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Traditional Use, Phytochemical Composition, and Biological Activities of *Sonchus arvensis*

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ABSTRACT

Medicinal plants are now widely used for various purposes, such as preventing and treating diseases. One of the medicinal plants widely used as traditional medicines and already commercialized is *Sonchus arvensis*, known as show thistle and *S. arvensis* in Indonesia. This review will highlight information about the traditional uses, phytochemical compounds, and biological activities of *S. arvensis* to increase our knowledge and understanding of this plant. We prepared this mini-review by finding sources of information in several scientific paper databases. As a traditional medicine, *S. arvensis* could be consumed to cure or prevent diseases. Secondary metabolites present in *S. arvensis* such as alkaloids, phenolics, flavonoids, and terpenoids are responsible for some biological activities of *S. arvensis*, such as antioxidant, antibacterial, antiinflammatory, antihypertensive, antihyperuricemic, and antidiabetic activities.

Keyword: Sonchus arvensis, medicinal plant, metabolite profile, biological activity

INTRODUCTION

Sonchus arvensis is a medicinal plant that belongs to the Asteraceae family. This plant can grow wild in open or slightly protected places and on slightly damp soil, such as on the edges of ditches, cliffs, wall edges, or between rocks. *S. arvensis* can grow at an altitude of 50-1650 meters above sea level. *S. arvensis* has its name in each country, for example, *niu she tou* in China, *laitron des champs* in France, sow thistle in the United Kingdom, and *S. arvensis* in Indonesia. Wahjono *et al*. (2021) stated that the leaves and all parts of *S. arvensis* are widely used for medicine for various diseases, such as urinary tract stones and gallstones, appendicitis, inflammation of the breast, dysentery, hemorrhoids, spermatorrhoea, hypertension, deafness, rheumatism gout, and bruises.

Several chemical compounds in *S. arvensis* belong to the triterpenoid, flavonoid, inositol, and mannitol groups. In the ethyl acetate leaves extract, compounds from the sesquiterpene group were detected (Xia *et al*., 2012). Also, a flavonoid compound, 6,7,4'-trihydroxy aurone, was identified in the ethyl acetate extract (Ramadhani *et al*., 2013) and lupeol, a triterpenoid compound, was detected in the *n*-hexane extract (Rumondang *et al*., 2013). In addition, Sudewei (2015) reported that one polyphenol compound in the form of tannins was found in the traditional drink of *S. arvensis* leaves. There is also detected luteolin (flavonoids) from the leaves (Suryani *et al*. 2020) and phytol, which are a terpenoids compound (Delyan 2021).

Several papers reported many biological activities of *S. arvensis*, such as antibacterial (Yanuarisa *et al*., 2016), antihyperuricemic (Hendriani *et al*. (2017), antioxidant (Lestari *et al*. 2020), antiinflammatory (Hidayat *et al*., 2020), antihypertensive (Suryani *et al*., 2020), and antidiabetic (Dutta *et al*., 2020). This biological activity is caused by the presence of bioactive metabolites contained in *S. arvensis*. These bioactive compounds can be found in *S. arvensis* in the roots, stems, and leaves. Therefore, this review will provide information related to traditional uses, phytochemical compounds, and biological activities influenced by the role of bioactive metabolites in *S. arvensis*. Also, complement the previous article review, which did not explain in detail the methods of each research, and further enriches the sources of reference journals in obtaining traditional uses, phytochemical compounds, and biological activities of *S. arvensis*.

METHODS

This review was conducted by searching for traditional uses, the content of phytochemical compounds, and the biological activity of *S. arvensis* in scientific databases such as Scopus (http://www.scopus.com/) with the keyword "Biological activity of *S. arvensis*", "Phytochemical compounds in *S. arvensis*", and "*S. arvensis* traditional uses". In Google Scholar and Google advance search with the keyword "antioxidant, antiinflammatory, antihypertensive, antibacterial, and antidiabetic activity of *S. arvensis*".

RESULTS AND DISCUSSIONS

Traditional Uses

S. arvensis has traditionally been widely used to prevent or cure various diseases. *S. arvensis* is one medicinal plant and an important weed among chronic weeds because of its fast reproductive system was used to treat some diseases such as gout, urinary stones, kidney stone crusher, swelling medicine, cough, asthma, fever, inflammation, and antibacterial (Evizal, 2013). *S. arvensis* is one of the selected medicinal plants that the people of Indonesia widely use because it has many properties in each part of the plant.

Figure 1. *Sonchus arvensis*

S. arvensis leaves and the whole plant parts have efficacy, and the public can consume it easily. *S. arvensis* can be consumed as medicine using 15-60 g of leaves or all plant parts boiled and then drunk. For external use, fresh herbs can be ground finely and then applied to the sore or squeezed, and the juice is used to compress wounds, inflammation, or hemorrhoids (Wahjono *et al*., 2021).

In addition, *S. arvensis* can be used traditionally in herbal medicine. Ardiyanto *et al*. (2018) conducted a study on the effect of obesity herbal medicine on body mass index, abdominal circumference, and arm circumference. This herbal medicine consists of *Guazuma ulmifolia* leaves, *Murraya paniculata* leaves, *Rheum officinale* root, and *S. arvensis* leaves. The herbal medicine was given for 56 days and showed a decrease in body mass index (BMI), waist circumference (WC), and upper arm circumference (UAC) and was proven safe for consumption.

Phytochemical Compounds

Phytochemical compounds are naturally found in plants and play an active role in their growth. These phytochemical compounds play a role in giving the plants' color, aroma, and taste. In addition, these phytochemical compounds also work as a protector of plant cells from extreme environmental conditions such as heat, pollution, exposure to UV rays, drought, and pathogen attacks (Saxena *et al*., 2013).

Several phytochemical compounds in *S. arvensis* have been discovered by several researchers, such as terpenoids, flavonoids, phenols, alkaloids, lactones, alkanes, esters, ketones, and others (Table I). Phytochemical compounds in *S. arvensis* can be identified in various ways. The simplest way to be used is by doing a qualitative phytochemical test. This qualitative phytochemical test will detect the presence or absence of the target compound that you want to know its existence. In addition to qualitatively, phytochemical compounds in plants can also be identified quantitatively using various instruments such as spectrophotometer UV-Vis, HPLC, GC-MS, LC-MS, LC-MS/MS, and other supporting instrumentation. The results obtained from this instrumentation can be in the form of levels of the compounds identified. In addition, unknown or previously discovered compounds (untargeted molecules) may also be found, which may dominate in plants.

Phytochemical compounds found in *S. arvensis* have an important role in the level of given biological activity, such as antioxidant, antibacterial, antiinflammatory, antihypertensive, antihyperuricemic, and antidiabetic powers. The effectiveness of this biological activity can be determined in vivo and *in vitro* in experimental animals and clinical trials if it is to be used in humans as traditional medicine.

Table I. Phytochemical compounds in *S. arvensis* (No. 1-24)

No	Plant Parts	Compound Groups	Phytochemical compounds	Researcher
1	All parts	Ester	Quinic acid ester	Xu *et al*. 2008
2	All parts	Terpenoid	Sesquiterpene	Xu *et al*. 2008
3	All parts	Terpenoid	Sesquiterpene : (a)1β,15-diacetoxy-5,7α,6,11β(H)-eudesm-3,4-en-6,12-olida	Xia *et al*. 2012
4	All parts	Terpenoid	(b)1β-hidroxy-3,4-en-15-O-β-glucopyranosyl-5,7α,6,11β(H) eudesm-6,12-olida	Xia *et al*., 2012
5	Leaves	Terpenoid	Lupeol octanoate	Rumondang *et al*., 2013
6	Leaves	Flavonoids	6,7,4'-trihidroxy auron	Rahmadani *et al*., 2013
7	Leaves	Flavonoids	Luteolin	Suryani *et al*., 2020
8	Root, stem, dan Leaves	Flavonoids	Orientin, hiperoside, rutin, apigenin, miricetin, luteolin, quercetin, dan kaempferol	Khuluk *et al*., 2021
9	Leaves	Flavonoids	Catechin, miricetin, kaempferol, dan quercetin	Seal, 2016
10	Leaves	Phenolic	Gallic acid	Seal, 2016
11	Leaves	Lactone	Ascorbic acid	Seal, 2016
12	Leaves	Phenolic	Total phenol	Hapsari *et al*., 2018
13	Leaves	Alkaloids	Isoquinoline	Murtadlo *et al*., 2013
14	Leaves	Alkanes	Pentacosane, tricosan, Eicosane, Tetradecane, Hexadecane, Heptadecan, Octadecane, Nonadecan, Hexacosane, 9-tricosene	Delyan, 2021
15	Leaves	Alkenes	3-tetradecene, 10-heneicosene, Heneicosene	Delyan, 2021
16	Leaves	Ester	1,2-benzenedicarboxylic acid Diisobutyl adipate 2-ethylhexyl ester 9,12,15-octadecatrienoic acid Bis(2-methylpropyl)ester Hexadecanoic acid Ethyl ester Benzoic acid	Delyan, 2021
17	Leaves	Ketone	6,10,14-trimethyl-2-pentadecanone	Delyan, 2021
18	Leaves	Aldehyde	Decanal, 2,4-decadienal, Tetradecanal	Delyan, 2021
19	Leaves	Alcohol	1-hexadecanol	Delyan, 2021
20	Leaves	Terpenoids	Phytol	Delyan, 2021
21	Leaves	Fatty acid	Tetradecanoic acid	Delyan 2021
22	All parts	Terpenoids	Sesquiterpene lactone glycosides	Asif & Saeed, 2020
23	Leaves	Alkanes	3-Methylhexane, Heneicosane, *n*-Heptane, 3-Methylheptane, *n*-Octane, 5-Methylnonane, 3-methylnonane, *n*-dodecane, *n*-decane, *n*-tetradecane, Nonacosane	Kanaani *et al*., 2015
24	Leaves	Alkenes	α - Methyltoluene	Kanaani *et al*., 2015

Table I. Phytochemical compounds in *S. arvensis* (No. 25-31)

No	Plant Parts	Compound Groups	Phytochemical compounds	Researcher
25	Leaves	Ester	Isobutyl phthalate, Methyl ester, Mono(2-ethylhexyl) phthalate	Kanaani *et al*., 2015
26	Leaves	Fatty acid	Palmitic acid, Linolenic acid	Kanaani *et al*., 2015
27	Leaves	Terpenoids	α-pinene, Eucalyptol, Borneol	Kanaani *et al*., 2015
28	Leaves	Benzene	o-xylene	Kanaani *et al*., 2015
29	Leaves	Cycloalkanes	1-Ethyl-3-methylcyclopentane Trans-1,3-Dimethylcyclopentane Cis-1,3-Dimethylcyclopentane Trans-1,2-Dimethylcyclopentane Toluene hexahydride	Kanaani *et al*., 2015
30	Leaves	Benzene	p-xylene	Kanaani *et al*., 2015
31	Leaves	Alcohol	3-(2-Methoxyethyl)-1-nonanol, 1-Hexacosanol	Kanaani *et al*., 2015

Xia *et al*. (2012) reported that *S. arvensis* contains two kinds of sesquiterpenes and ten other compounds. All plant parts were used and extracted using the reflux method with 85% ethanol solvent. The first sesquiterpene identified was derived from the isolation of the yellow part of the oil and its molecular formula was determined using HR-ESI-MS as $C_{19}H_{29}O_6$, and correlation was carried out using 2D NMR (HMBC and ROESY) and found the structure, namely 1β-15-diacetoxy-5,7α,6,11β(H)-eudesm-3,4-en-6,12-olide. The second sesquiterpene, whose molecular formula was successfully determined, was isolated from the yellow sap-like part using HR-ESI-MS as $C_{21}H_{32}O_9$. Then correlation using 2D NMR (HMBC and ROESY) and found the structure, namely 1β-hydroxy-3,4-en-15-O-β-glucopyranosyl-5,7α,6,11β(H)-eudesm-6,12-olide.

Based on other studies that have been carried out, the ethyl acetate extract of *S. arvensis* leaves has compounds included in the alkaloids, flavonoids, phenols, and saponins according to the qualitative test phytochemical screening. Furthermore, the flavonoid compounds were separated using TLC, column chromatography, and preparative TLC, and purification was carried out using 2-dimensional chromatography. Pure isolates from ethyl acetate extract of *S. arvensis* leaves were analyzed using the UV-Vis spectrophotometry method with maximum wavelengths at two points, namely 253 nm and 437.5 nm, which indicated the presence of auron group flavonoids. Further analysis was carried out using FTIR to determine what functional groups were present in the isolates. Based on the results of the analysis that has been carried out, the isolate is suspected to be 6,7,4'−trihydroxyauron (Ramadhani *et al*., 2013).

Murtadlo *et al*. (2013) have also isolated and identified total alkaloid compounds in the ethanol extract of *S. arvensis* leaves. Identification by UV-Vis spectrophotometer showed absorption peaks at three wavelengths, namely 225 nm, 253 nm, and 352 nm, which indicated the presence of a benzene ring and a compound in the form of a homoanular diene. Meanwhile, based on the FTIR spectrum, there are absorptions at wavenumbers of 3448.72 cm-1 (OH stretching vibration), 1627.92 cm-1 (C=N stretching vibration), 1103.28 cm-1 (C−N bending vibration which is symmetrical with C−O stretching vibration), 2924 cm-1 and 2854.65 cm-1 (aliphatic C−H stretching vibration), 1472.67 cm-1 and 1347.4 cm-1 (C−H group), 1720.50 cm-1 (C=O stretching vibration), 1650.92 cm-1 (conjugated C=C stretching vibration), and 794.67 cm-1 (out-of-plane aliphatic C−H). LC-MS analysis resulted in the MS spectrum of *S. arvensis* leaves, an alkaloids compound with a molecular weight is 444 g/mol. The identification results indicate the presence of a benzene ring, homoanular diene, C=N bonds, and the MS spectrum in the form of alkaloids, allowing the alkaloid compounds contained in *S. arvensis* leaves to have an isoquinoline basic framework.

Rumondang *et al*. (2013) have also isolated and identified triterpenoid compounds from the n-hexane extract of *S. arvensis* leaves. Identification of isolated compounds using FTIR and GC-MS spectra. The FTIR spectrum of the isolated compound

showed the presence of C=O ester, CH_3, CH_2, and C−O ester groups. The results of GC-MS showed that there were five peaks and peak number one was obtained at a retention time of 21.117 minutes with the largest percentage of peak area (40.69 %), which is supposed to be the peak of triterpenoid compounds. The peak is then analyzed further to determine its structure. Based on its mass spectrum, peak number 1 has an M^+ value of 552 and according to the literature, it is likely to be a lupeol octanoate compound with a molecular weight of 552 g/mol. In addition, an ester linkage with an m/z 408 fragment which is considered to be missing a saturated fatty acid, namely octanoic acid (*m/z* 144), is found in the Asteraceae family. The base peak obtained with *m/z* 43 is the ester chain, which is assumed to be lupeol. However, nobody knows these triterpenoids' absolute structure, so further analysis is needed to elucidate the compound structure.

Seal (2016) has also researched a quantitative analysis of the content of phenolic acids, flavonoids, and ascorbic acid in four types of *S. arvensis* leaf extract using HPLC. The extracting solvents used were chloroform, methanol, 80% ethanol, and 1% acetic acid. The HPLC system used is a reversed-phase HPLC with an AcclaimTM 120 C18 column and a diode array detector. The results showed the presence of compounds in the form of phenolic acids, flavonoids, and ascorbic acid in various extracts. The chloroform extract contained 0.058 ± 0.0004 mg/g extract of quercetin and 0.045 ± 0.0003 mg/g of kaempferol extract. Furthermore, the methanol extract contained quercetin at 0.028 ± 0.0003 mg/g extract. Then the 80% ethanol extract was found to have ascorbic acid at 6.23 ± 0.05 mg/g extract, gallic acid at 0.05 ± 0.0003 mg/g extract, catechins at 0.136 ± 0.004 mg/g extract, myricetin at 0.110 ± 0.004 mg/g extract, and kaempferol at 0.157 ± 0.002 mg/g extract. Finally, in 1% acetic acid extracting solvent, ascorbic acid was found at 12.11 ± 0.15 mg/g extract, gallic acid at 0.281 ± 0.05 mg/g extract, quercetin at 0.043 ± 0.0003 mg/g extract, and kaempferol of 0.094 ± 0.0002 mg/g extract.

Delyan (2021) also studied the composition of volatile compounds in *S. arvensis* leaves using GC-MS. The column used is a capillary column DB-5 (inner diameter 30 m x 0.25 mm, with a film thickness of 0.25 mm). Oven temperature from 50 ^{0}C (hold for 3 minutes) to 320 ^{0}C with 4 ^{0}C/min change. Injector temperature was 250 ^{0}C, helium carrier gas, flow rate 1.2 mL/min, and injection volume 1.5 L. The results of the analysis showed that 42 compounds were identified. There are several compounds found in high amounts, namely pentacosan at 75 mg/kg, 1,2-benzenadicarboxylic acid-di-n-butyl ester at 55 mg/kg, 6,10,14-trimethyl-2-pentadecanone at 38 mg/kg. and n-tricosane at 24 mg/kg

Suryani *et al*. (2020) has also researched evaluating the effect of polarity of compounds on *S. arvensis* leaves as inhibitors of hypertension. Phytochemical analysis was carried out to determine the class of compounds in polar, semipolar, and nonpolar fractions in *S. arvensis* leaves. The results showed that the semipolar fraction, namely the ethyl acetate fraction of *S. arvensis* leaves, contained luteolin which belonged to the flavonoid group. This is evidenced by the characterization of this semipolar fraction using TLC and the results show that the Rf value is the same as the Rf of luteolin, which is 0.34. This result is not found in the polar and nonpolar fractions. After that, the weight of the luteolin in the extract was also determined using a densitometer. The luteolin weight obtained was 0.65±0.059 mg luteolin/gram fraction.

Khuluk *et al*. (2021) did a study to determine the levels of eight types of flavonoids found in the roots, stems, and leaves of S. arvensis based on the geographical origin of this plant. Determination of flavonoid content was carried out using HPLC. The eight flavonoid compounds were separated using an inverted phase with a C-18 column, 1 mL/min flow rate, and gradient elution using methanol and 0.2% aqueous formic acid. The types of successfully separated flavonoids were myricetin, luteolin, quercetin, kaempferol, orientin, hyperoside, apigenin, and rutin from Bogor and West Bandung districts with different concentration levels for each plant part. The flavonoid compound with the minor concentration found in the leaves, stems, and roots in both regions was kaempferol and the largest was apigenin.

Based on the results obtained from several researchers, the *S. arvensis* has various kinds of phytochemical compounds found in all parts of the plant. The content of these phytochemical compounds in plants can be affected by several factors such as the part of the plant used (Rahayu *et al*., 2022), harvest time (Hasan *et al*., 2017), extracting solvent, and the amount of concentration used (Fidiyani *et al*., 2015), extraction method (Utami *et al*., 2020), and environmental factors where it grows (Utomo *et al*., 2020). Different harvest times and plant parts can affect the number of phytochemical compounds

detected (Hasan *et al*., 2017). The extraction solvent used will affect the phytochemical compounds taken because it follows the like dissolve-like principle. Polar solvents will attract more polar compounds present in plants so that nonpolar compounds may be slightly taken up or even undetected (Altemimi *et al*., 2017)

The extraction method also affects the phytochemical compounds taken. Phytochemical compounds sensitive to heat will be better extracted using the maceration technique than reflux. The reflux method will damage the phytochemical compounds so that what should be detected becomes undetectable. However, if the target compound is resistant to heat, the reflux extraction method is preferred because the time required for extraction will be less and more efficient. Extracted phytochemical compounds can be analyzed using various methods such as preliminary tests, namely qualitative tests to determine what groups of compounds exist and quantitative tests to determine how many phytochemical compounds are present.

Biological Activities

Antioxidant

Antioxidants are compounds that can slow down or prevent the oxidation of other molecules. Antioxidants can stop chain reactions by eliminating free radicals and stop the oxidation of other compounds by oxidizing themselves (Hassanbaglou *et al*., 2012). The number of free radicals can increase due to several factors, such as pollution, alcohol, tobacco smoke, heavy metals, transition metals, industrial solvents, pesticides, certain drugs, and radiation (Phaniendra *et al*., 2015). The antioxidant activity can be measured based on the IC_{50} value, which is the concentration required by the sample to inhibit 50% of free radicals. The smaller the IC_{50} value, the greater the antioxidant activity of the sample and vice versa. The IC_{50} value in a sample may vary depending on the sample used. Samples that have an IC_{50} value of less than 50 ppm include a group with very strong antioxidant activity, an IC_{50} value between 50–100 ppm including a strong antioxidant activity group, a moderate group with an IC_{50} value of 101–150 ppm, and a weak group with an IC_{50} value between 151–200 ppm (Blois, 1985).

Yuliarti *et al*. 2013 isolated, identified, and determined the antioxidant activity of the phenolic acids in the ethanol extract of *S. arvensis* leaves using the DPPH method. Isolation was carried out in three stages, namely, without hydrolysis (HT), acid hydrolysis (HA), and alkaline hydrolysis (HB). Then isolate B was found purified using preparative TLC, which was then identified using spectrophotometer UV-Vis, FTIR, and LC-MS. The results showed that isolate B was *p*-coumaric acid (Figure 2). The antioxidant activity was determined on the ethanol extract of *S. arvensis* leaves and isolate B, isolated by alkaline hydrolysis treatment (HB fraction). The IC_{50} value obtained using the DPPH method for the ethanol extract was 150,860 ppm, and for isolate B, which was 428,718 ppm. These results indicate that the ethanol extract has a higher antioxidant activity value than isolate B. Although the results of the antioxidant activity of isolate B are in the moderate category, isolate B still has the potential to be developed as a source of antioxidant compounds.

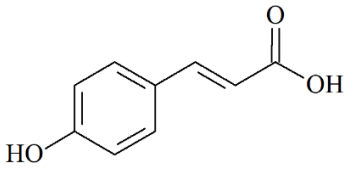

Figure 2. *p*-Coumaric acid

Other studies have determined the antioxidant activity of 70% ethanol extract of *S. arvensis* leaves by DPPH and ABTS methods. This determination used vitamin C as a positive control. Vitamin C showed IC_{50} values with the DPPH method of 5.40 g/mL and 2.17 g/mL with the ABTS method. Testing the antioxidant activity of ethanol extract using DPPH as a free radical source showed an IC_{50} value of 64.97 g/mL, and a test using ABTS as a radical source is 138.26 g/mL. These results indicate that a greater concentration is needed to reduce 50% of ABTS radicals compared to DPPH radicals (Istikhara, 2015). Therefore, it can be stated that the 70% ethanol extract of *S. arvensis* leaves has a strong category of antioxidant activity against DPPH radicals and moderate categories against ABTS radicals.

Lestari *et al*. (2020) have also reported on the antioxidant activity through the effect of extraction time using the ultrasonication method on 96% ethanol extract of *S. arvensis* leaves. The sonicator's extraction time variation was 10, 20, 30, 40, and 50 minutes. Determination of phenol, flavonoid, and total tannin levels were determined using a UV-Vis spectrophotometer, and antioxidant activity was determined using the DPPH method. Based on the results obtained, the extraction time of 50 minutes gave the largest extract yield, which was 18.60%. The levels of phenol, flavonoid, total

tannin, and antioxidant activity resulted in the highest value when using an extraction time of 30 minutes. The total phenol, flavonoid, and tannin levels were 55.05 mg GAE/g, 38.14 mg QE/g, and 8.82 mg TAE/g, respectively. Antioxidant activity measured using the DPPH method, which works by inhibiting DPPH free radicals by 50%, produces an IC_{50} value of 262.82 mg/L. These results indicate that the antioxidant activity of the 96% ethanol extract of *S. arvensis* leaves in this study is in the weak category.

Sukweenadhi *et al*. (2020) performed a study on screening for antioxidant activity in *S. arvensis*. The total phenol content in *S. arvensis* from 80% ethanol extract was 7.22±0.15% GAE, and the total flavonoid content was about 3.78±0.01% QE. Antioxidant activity was measured using three methods, namely DPPH, ABTS, and FRAP. The antioxidant activity using the DPPH method gave an IC_{50} value of about 1118±7.1 ppm, which was included in the very weak category. Using the ABTS method, they obtained an antioxidant activity value with an IC50 value of about 143±1.85 ppm, which was included in the medium group. Finally, the antioxidant activity using the FRAP method was carried out at various extract concentrations, 200, 400, 600, 800, and 1000 ppm, which resulted in IC_{50} values of 27.88±0.31; 47.63±0.89; 54.61±0.36; 61.02±1.32; and 63.68±0.63 ppm AEAC/ppm extract which belonged to the very strong group at concentrations of 200 and 400 ppm while the strong group at concentrations of 600, 800, and 1000 ppm.

Based on several research results that have been reviewed, the smallest IC_{50} value, which is 64.97 ppm, was obtained in the Istikharah work (2015) using 70% ethanol solvent, maceration extraction method, and DPPH method as a method of determining antioxidants. This may indicate that the compound that plays a role in its biological activity is polar compounds. The same study also used ABTS as a source of radical compounds. However, the IC_{50} value obtained is greater than the DPPH method, which is 138.26 ppm. This may be because a higher concentration is required to scavenge 50% of ABTS radicals than DPPH radicals. The biggest IC_{50} value was obtained in Sukweenadhi *et al*. (2020) research, which is 1181 ppm using 80% ethanol solvent, reflux extraction method, and DPPH antioxidant activity method. This large IC_{50} value may be due to the compounds that act as antioxidants in this study being sensitive to heat and being damaged during the extraction process. The FRAP method was used to determine the antioxidant activity in the same study. However, it can't be compared with other studies because it doesn't determine the IC_{50} value.

Antibacterial

Antibacterial is a substance or compound used to inhibit bacteria. The compounds act as antibacterial by damaging cell walls, changing membrane permeability, interfering with protein synthesis, and inhibiting the work of enzymes from bacteria (Septiani *et al*., 2017). A medicinal plant can have various benefits and one of them acts as an antibacterial. This antibacterial activity occurs because of these medicinal plants' secondary metabolites' content (Muharni *et al*., 2017).

The antibacterial activity in thick n-hexane extract of *S. arvensis* leaves was investigated. The thick n-hexane extract yielded five fractions obtained from column chromatography. Fraction 4.1 can inhibit the growth of *S. aureus* bacteria by 2.5 mm and inhibit the growth of *E. coli* bacteria by 2.0 mm at a concentration of 100 ppm compared to other fractions. Tetracycline as a positive control with a 30 g had an inhibition zone of 20 mm against *S. aureus* and 17 mm against *E. coli*. Based on the identification using GC-MS and the WILEY 7 database, fraction 4.1 was successfully isolated, consisting of a mixture of bis(2-Ethylhexyl) ester (Figure 3) and a triterpenoid group compound with the molecular formula $C_{32}H_{66}O_6$. The two components in fraction 4.1 have greater antibacterial potential than other fractions (Sukadana and Santi 2011).

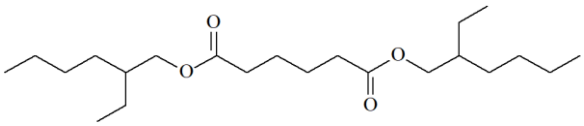

Figure 3. Bis(2-Ethylhexyl) ester structure

Kanani *et al*. (2015) also conducted a study on the antibacterial activity of methanol extract of *S. arvensis* leaves by in vitro method. The methanol extract was tested for its antibacterial activity using the disc diffusion technique to determine the diameter of the zone of inhibition of bacterial growth and the broth microdilution method to determine the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC). The gram-positive bacteria *B. cereus* and *S. aureus* and gram-negative bacteria, *S. enterica,* and *E. coli*. The analysis results showed no growth inhibition zone on the addition of *S. arvensis* leaves

methanol extract by the disc diffusion method. In determining MIC and MIB, methanol extract of *S. arvensis* L. succeeded in preventing the growth of all bacteria. From the results obtained, the highest sensitivity was seen in *B. cereus* and *S. aureus,* and the least was seen in *S. enterica* and *E. Coli*.

Yanuarisa *et al*. (2016) also researched the antibacterial activity and minimum inhibitory concentration (MIC) of the ethanol extract of *S. arvensis* leaves against *S. typhi* bacteria by in vitro method. The ethanol extract was made in eight concentrations and four repetitions. Chloramphenicol was used as a positive control and DMSO as a negative control. The study showed that the positive control had an average inhibitory zone of 28.5 mm and the negative control did not form an inhibitory zone around and under the disc. Ethanol extract at concentrations of 10 g/disk, 20 g/disk, 30 g/disk, 40 g/disk, 60 g/disk, and 80 g/disk had antibacterial activity by forming a clear zone around and under the disc. The clear zone indicates the inhibition of the growth of *S. typhi*. Based on these results, the minimum inhibitory concentration of ethanol extract of *S. arvensis* leaves was 10 g/disk with an average inhibition zone diameter of 7.1 mm.

The antibacterial activity of the combination of antibiotics, namely tetracycline with *S. arvensis* leaves extract as anti-dysentery against *Shigella flexneri* bacteria, has been carried out using the microdilution method. The results of the checkboard method showed that the combination of tetracycline with *S. arvensis* leaves extract reduced the MIC (Minimum Inhibitory Concentration) value, which was 1/8 for *S. arvensis* leaves extract and 1/2 for tetracycline. To assess the effect by in vivo method, a combination of the two was administered to mice orally infected with *Shigella flexneri* for seven consecutive days. From the results obtained, a combination of the two can reduce the number of bacteria found in rat droppings significantly compared to positive controls and tetracycline alone for six-day after drug administration (Sukandar *et al*., 2016).

Based on the above research results, the antibacterial activity of *S. arvensis* extract can have various effects. This may occur because the use of polar, semipolar, or nonpolar extracts can affect the extracted phytochemical compounds and the strength of these phytochemical compounds as antibacterial. In addition, the bacteria used also gave different results. Gram-positive bacteria are bacteria that are primarily composed of peptidoglycan and simple layers. At the same time, gram-negative bacteria are composed of more complex layers, such as lipopolysaccharide, outer membrane, peptidoglycan, and inner membrane. Therefore, gram-negative bacteria are more difficult to inhibit by treating phytochemical compounds than gram-positive bacteria. This is following a study conducted by Sukandana and Santi (2011), where the inhibition zone produced was greater in *S. aureus* bacteria, a gram-positive bacterium, than *E. coli*, a gram-negative bacterium.

Antiinflammatory

Inflammation is the body's response to infection, irritation, and other injuries or can also be referred to as a non-specific immune response. The presence of inflammation can produce a response of the body, such as swelling, redness, and pain (Stankov, 2012). Therefore, an antiinflammatory is needed to reduce symptoms such as inflammation or swelling.

Research on antiinflammatory activity in Nepal has been carried out on parts of the *S. arvensis* exposed to air. The study was conducted to determine the analgesic effect of *S. arvensis* methanol extract using mice *in vivo*. The technique used to analyze the effect of *S. arvensis* methanol extract on analgesic activity in mice, namely hot plate and chemical writhing. In the hot plate method with doses of 62.5 mg/kg BW, 125 mg/kg BW, and 500 mg/kg BW, both methanol extract and standard (aspirin) showed that both methanol extract and standard (aspirin) showed percent protection, respectively, 55%, 86.11%, and 96.65%. The results of the chemical writhing method with doses of 62.5 mg/kg BW, 125 mg/kg BW, and 500 mg/kg BW, both methanol extract and standard (aspirin), showed the percent protection, respectively, 35.14%, 51, 38%, and 79.84%. The larger the dose given, the higher the resulting protective effect (Prasad *et al*., 2015).

Poudel *et al*. (2015) did a pharmacological study on the methanol extract of *S. arvensis* originating from Kathmandu. The part of the *S. arvensis* used is the part that is exposed to air. The results showed that methanol extract could inhibit carrageenan-induced acute leg edema, which was also dose-dependent, indicating the presence of antiinflammatory activity. The antiinflammatory activity was higher in methanol extract at a 400 mg/kg dose than diclofenac as a positive control at 10 mg/kg. However, the methanol extract did not have skeletal muscle relaxant activity based on the traction test and inclined plane test results at all doses given, 125, 250, and 500 mg/kg BW.

Hidayat *et al*. (2020) did a study in the form of antiinflammatory effects of ethanol extract of *S. arvensis* leaves on gouty arthritis white rats induced by monosodium urate (MSU) crystal. The results obtained, the ethanol extract gave an effect in the form of a reduction in the inflammatory response due to MSU induction in the joints. In addition, the ethanol extract was able to reduce the expression of proinflammatory cytokines, namely IL-1β and TNF-α. Recruitment and infiltration of neutrophils into the joint and synovial fluid are the hallmarks of gouty arthritis. Histopathological test results showed that a dose of 100 mg/kg BW could significantly weaken the infiltration of inflammatory cells into the synovium induced by MSU crystals and increase synovial hyperplasia. Even the effect given by this dose was comparable to the effect of colchicine which was a positive control.

Based on several studies that have been carried out, polar compounds in *S. arvensis* have antiinflammatory activity by protecting or reducing inflammation at various doses given. Further analysis is needed regarding what secondary metabolite compounds play an important role in providing this antiinflammatory effect. Semipolar and nonpolar compounds may have the same effect or even better than the effect given to polar compounds with lower doses. Therefore, further analysis is needed to determine what compounds play an important role as an antiinflammatory.

Antihypertensive

Hypertension is a condition where there is an abnormal increase in blood pressure which can be a triggering factor for diseases such as cardiovascular disease. A person's blood pressure is high if it exceeds 140 mmHg (systolic) (Ansar *et al*., 2019). According to the Ministry of Health (2013) data, hypertension is the number 3 cause of death in Indonesia after stroke and tuberculosis, with 6.7% of deaths at all ages. Therefore, drugs are needed to prevent hypertension and one of them can be obtained from the *S. arvensis* herbal plant.

Iswantini *et al*. (2015) studied the activity of aqueous extract of *S. arvensis* in inhibiting Angiotensin-Converting Enzyme (ACE) using *in vitro* method. ACE can act by converting the inactive decapeptide angiotensin I to angiotensin II as its active form. The formation of angiotensin II will cause constriction of blood vessels, which can trigger hypertension. Based on the toxicity test of shrimp larvae using the BSLT method, the aqueous extract of *S. arvensis* produced an LC_{50} value of 1657.44 ppm. Furthermore, the ACE inhibitory activity using the ACE Kit-WST method gave 88.34% results for captopril at a concentration of 25 ppm as a positive control and 39.67% for water extract of *S. arvensis* with a concentration of 50 ppm. Based on these results, the water extract of *S. arvensis* had the potential to inhibit ACE, although it had lower yields than the positive control.

Suryani *et al*. (2017) studied the antihypertensive activity of 96% ethanol extract of *S. arvensis* leaves in inhibiting ACE, using the Chusman and Cheng method with hipuryl-histidyl-leucine or HHL as a substrate. The results showed that the percent inhibition of captopril and ethanol extract against the ACE enzyme was the greatest, at a concentration of 75 g/mL with a percent of inhibition, respectively, 92.34% and 60%. In addition, captopril as a positive control had an IC_{50} value of 1.26 g/mL and ethanol extract had an IC_{50} value of 46.71 g/mL. Therefore, ethanol extract is potentially an antihypertensive, although it has a smaller percentage of inhibition and IC_{50} than the positive control.

Suryani *et al*. (2020) evaluated the effect of polarity of *S. arvensis* leaves extract as an antihypertensive. There are three fractions used, *n*-hexane (nonpolar fraction), ethyl acetate (semipolar fraction), and water (polar fraction) (1:1). The results showed that the given of epinephrine 0.25 mg/kg BW in positive controls was able to induce blood pressure in diastolic blood pressure (DBP), systolic blood pressure (SBP), and average blood pressure (MBP). Then the semipolar fraction gave the highest results in inhibiting hypertension activity at the same dose, which was 16 mg/kg BW compared to other fractions.

Based on the results obtained, hypertension can be prevented in various ways, namely by adding a compound that can act as a renin inhibitor that functions to prevent the formation of angiotensin I from angiotensinogen. In addition, it can also be prevented by the addition of an ACE inhibitor which functions to prevent the formation of angiotensin II from angiotensin I. The addition of compounds that act as angiotensin receptor blockers (ARBs) can also prevent hypertension by blocking the binding of angiotensin II to the AT-1 receptor so that it can't be converted to aldosterone. Then the addition of compounds that act as aldosterone blockers can also prevent sodium and fluid retention in blood vessels, which can cause blood pressure to rise. Therefore, further analysis is needed regarding secondary metabolites in *S. arvensis*, which have an antihypertensive effect.

Antihyperurichemic

Hyperuricemia is a condition when the uric acid level in the blood exceeds the proper concentration, which is around 6.8 mg/dL (Boleu *et al*., 2018). Hyperuricemia can be caused by excessive intake of foods containing protein, purines, and nucleic acids (Artini & Yanti 2019) so that the synthesis or formation of uric acid in the body becomes excessive. The effects can arise when a person has long suffered from hyperuricemia, namely joint damage, soft tissue, and kidney disorders (Dianati, 2015). Therefore, drugs are needed to treat hyperuricemia. Various studies on the effect of antihyperuricemia on traditional plants such as *S. arvensis* have been carried out.

Cendrianti *et al*. (2014) reported the antihyperuricemic activity of *S. arvensis* leaves from a maceration of extracts of *n*-hexane (nonpolar), ethyl acetate (semipolar), and 70% ethanol (polar) in hyperuricemic male mice. Based on the research, 18 male white mice were used at 2.5–3.5 months and body weight of about 20–30 grams. The positive control was used as allopurinol. The results obtained on day 12 after administration of *n*-hexane, ethyl acetate, and 70% ethanol extract of *S. arvensis* leaves showed a decrease in uric acid levels in mice with hyperuricemia compared to day 9. The percentage decrease in uric acid levels in administering *n*-hexane, ethyl acetate, and 70% ethanol extracts was 23.905 ± 7.808%, 56.482 ± 6.778%, 58.764 ± 4.153%, respectively. The antihyperuricemic activity of 70% of ethyl acetate and ethanol extracts was still lower than allopurinol, which may be due to fewer compounds that have the potential for antihyperuricemia, but 70% of ethyl acetate and ethanol extracts still have potential as antihyperuricemics.

Hendriani *et al*. (2017) also observed a study to determine the activity of quercetin in the 96% ethanol extract of *S. arvensis* leaves in inhibiting the activity of xanthine oxidase, which is an essential enzyme for the synthesis of uric acid. This analysis was carried out using in vitro and *in silico* methods. In vitro test was performed using a UV-Vis spectrophotometer at λ_{max} = 295 nm. The analysis results showed that the IC_{50} value in the ethanol extract containing quercetin (Figure 5) was 4.39 g/mL and 4.84 g/mL in allopurinol. These results indicate that quercetin is a xanthine oxidase inhibitor. The results of the in silico analysis show the RMSD (Root-Mean-Square Deviation) value of 0.91Å, which means that the calculation method and parameter settings meet the criteria for the validity of the docking method is smaller than 2Å. In addition, based on the analysis, it is known that the binding energy of quercetin is more negative than allopurinol. This shows that quercetin (Figure 4) has more affinity for the enzyme's active site than allopurinol and has the potential as an inhibitor in uric acid synthesis.

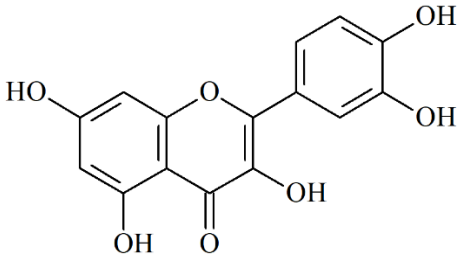

Figure 4. Quercetin

Based on several studies that have been carried out, polar compounds in *S. arvensis* play a role in inhibiting the work of the xanthine oxidase enzyme in converting xanthine into uric acid. However, only one study explains the content of polar compounds in the form of quercetin, which has the activity to inhibit uric acid form. Therefore, further research is needed regarding other polar compounds in their activity as antihyperuricemia. Semipolar compounds and nonpolar compounds may have the same activity. This may be done by using the appropriate concentration of solvent and dosage of extract. Furthermore, an analysis of the secondary metabolites that play a role in each extract also needs to be carried out.

Antidiabetic

Diabetes mellitus is a degenerative disease when blood sugar (blood glucose) levels exceed normal limits (200 mg/dL) when not fasting or 126 mg/dL when fasting (Hestiana, 2017). There are several types of diabetes, namely type 1, which occurs due to a problem with the function of the pancreas, which cannot produce insulin. Type 2 diabetes is because there is a problem of insufficient insulin and is not caused by pancreatic damage but by an unfavorable lifestyle (Nugroho, 2012). Therefore, drugs are needed to improve insulin production by the body, which can be derived from traditional plants, which are more economical and have an effect comparable to synthetic drugs.

Dutta *et al*. (2020) conducted a study on the antidiabetic activity of *S. arvensis* leaves in Wistar rats induced by alloxan. Extraction was carried out by maceration using 95% ethanol. The male Wister

rats used weighed 210–250 grams and were 5–8 months old. The rats were divided into several groups, namely group 1 as normal control which was given saline 10 mL/kg BW, group 2 given alloxan 150 mg/kg BW, group 3 given alloxan 150 mg/kg BW + ethanol extract 100 mg/kg BW, group 3 4 were given alloxan 150 mg/kg BW + ethanol extract 150 mg/kg BW, and group 5 was given alloxan 150 mg/kg BW + ethanol extract 200 mg/kg BW. Blood samples were taken from the rats' tails on days 0, 3, 7, and 15. The analysis results showed that the effect of decreasing the concentration of glucose in the blood of rats was greatest given at a dose of 200 mg/kg BW after 14 days of treatment, from 190 ± 0.8 mg/dL to 93.1 ± 1.7 mg/dL. These results indicate that the antidiabetic activity had the most effective effect at the largest compared to other doses.

The antidiabetic activity of *S. arvensis* leaves phytochemical compounds that play a role in lowering blood sugar levels in the body and the dose given. For example, sulfonylurea compounds play a role in closing the K^+ channel in the pancreas so that Ca^{2+} from outside the pancreas can enter and encourage insulin secretion, which can bind to glucose in the blood and become energy when it enters a cell. Therefore, excess blood sugar in the body can be prevented in various ways and mechanisms according to the drugs given. The drugs given are tightly bound to phytochemical compounds and functional groups that play an important role in antidiabetic activity.

CONCLUSION

This review highlights the potential of *S. arvensis,* which can be used as traditional medicine by the community and can be consumed or used externally. Based on the content of compounds such as flavonoids, alkaloids, terpenoids, etc, this plant has various biological activities found. This biological activity is in the form of antioxidant, antibacterial, antiinflammatory, antihypertensive, antihyperuricemic, and antidiabetic activities. Therefore, *S. arvensis* has the potential to be investigated further regarding the chemical composition and concentration and related biological activities

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