidant properties (Takaidza et al. 2018).

There is still limited information on the morphological traits of *Adenostemma* plants, as well as their phenolic and flavonoid content. Therefore, it is meaningful to investigate the variation of morphology traits in different *Adenostemma* species, and their relation to phenolic and flavonoid compounds. This study aims to observe the qualitative and quantitative morphological characteristics, and phenolic and flavonoid content of three species of *Adenostemma*, i.e. *A. lavenia*, *A. madurense*, and *A. platyphyllum*. This study will be the first to report and expect to obtain useful information about various species of *Adenostemma* with different morphological traits that substantially impact the content of their chemical compounds, such as phenolic and flavonoid.

MATERIALS AND METHODS

Plant material

Three species of *Adenostemma* used in this study were *A. lavenia, A. madurense, A. Platyphyllum*, collected from Biopharmaca Conservation and Cultivation Station, Tropical Biopharmaca Research Center, Bogor Agricultural University (IPB). The identification of these plants was carried out by the curator of herbarium Bandungense (FIPIA) SITH ITB. Voucher specimens were deposited at herbarium Bandungense (FIPIA) SITH ITB under collection numbers FIPIA-DEP32 (*A. lavenia*), FIPIA-DEP33 and 34 (*A. madurense*), FIPIA-DEP35, 36, and 37 (*A. platyphyllum*).

Field experiment

The field experiment was conducted at the Biopharmaca Conservation and Cultivation Station, Tropical Biopharmaca Research Center, Bogor Agricultural University (IPB), West Java, Indonesia, from March-April 2022 (6°32'25.47" N and 106°42'53.22" E, at 142.60 m altitude). The experiment was set in a randomized complete block design with three replication for each species. Plants were grown in the same conditions by stem cutting in the latosol soil with pH of 4.69, organic C of 2.05, N of 0.20%, P of 8.0 ppm, plants spacing 30 x 30 cm, and treated with no fertilizer. The plants were harvested after six weeks after planting.

Morphology observation

Morphology characters observed were: plant height, number of leaves, leaf length, leaf width, number of branches, and distance between nodes.

Total phenolic content

Total phenolic content was measured according to Batubara et al (2020). Briefly, 10 µL of leaves extract solution was mixed with 10 µL of 10% Folin–Ciocklteu reagent, 20 µL of 10% Na_2CO_3, and 150 µL of aquabidest were added to the microplate well. After homogenization, the mixture was incubated at room temperature for 30 minutes. The absorbances were determined at 750 nm using a microplate reader (Epoch Biotek, Winooski, VT, USA). The phenolic content was measured in milligrams of gallic acid equivalent per gram of dried extract (mg GAE/g DW) using a gallic acid calibration curve. All samples were determined in triplicate.

Total flavonoid content

Total flavonoid content (TFC) was determined according to Batubara et al. (2020), 60 µL of leaves extract solution was added to the microplate well, along with 10 µL of 10% $AlCl_3$, 10 µL of CH_3COOK, and 120 µL of aquabidest. Then, the sample solution was homogenized and incubated for 30 minutes at room temperature. The measurement of absorbances using a microplate reader at 415 nm. The quercetin standard was used to generate a calibration curve, and total flavonoid content was determined as milligrams of quercetin equivalent per gram of dried extract (mg QE/g DW). The total flavonoid content of all samples was analyzed in triplicate.

Data analysis

The data of morphology characters, total phenolic content, and total flavonoid content were subjected to ANOVA followed by Duncan's Multiple Range Test (DMRT), the correlation between morphology characters and total phenolic content, and also total flavonoid content was analyzed using the Statistical Tool for Agricultural Research (STAR) 2.0.1.

RESULTS AND DISCUSSION

Qualitative characters

The qualitative traits of three species of *Adenostemma* i.e. *A. lavenia*, *A. madurense*, *A. platyphyllum* were observed and presented in Figure 1. The roots of all species exhibited the same type of fibrous root. All three species of *Adenostemma* have herbaceous, erect and branched stems but are slightly different in colour. *Adenostemma lavenia*

and *Adenostemma madurense* have a green stem, whereas *A. platyphyllum* has purplish-green stems. In addition, the number of branches and internodes distance showed various results as evaluated on quantitative characters in the following discussion. All species have opposite leaves, petiolate or sessile, base attenuate, margins coarsely dentate, serrate or biserrate, acuminate or acute apex, pinnate leaf venation. However, the differences were *A. lavenia* has ovate, slightly shiny in the upper part, and light green leaves, *A. madurense and A. platyphyllum* have broadly ovate or ovate-oblong, slightly rough in the upper part. Also, *A. platyphyllum* has darker green leaves than two other species. Inflorescence terminal, corymb or panicle, involucral bracts obtuse; heads many white-flowered and sticky, 4-8 mm long for *A. lavenia* and *A. madurense*, 3-5 mm long with smaller diameter, purplish-white or yellowish-white flowered for *A. platyphyllum*. Corolla campanulate-funnel shaped, small flowers, floret zygomorphic, calyx modified into pappus.

Quantitative characters

The quantitative traits of three species of *Adenostemma* significantly varied ($p \leq 0.05$) for plant height, leaf length, leaf width, and internodes distance (Table 1). However, the number of leaves and branches of all species showed a non-significant difference. *Adenostemma platyphyllum* exhibited the highest plant height of 30.80 cm and had the longest internodes distance of 8.10 cm, significantly different from the other two species. *A. madurense* displayed the longest (13.63 cm) and widest (7.13 cm) leaf, significantly different from the other two species. *A. madurense and A. platyphyllum* have broadly ovate or ovate-oblong as observed in qualitative morphology characters (Figure 1). At the same time the leaf width of *A. lavenia* was not significantly different from that of *A. platyphyllum*.

Total phenolic and total flavonoid content

Variations in total phenolic and total flavonoid contents of three species of *Adenostemma* are shown in Table 2. A significant difference was detected between *A. lavenia* and *A. madurense*, *A. platyphyllum* for phenolic content. The highest total phenolic content (14.40 mg GAE/g DW) was analyzed in *A. lavenia*, significantly different from *A. madurense* and *A. platyphyllum*. Whereas the *A. madurense* had the lowest total phenolic content (4.51 mg GAE/g DW) but was not significantly different from *A. platyphyllum* (5.01 mg GAE/g DW).

Adenostemma lavenia has a total flavonoid content (4.73 mg GAE/g DW) that is not significantly different from *A.madurense* (4.74 mg GAE/g DW). Whereas, *A. platyphyllum* had the lowest total flavonoid level (3.48 mg GAE/g DW).

Discussion

The morphological characteristics of *A. lavenia* reported in this study were similar and relatively consistent with those described by Backer and Bakhuizen van den Brink (1965), Tjitrosoedirjo (2002), and Orchard (2011). Backer and Bakhuizen van den Brink (1965) described *A. lavenia* in Java, Indonesia has heads 3-7 mm long, 5-7 mm in diameter, in lax corymbs, involucral bract obtuse with scattered glands, corolla 1-2 mm, campanulate-funnel-shaped; stem glandular-hairy or subglabrous; leaves ovate with a narrowed base and an acuminate, obtuse or acute apex, dentate or serrate, sometimes biserrate. In addition, Tjitrosoedirdjo (2000) recognized three species of *Adenostemma* in Sumatera, Indonesia. Based on her key and description, *A. lavenia* is distinguished from the other two species by having a corolla that is 1.5 to 2 mm long, an obconical, 5-lobed limb, and glandular tissue, especially in the lower section. Moreover, Orchard (2011) reported that Australian *A. lavenia* is an annual or perhaps perennial herb that grows to approximately 60 cm tall and thrives in open areas with lots of shade and damp conditions. The stems are branching, the leaves are ovate or narrowly ovate to lanceolate, serrated, upper surface dull or slightly shiny when dried, densely muricate when mature, and sometimes also sparsely glandular.

Table 1. Morphology characters (quantitative traits) of three species of *Adenostemma*

Species	Plant height (cm)	Number of leaves	Leaf length (cm)	Leaf width (cm)	Number of branches	Internodes distance
A. lavenia	25.83^{b}	29.67^{a}	6.20^{c}	3.67^{b}	3.33^{a}	4.80^{b}
A. madurense	20.83^{c}	23.67^{a}	13.63^{a}	7.13^{a}	4.00^{a}	2.47^{c}
A. platyphyllum	30.80^{a}	29.67^{a}	9.27^{b}	5.37^{b}	3.67^{a}	8.10^{a}

Note: Different superscripts among mean values in the column indicated a significant difference ($p \leq 0.05$)

Table 2. Variation in total phenolic and total flavonoid contents of three species of *Adenostemma*

Species	Total phenolic content (mg GAE/g DW)	Total flavonoid content (mg QE/g DW)
A. lavenia	14.40^{a}	4.73^{a}
A. madurense	4.51^{b}	4.74^{a}
A. platyphyllum	5.01^{b}	3.48^{b}

Note: Different superscripts among mean values in the column indicated a significant difference ($p \leq 0.05$)

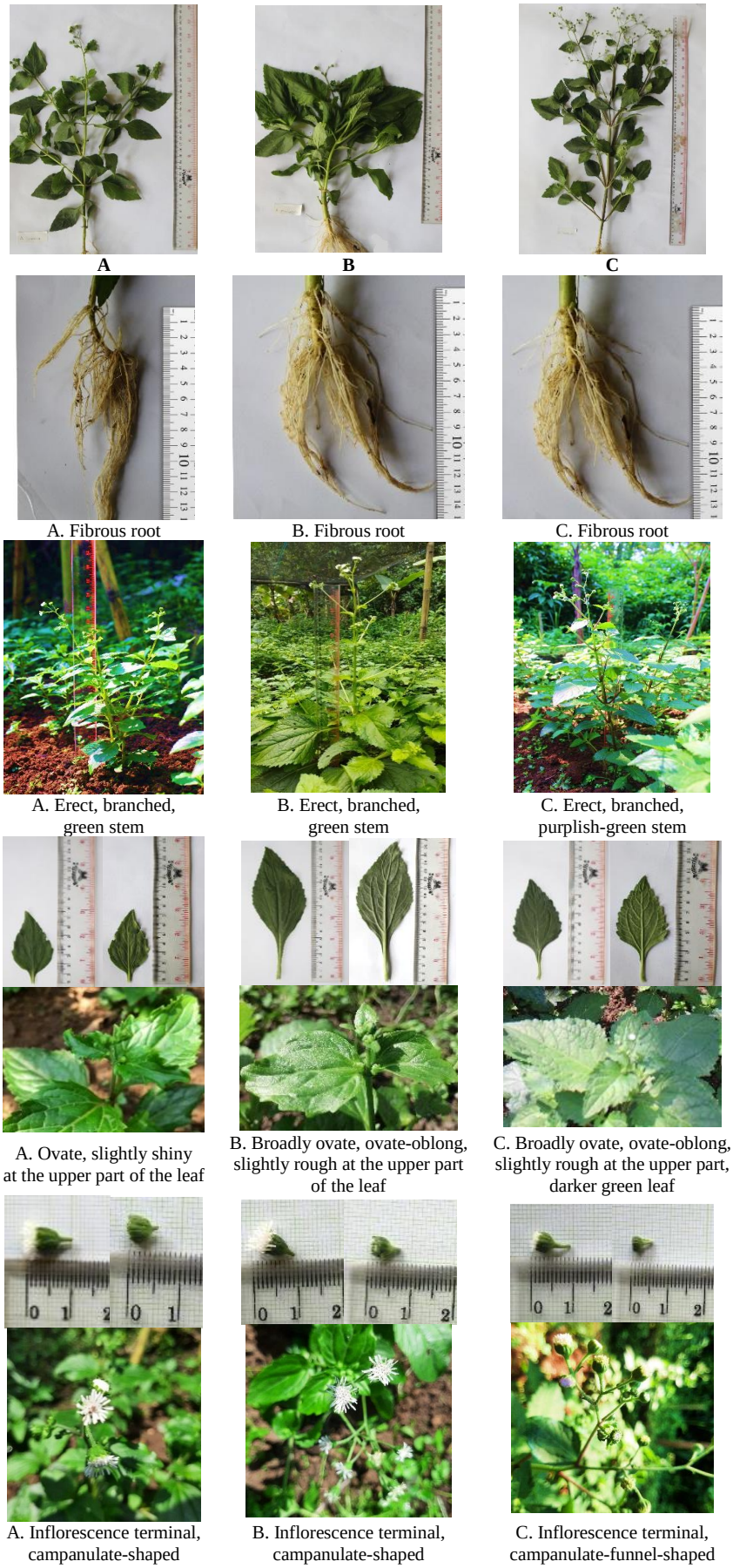

Figure 1. Variation in the qualitative morphology of *Adenostemma*. A. *A. lavenia*, B. *A. madurense*, C. *A. platyphyllum*

Table 3. Correlation coefficients among morphology characters, total phenolic content, and total flavonoid content of three species of *Adenostemma*

Correlations	TPC	TFC	Plant height	Number of leaves	Leaf length	Leaf width	Number of branches	Internodes distance
Total phenolic content (TPC)	1							
Total flavonoid content (TFC)	0.470	1						
Plant height	0.005	-0.852**	1					
Number of leaves	0.361	0.009	0.331	1				
Leaf length	-0.733*	0.052	-0.444	-0.314	1			
Leaf width	-0.751*	-0.029	-0.413	-0.364	0.863**	1		
Number of branches	-0.070	0.113	0.011	0.539	0.317	0.209	1	
Internodes distance	-0.018	-0.847**	0.926**	0.288	-0.458	-0.362	-0.030	1

Note: * Correlation is significant at the 0.05 level (2-tailed); ** Correlation is significant at the 0.01 level (2-tailed)

Characteristics of the morphology of *Adenostemma madurense* were similar to the qualitative and quantitative traits that were recorded by Koyama et al. (2002) and Jeong et al. (2017), that *A. madurense* is morphologically distinguished from *A. lavenia* by the characteristics of a plant height of 30-150 cm. The leaves are ovate or ovate-oblong with a length of 15-21 cm, and a width of 7-12 cm, the upper surface of the leaves is slightly rough. *A. madurense* is generally found in moderately dry areas, such as mountain slopes and forests, while *A. lavenia* is usually found in humid areas.

Adenostemma platyphyllum Cass is an annual herbaceous plant, erect, up to 100 cm tall, petiole up to 8 cm, leaves opposite, broadly ovate up to 18 cm long and up to 13 cm wide, rough leaf surface, white flowers, with slightly purple leaves (Blair and Madrigal 2005). These morphological characteristics are identical to those described in this study for *A. platyphyllum*.

Plant species, environmental, and growing conditions have a significant impact on bioactive compounds (Ezez and Tefera 2021; Chumroenphat et al. 2021). Because the current investigation was carried out in the same environment and under the same growing conditions, a genetic variation in different species could be a main contributing factor in total phenolic and flavonoid content variation. Phenolic compounds are the most abundant secondary metabolites in plants. Plant phenolics are thought to play a significant role as defensive compounds when environmental stresses, such as strong light, low temperatures, pathogen infection, herbivores, and nutrient deficiency, can lead to increased formation of free radicals and other oxidative species in plants (Lattanzio 2013). Flavonoids are the most represented group of phenolic compounds, and come in a variety of forms, including aglycones, glycosides, and methylated derivatives (Kumar and Pandey 2013; Ahmed et al. 2016). Flavonoids and other phenolic compounds have been reported as effective antioxidants, anti-inflammation, antibacterial, anticancer, cardioprotective agents, immune system boosting, skin protection from UV radiation, and fascinating candidate for pharmaceutical and medical use (Svobodova et al. 2017; Tungmunnithum et al. 2018; Złotek et al. 2019).

Many reports on chemical compounds and bioactivity of plants belonging to the Asteraceae family have been published. However, information on *Adenostemma* is still limited. Leaves of *A. lavenia* are widely utilized because they contain a variety of secondary metabolites such as terpenoids, flavonoids, alkaloids, and polyphenols, as well as essential oils (Batubara and Prastya 2020b). *A. lavenia* contains phenolic and flavonoid compounds that have the potency as an anti-inflammatory by inhibiting COX-2 activity (Iswantini et al. 2021). The present study (Table 2) showed that *A. lavenia* has the highest total phenolic content (TPC). In comparison to *A. lavenia*, there are fewer reports of secondary metabolites in *A. madurense*. In this current study, *A. madurense* had the lowest TPC. According to (Maeda et al. 2022), *A. madurense* contains terpenoids, specifically kaurenoic acid, which possesses anti-inflammatory, antimelanogenic, and antioxidant properties. On the other hand, *A. platyphyllum* has a higher TPC than total flavonoid content (TFC). This finding was similar to the metabolite profiling analysis reported by Fauzan et al. (2018). They recorded that the main compound of *A. platyphyllum* is a phenolic compound. The study conducted by Moncayo et al. (2021) showed that *A. platyphyllum* contains a phenolic and flavonoid compound with a great antioxidant capacity. In this study (Table 2), the phenolic and flavonoid content of different species exhibited varied results. This finding was similar to Praptiwi et al. (2021), in that the total phenolic and flavonoid content varied in the three species of Rubiaceae.

Correlations between the evaluated morphology traits, TPC and TFC of *A. lavenia*, *A. madurense*, and *A. platyphyllum* were given in Table 3. Results exhibited a negative and significant ($p \leq 0.05$) correlation between leaf length, leaf width and TPC. The longer and broader the leaves of *A. lavenia*, *A. madurense*, and *A. platyphyllum*, the lower their TPC. On the other hand, the shorter the length and width of the leaf, the higher its TPC. Moreover, plant height and internodes distance were significantly negatively correlated with TFC ($p \leq 0.01$). The taller the plant and the farther the internode distance, the lower TFC of the three *Adenostemma* species. Conversely, the shorter the plant and the closer the internode distance, the greater TFC. Whereas, the plant height showed a positive and significant ($p \leq 0.01$) correlation with internodes distance. Also, leaf length was significantly ($p \leq 0.01$) positively correlated with leaf width. The higher the plant, the farther the internode distance, and the longer the leaves, the broader the leaf width. Other parameters have a positive

and negative correlation but are not significant. Therefore, leaf length and width in *Adenostemma* might be considered essential selection criteria for high TPC. This is supported by the morphological traits of *Adenostemma lavenia*, which has the smallest leaf length and width of the three *Adenostemma* species but the highest TPC (Table 1 and Table 2). On the other hand, for high total flavonoid content in *Adenostemma*, plant height and internodes distance can be important selection criteria. This study (see Table 1 and Table 2) showed that TFC was higher in *A. lavenia* and *A. madurense*, which had a shorter plant height and internode distance than *A. platyphyllum*.

The present study revealed variation in morphological traits of three species of *Adenostemma,* i.e., the color of the stem; shape, color, and the upper part surface of the leaf; the size of the head; plant height, length and width of leaf, and internodes distance. The leaf length and width, plant height and internodes distance could be used as important selection criteria in *Adenostemma* for obtaining high phenolic and flavonoid content. The findings showed that diverse species with varying morphological traits have a substantial impact on the chemical composition of these plants. In this study, *A. lavenia* contains the highest TPC and TFC. The results are expected to be useful information for the potential use of *Adenostemma* as alternative sources of bioactive compounds as functional foods or medicinal plant products.

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