Advances in Traditional Medicine (2022) 22:383–394
https://doi.org/10.1007/s13596-021-00553-y

RESEARCH ARTICLE

Algerian *Sonchus oleraceus* L.: a comparison of different extraction solvent on phytochemical composition, antioxidant properties and anti-cholinesterase activity

Fatine Aissani[1] · Nedjoud Grara[2] · Chawki Bensouici[3] · Aissam Bousbia[2] · Hayette Ayed[2] · Muhd Hanis Md Idris[4,5] · Lay Kek Teh[4,5]

Received: 21 October 2020 / Accepted: 5 January 2021 / Published online: 17 February 2021

Abstract
Aerial parts of *Sonchus oleraceus* L. were studied for the antioxidant and anti-cholinesterase activities in different solvent and fractions. Extracts/fractions were analysed for total phenolic, flavonoid and flavonol contents. The chemical constituents of the most active extracts/fractions were analysed using LC–MS/QTOF in the positive ion mode. Ethyl acetate and butanolic fractions exhibited the highest antioxidant activity in DPPH, galvinoxyl and phenanthroline assays due to high contents of phenolics, flavonoids and flavonols. Whereby total alkaloid extract had the highest scavenging activity in ABTS•+assay. Besides, methanolic extract was noted for the highest inhibitory effect against acetylcholinesterase. Total 24 compounds were identified by LC–MS/QTOF which were phenolic acids, sesquiterpene lactones and phenylpropanoid derivatives. As conclusion, the study revealed that the aerial parts of *S. oleraceus* are potential sources of natural antioxidant and anti-cholinesterase compounds.

Keywords LC–MS/QTOF · Sowthistle · Antioxidant · Anti-cholinesterase · Phenolic compounds

Introduction

Sonchus oleraceus L. (family; Asteraceae), commonly known as Sowthistle (Arabic name; Tilfaf), is an edible leaf vegetable. It is frequently consumed in Mediterranean countries (Guil-Guerrero et al. 1998). It is cosmopolitan and its native is Europe and North Africa (Vieira and Barreto 2006). Traditionally, it used to treat central nervous system dysfunction, and mental disorders (Lane et al. 2006). Several pharmacological properties such as antioxidant, anti-diabetic and anti-inflammatory of *S. oleraceus* (SO) had been reported before (Schaffer et al. 2005; Teugwa et al. 2013; Li et al. 2017). Phytochemical studies of SO have revealed the presence of sesquiterpene lactones, essential oils, flavonoids, flavonols, proanthocyanidins, phenols, saponins and alkaloids (Miyase and Fukushima 1987; Guarrera et al. 2008).

Plant secondary metabolites plays a crucial role in the treatment of Alzheimer's disease (AD) (Oken et al. 1998); the most prevalent neurodegenerative disorder. AD is defined by the neuropathological deposition of extracellular amyloid-beta (Aß) senile plaques, intracellular neurofibrillary tangles (NFTs) (Castellani et al. 2010). The protein aggregates (Aß) provoke neuronal damage and synaptic dysfunction like the cleavage of the neurotransmitter acetylcholine (Ach) into acetate and choline. Hence, the inhibition of their formation remains one of the potential therapeutic approach for the treatment of AD which can be achieved by the inhibition of acetylcholinesterase (AChE) (Whittaker 1990). Unfortunately, synthetic AChE inhibitors have side

✉ Muhd Hanis Md Idris
muhd_hanis@hotmail.com

1 Laboratoire Biologie, Eau et Environnement (LBEE), Université 8 Mai 1945, Guelma, P.B. 401, 24000 Guelma, Algeria

2 Faculté des Sciences de la Nature et de la Vie et Sciences de la Terre et de l'Univers, Université 8 Mai 1945 Guelma, P.B. 401, 24000 Guelma, Algeria

3 Biotechnology Research Center (CRBT), Ali Mendjli New Town UV 03, P.B. E73, Constantine, Algeria

4 Integrative Pharmacogenomics Institute (iPROMISE), Universiti Teknologi MARA (UiTM) Selangor, Puncak Alam Campus, 42300 Bandar Puncak Alam, Selangor, Malaysia

5 Faculty of Pharmacy, Universiti Teknologi MARA (UiTM) Selangor, Puncak Alam Campus, 42300 Bandar Puncak Alam, Selangor, Malaysia

effects and can be potentially toxic to the patients causing gastrointestinal disturbances, hepatotoxicity and short bioavailability (Alva and Cummings 2008).

In fact, oxidative damage has been proposed to be a primary event in AD (Nunomura et al. 2001). This is because brain is quite vulnerable to oxidative injury as it is composed of easily oxidized lipids with a higher oxygen consumption rate (Nunomura et al. 2001). The oxidation of nucleic acid, lipid and protein was found in the neurons of AD patients in which is the common pathological feature of AD (Lovell and Markesbery 2007). Therefore, antioxidant can ameliorate these pathological conditions (Feng and Wang 2012). Further, antioxidant activity was found to be associated with AChE activity (Ferreira et al. 2006). Precedent study also revealed that antioxidants had substantial potential to reduce the symptoms and the frequency of AD (Gutzmann and Hadler 1998). For this reason, the antioxidant had been investigated with AChE activity in the aim of searching for novel AD drugs candidates from natural sources. Thus, the aim of the present work was to determine the antioxidant and AChE properties as well as the chemical constituents obtained from different solvent extractions of the aerial parts of the Algerian SO.

Materials and methods

Chemicals and reagents

In the present study, 1,1-diphenyl-2-picrylhydrazyl (DPPH), butylated hydroxyanisole (BHA), butylated hydroxyl toluene (BHT), α-tocopherol, gallic acid (GA), quercetin, trichloroacetic acid (TCA), potassium ferricyanide, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS), galvinoxyl (GOX), 1,10-phenanthroline, acetylthiocholine iodide (ATChI), galantamine, 4-nitrophenyl-α-D-glucopyranoside (≥ 99%), 5,5′-dithiobis(2-nitrobenzoic) acid (DTNB) and Folin-Ciocalteu's reagent (FCR) were purchased from Biochem Chemopharma. Acetylcholinesterase (AChE) from electric eel (EC 3.1.1.7, Type VI-S, 827.84 U/mg) and all other chemicals and solvents unless stated were analytical grade and were purchased from Sigma-Aldrich, Inc. (St. Louis, MO, USA).

Collection of plant material

The aerial parts of SO were collected in January 2018 at Boumahra ahmed commune (36° 27′ 16.8″ North, 7° 32′ 55.6″ East), City of Guelma, which is in the Northeastern of Algeria. The plant was authenticated by the botanist, Prof. Gérard De Belair (Faculty of Sciences, University of Annaba, Algeria), where a voucher specimen was deposited (LBEE.22.01.18).

Preparation of extracts/fractions

The aerial parts of SO were air-dried under the shade area at room temperature until completely dried before crushed into a fine powder (diameter < 250 µm) using an electric mill (KWCG-102, China). Then, 200 g of SO powder was macerated in 2 L of hydro-methanolic solution (80%) for 72 h at room temperature and filtered. This combination of solution was used as it can extract the most flavonoids from the plant (Baatouche et al. 2019). The process was repeated in three times. The filtrates were then concentrated and evaporated under pressure in a rotary evaporator (R-215, Büchi Labortechnik AG, Flawil, Switzerland) at 40 °C to obtain crude extract (M.E). A part of the extract was suspended in distilled water and successively partitioned to a liquid–liquid extraction in a funnel using different solvents of increasing polarity: chloroform, ethyl acetate and n-butanol. This yielded chloroform fraction (C.F), ethyl acetate fraction (EA.F) and butanolic fraction (B.F) while the residual represented aqueous phase fraction (AP.F).

For the hot aqueous extract (HAE), 20 g of SO powder was extracted in 100 mL of distilled water for 4 h until boiling. The mixture was filtered and centrifuged at $2000 \times g$ for 15 min. The supernatant was dried using a lyophilisation apparatus (Smach et al. 2015). HAE was kept in dry place. In the preparation of the ethanolic extract (E.E), 20 g of SO powder were mixed with 500 mL of ethanol by constantly shaking for 72 h. After that, it was filtered and concentrated in a rotary evaporator at 40 °C. It was lyophilised to give crude EE. Similarly, the macerated aqueous extracts (MAE) were prepared by mixing 50 g of SO powder with 500 mL of distilled water and constantly shaking for 72 h. Then, it was filtered and frozen before finally lyophilised. Both E.E and MAE were weighed and kept at 4 °C. The methods of extraction for E.E and MAE were modified from Dos Santos et al. (2019).

The extraction of total alkaloid was conducted according to the method reported by Dehmlow et al. (1999). 100 g of SO powder was extracted in 1 L methanol. The methanol was then removed under reduced pressure using a rotary evaporator. 4% acetic acid (500 mL) was added to the residue and it was extracted for three times in petroleum ether (100 mL each time) to remove neutral compound. 120 mL of ammonia was poured on the aqueous layer to alkalinize it until the pH reach 11. It was extracted again in 50 mL of petroleum ether for 10 times. The organic phase was evaporated to give the total alkaloid extract (TAE).

Quantification of total phenolic content

The total phenolic content (TPC) of SO samples was evaluated by using the FCR method as described by Singleton and Rossi (1965) with some modifications (Müller et al. 2010). Briefly, 10 mg of the extracts/fractions was dissolved in 10 mL of methanol using sonicator to yield a concentration of 1 mg/mL. Then, 20 µL of the extracts/fractions (1 mg/mL) were mixed with 100 µL of FCR (1:10 in distilled water) and 75 µL of sodium carbonate solution (7.5%) in the wells of 96-well microplate. After 2 h of incubation in the darkness at room temperature, the absorbance was measured using microplate reader (EnSpire® Multimode Plate Reader, PerkinElmer, Inc., Massachusetts, USA) at 765 nm against a blank. The tests were performed in triplicate. A calibration curve was generated by using the optical density (OD) of the know concentration of GA as standard. TPC was expressed as µg gallic acid equivalents/mg dried extract weight (µg GAE/mg of extract) which was based on the calibration curve of gallic acid with the linearity range from 10 to 100 µg/mL ($R > 0.99$).

Quantification of total flavonoid content

The total flavonoid content (TFC) of plant extracts was determined using the microplate method as described by Topçu et al. (2007). A volume of 50 µL of the extracts/fractions (1 mg/mL in methanol) was mixed with 130 µL of MeOH. This was followed by the addition of 10 µL of acetate potassium and 10 µL of aluminium nitrate. After 40 min at room temperature, the absorbance was measured at 415 nm using microplate reader (EnSpire® Multimode Plate Reader, PerkinElmer, Inc., Massachusetts, USA). All samples were performed in triplicate. TFC was expressed as µg of quercetin equivalents per milligram of dried extract weight (µg QE/mg of extract) which based on the calibration curve of quercetin with the linearity range from 25 to 200 µg/mL ($R > 0.99$).

Quantification of total flavonol content

Total flavonol content (TFLC) was measured using the method of (Kumaran and Joel Karunakaran 2007). Briefly, a volume of 50 µL of the extracts/fractions was mixed with 50 µL of aluminium chloride and 150 µL of sodium acetate solution (in water). After 2.5 h of incubation, the absorbance was measured at 440 nm. All tests were carried out in triplicate. The results were expressed as µg of quercetin equivalents per milligram of dried extract weight (µg QE/mg of extract) which based on the calibration curve of quercetin with the linearity range from 25 to 200 µg/mL ($R > 0.99$).

DPPH radical scavenging activity

The scavenging ability of the extracts/fractions towards the DPPH radical was determined using the method of (Blois 1958) with modifications involving the use of a high-throughput microplate system. In a 96-well microplate, 160 µL of the methanolic DPPH solution was mixed with 40 µL of the samples in methanol at different concentrations (12.5–800 µg/mL). After 30 min at room temperature in the darkness, the absorbance was recorded at 517 nm against a blank using a microplate reader (EnSpire® Multimode Plate Reader, PerkinElmer, Inc., Massachusetts, USA). BHA, BHT and α-tocopherol were used as comparison while methanol was used as a control. The percentage of inhibition of radical scavenging activity was calculated using Eq. 1. The concentration of samples providing 50% inhibition (IC_{50} of the samples) was obtained from the plotted graph of the percentage of inhibition versus the concentrations of samples.

$$\text{Percentage of Inhibition}\,(\%) = \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}} \times 100 \quad (1)$$

where A_{control} is the absorbance of the control reaction and A_{sample} is the absorbance of the test samples.

ABTS radical scavenging assay

The ABTS radical cation ($ABTS^{\bullet+}$) decolourisation assay was performed according to the method described by Re et al. (1999) with slight modifications. At first, ABTS was diluted in water to 7 mM concentration. Next, $ABTS^{\bullet+}$ solution was prepared by reacting ABTS solution with potassium persulfate (final concentration: 2.45 mM). The mixture was allowed to stand in the dark at room temperature for 16 h before use. After that, the mixture was diluted in water to get an absorbance equal to 0.700 ± 0.020 at 734 nm. Then, 40 µL of the extracts/fractions in methanol at different concentrations and 160 µL of diluted $ABTS^{\bullet+}$ solution were added to each well of microplate. After 10 min, the absorbance at 734 nm was recorded using a microplate reader (EnSpire® Multimode Plate Reader, PerkinElmer, Inc., Massachusetts, USA). The percentage of inhibition was calculated using the Eq. 1 and the IC_{50} values were deducted from the plotted graph. BHA and BHT were used as the positive controls.

Phenanthroline assay

The (Szydłowska-Czerniak et al. 2008) method was adopted for this assay. This assay measured the formation of tri-phenanthroline complex. In the presence of hydroxyl radical, Fe^{2+}

was oxidized to Fe^{3+} and combined with 1,10-phenanthroline to form tri-phenanthroline. Otherwise, this reaction was disrupted if the antioxidant was able to scavenge the hydroxyl radical. The reaction mixture containing 10 µL of different concentration of the extracts/fractions in methanol, 30 µL of 1,10-phenanthroline solution in methanol (0.5%), 50 µL ferric chloride ($FeCl_3$) (0.2%) and 110 µL of MeOH was incubated in the dark for 20 min at 30 °C. The absorbance of the reaction mixture was then read at 510 nm. The percentage of inhibition was calculated according to the Eq. 1 and compared with BHT as a classical metal chelator. The results were presented as IC_{50} value in µg/mL.

GOX free radical scavenging assay

This assay was performed as shown by Shi et al. (2001). It measured the scavenging ability of the antioxidants toward the stable GOX radicals by donating hydrogen in the hydroxyl groups to form resonance-stabilized GOX radicals. Basically, GOX solution was appeared in deep blue and decolourised to become purple over the time as its odd electron was paired off. In brief, 160 µL of GOX (0.1 mM) was mixed with 40 µL of each sample at different concentrations. The reaction was carried out at room temperature and monitored for 2 h. The decrease in GOX concentration was recorded by measuring the absorbance at 428 nm.

AChE inhibition assay

The inhibitory activity of AChE was investigated using a modified version of (Ellman et al. 1961) in a 96-well microplate. 150 µL of Tris buffer (0.1 M, pH 8.0), 10 µL of the extracts/fractions in ethanol with different concentrations (3.125 – 200 µg/mL) and 20 µL of AChE enzyme solution (5.32×10^{-3} U) were mixed and incubated for 15 min at 25 °C. Subsequently, the reaction was started by adding 10 µL of DTNB (0.5 mM) and 10 µL of ATChI substrate solution (0.71 mM). The absorbance of the mixture was measured spectrophotometrically at 412 nm in every 5 min for 15 min. A blank containing Tris buffer and ethanol instead of enzyme solution was used. A control mixture was also prepared by replacing ethanol instead of extract and was considered as 100% enzyme activity. The percentage of inhibition was calculated as in Eq. 2. The concentration of extracts/fractions providing 50% of inhibition (IC_{50}) was determined by plotting the percentage of inhibition versus the concentrations of extracts/fractions.

$$\text{Percentage of inhibition}(\%) = \frac{(E-S)}{E} \times 100 \quad (2)$$

where E is the activity of the enzyme without the sample (100% enzyme activity) and *S* is the activity of the enzyme in the presence of the sample.

LCMS–QTOF analysis

The determination of the phytochemical constituents of the active extracts/fractions was carried out using LCMS-QTOF (LC 1200 Series, Agilent Technologies, Palo Alto, California, USA) equipped with a standard autosampler. The chromatography column was ZORBAX Eclipse Plus C18 (EPC-18) column (2.1 × 100 mm, 1.8 µm) from Agilent Technologies. Firstly, the samples were prepared by dissolving the extracts/fractions (4 mg) in methanol (HPLC grade). The samples were filtered by passing through a Millipore nylon filter disk (0.22 µm) using an injector to remove any particulates before they were injected into the LCMS system. The injection volume was 2 µL and the column temperature was set at 40 °C. The samples were run using a gradient elution programme at a flow rate of 0.25 mL/min. The mobile phases that were used consisted of ultra-purified water plus 0.1% formic acid (A) and 5% acetonitrile (B). The solvent gradient was applied as follows: 0 min, 5% B; 36 min, 95% B; 41 min, 95% B; 41.1 min, 5% B; 48 min, 5% B. The LCMS system was coupled to a Quadrupole-Time-of-Flight (QTOF) (Agilent Technologies, Palo Alto, California, USA) and a detector was equipped with an electrospray ionization source (ESI) operating in the positive ion mode. The optimum values of the ESI–MS parameters were: nitrogen in which was used as drying gas at a temperature of 325 °C, drying gas flow at 10 L/min; nebulising gas pressure at 30 psi; capillary voltage potential at 4000 V and finally, fragmentor voltage of 175 V was chosen and applied to the samples. The detection was carried out within a mass range of 100–1100 m/z. For analysis of the samples, the accurate mass data of the molecular ions were processed using Agilent Mass Hunter Qualitative Analysis B.05.00 software (Agilent Technologies, Palo Alto, California, USA). All products were recognized by interpreting their MS data and comparing them with the available bibliography.

Statistical analysis

All the experimental data were displayed as mean ± standard deviation (SD) of three trials. The one-way analysis of variance (ANOVA) followed by Tukey, Least Significance Difference (LSD) post-hoc tests, and the homogeneity test of variances by the Levene test were conducted using IBM SPSS Statistics V20 software (IBM Corporation, New York, USA). The level of significance was set at $p < 0.05$ value.

Table 1 The yield of extraction and antioxidant potential of the extracts/fractions of SO in different assays

Samples	Yield of extractions (%)	IC_{50}			$A_{0.5}$
		DPPH (µg/mL)	ABTS (µg/mL)	GOR (µg/mL)	Phen (µg/mL)
M.E	28.55	59.79 ± 1.86^{ab}	97.34 ± 1.76^{e}	96.37 ± 5.61^{ab}	97.55 ± 9.35^{c}
C.F	0.14	NA	263.30 ± 0.99^{a}	354.42 ± 2.50^{ab}	NA
EA.F	1.86	13.41 ± 0.15^{ab}	11.40 ± 0.60^{h}	23.37 ± 1.17^{ab}	25.17 ± 2.50^{e}
B.F	18.31	22.42 ± 0.75^{ab}	31.85 ± 0.35 g	34.60 ± 1.09^{ab}	42.89 ± 0.10^{d}
AP.F	41.73	59.50 ± 0.70^{ab}	77.33 ± 0.56^{f}	117.85 ± 1.34^{ab}	129.92 ± 1.13^{b}
MAE	6.50	NA	157.13 ± 1.82^{c}	541.61 ± 11.77^{ab}	NA
HAE	10.92	646.97 ± 25.41^{b}	136.33 ± 2.72^{d}	682.47 ± 0.58^{b}	NA
E.E	33.10	573.67 ± 52.21^{b}	197.93 ± 2.79^{b}	418.54 ± 2.59^{ab}	164.24 ± 6.06^{a}
TAE	7.82	NA	2.00 ± 0.05^{i}	NA	NA
BHT*	NIL	12.99 ± 0.41^{ab}	1.29 ± 0.30^{i}	6.82 ± 0.49^{a}	2.24 ± 0.17^{f}
BHA*	NIL	6.14 ± 0.49^{a}	1.81 ± 0.10^{i}	6.82 ± 0.49^{a}	0.93 ± 0.07^{f}
α-Tocopherol*	NIL	13.02 ± 5.17^{ab}	NT	NT	NT

The values were expresssed in mean ± SD of biological triplicates

DPPH: 2,2-diphenyl-1-picrylhydrazyl, ABTS: 2,2′-azino-bis(3-ethylbenzothiazoline-6 sulfonicacid), GOR: galvinoxyl radical, Phen: phenanthroline, M.E: methanolic extract, C.F: chloroformic fraction, EA.F: ethyl acetate fraction, B.F: butanolic fraction, AP.F: aqueous phase fraction, MAE: macerated aqueous extract, HAE: hot aqueous extract, E.E: ethanolic extract, TAE: total alkaloid extract, BHA: butylatedhydroxylanisole, BHT: butylated hydroxytoluene, NIL: not applicable, NA: no activity and NT: not tested

*Compounds used as positive control

$^{a-i}$ Results with different superscript letters were significantly different

Results and discussion

Yield of extractions

The extraction yields of different extracts/fractions of SO were reported in Table 1. Based on the results, AP.F produced the highest yield of extraction (41.73%) while the lowest amount of yield was C.F (0.14%). According to Dhanani et al. (2017), the amount of yield indicated the effects of the extraction conditions. Thus, the variations in the extraction yields was due to the differences in the polarity of the solvents that were used as well as the method of extractions which directly impacted the biological activities of the final extracts (Hayouni et al. 2007; Pellegrini et al. 2007). As the most polar solvent, water was the most efficient solvent in extracting the phytochemical constituents from the plant. In fact, the combination of water and organic solvent (methanol) which also had high polarity further enhanced the efficiency of the extraction. This was supported by the previous study that showed high polar solvent resulted greater percentage of yield as compared to less polar solvent (Abubakar et al. 2017). The study by Jacotet-Navarro et al. (2018) also found that hydro-alcoholic mixtures gave maximum yield of extraction.

However, there was a great reduction in the percentage of yield when different methods of extraction were used. The hot extraction (10.92%) and maceration method (6.50%) in aqueous condition caused the decrease in the percentage of yield by 4 and 7 times as compared to liquid–liquid extraction. In the case of different solvent extractions, ethanol yielded higher mass of extraction (33.10%) than water (6.50%). It was the second highest amount of yield. This is due to the plant material contains high levels of polar compounds that are more soluble

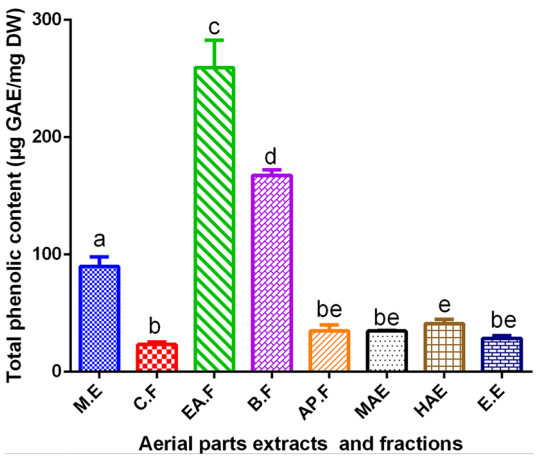

Fig. 1 Total phenolic content of different extracts/fractions from the aerial parts of SO. GAE: Gallic acid equivalent, DW: Dry weight of the samples, M.E: methanolic extract, C.F: chloroformic fraction, EA.F: ethyl acetate fraction, B.F: butanolic fraction, AP.F: aqueous phase fraction, MAE: macerated aqueous extract, HAE: hot aqueous extract, E.E: ethanolic extract and TAE: total alkaloid extract. $^{a-e}$: Results with different superscript letters were significantly different

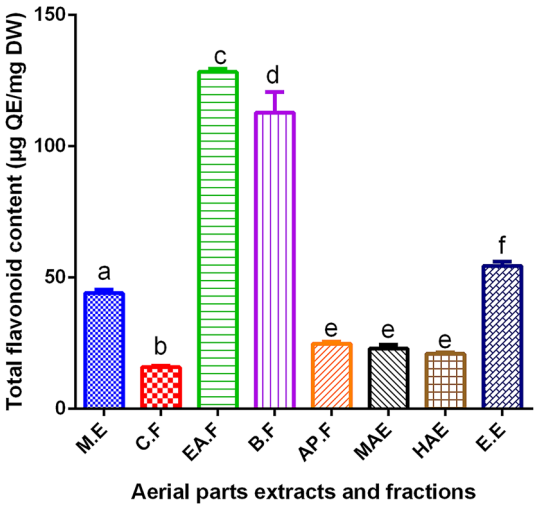

Fig. 2 Total flavonoid content of different extracts/fractions from the aerial parts of SO. QE: Quercetin equivalent, DW: Dry weight of the samples, M.E: methanolic extract, C.F: chloroformic fraction, EA.F: ethyl acetate fraction, B.F: butanolic fraction, AP.F: aqueous phase fraction, MAE: macerated aqueous extract, HAE: hot aqueous extract, E.E: ethanolic extract and TAE: total alkaloid extract. [a–f]: Results with different superscript letters were significantly different

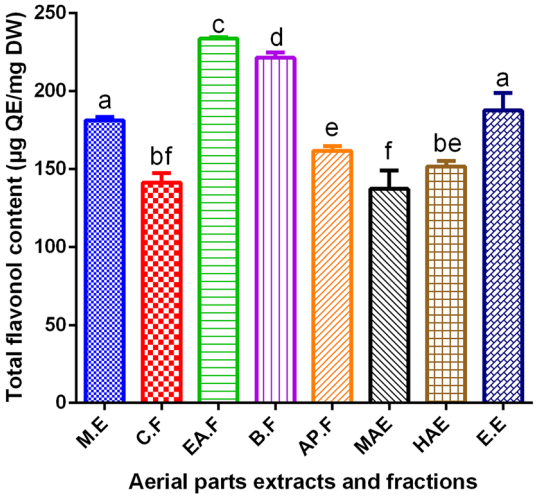

Fig. 3 Total flavonols content of different extracts/fractions from the aerial parts of SO. QE: Quercetin equivalent, DW: Dry weight of the samples, M.E: methanolic extract, C.F: chloroformic fraction, EA.F: ethyl acetate fraction, B.F: butanolic fraction, AP.F: aqueous phase fraction, MAE: macerated aqueous extract, HAE: hot aqueous extract, E.E: ethanolic extract and TAE: total alkaloid extract. [a–f]: Results with different superscript letters were significantly different

in ethanol rather than in water (Thakur & Arya 2012; Piechocka et al. 2020). Therefore, it can conclude that the use of organic solvent especially ethanol in solid–liquid extraction possessed the greatest performance in getting better yield for this plant.

Total phenolic, flavonoid and flavonol contents

The results of total phenolic, flavonoid and flavonol contents were presented in Figs. 1, 2 and 3 respectively. EA.F contained the highest amount of phenolic compounds (259.20 ± 23.51 µg GAE/mg) and followed by B.F (167.53 ± 4.57 µg GAE/mg). The lowest phenolic content was obtained from C.F (23.31 ± 2.21 µg GAE/mg) while the rest were between 28.51 µg GAE/mg and 89.98 µg GAE/mg. Similarly, EA.F and B.F exhibited the top amount of total flavonoid with the value of 128.33 ± 1.00 µg QE/mg and 112.85 ± 7.82 µg QE/mg respectively. The other samples demonstrated the value of total flavonoid content between 15.88 µg QE/mg and 54.45 µg QE/mg with the lowest amount was also in C.F. For the total flavonol content, the highest values were still in EA.F (233.73 ± 0.88 µg QE/mg) and B.F (221.38 ± 3.41 µg QE/mg) but MAE comprised the least amount of flavonol (137.21 µg QE/mg). Meanwhile, the range of flavonol content in the other samples were between 141.25 µg QE/mg and 187.54 µg QE/mg.

Our findings showed that EA.F and B.F had the highest total phenolic, total flavonoid and total flavonol content in despite of low extraction yield. In a study carried out by Teugwa et al. (2013), total phenolic content of the hydroethanolic and methanolic extracts of the whole plant of SO were measured at 616.89 ± 19.20 and 182.25 ± 16.76 µg catechine equivalent/g of dry extract respectively which were higher than the current results. In another research, high amounts of TPC and TFC had been obtained from the aerial parts of SO grown in China when methanol was used (Xia et al. 2011). Consistently, the methanolic extract of SO which was grown in Korea had the highest value of TPC, and the lowest values of TPC were obtained in ethanolic and water extracts (Yin et al. 2007). This was also not in line with our results. The differences may be due to geographical distribution and various environmental conditions, which can affect the synthesis of the phytochemicals in the plant (Hossain and Shah 2015).

Generally, those intermediate polar solvents such as ethyl acetate and butanol were found to be more potent in extracting phenolic compounds (Ajayi et al. 2017). In a study on *Armoracia rusticana*, it was revealed that ethyl acetate extraction possessed high TPC as ethyl acetate is the best solvent for selectively extracting polyphenols (Thavamoney et al. 2018). Moreover, most of the flavonoids are known to be less polar or semi-polar in nature. Because of that, a research on *Monotheca buxifolia* suggested that hexane is a poorer solvent for flavonoids recovery compared to those more polar solvents such as ethyl acetate and butanol (Jan et al. 2013). Furthermore, the ethyl acetate and the *n*-butanol fractions were reported to be more effective in extracting phenol compounds from crude extract according to the previous research. It could be suggested that phenol compounds mostly occupy the ethyl acetate fraction as compared to the

other fractions, resulting low extraction yield and high TPC (Nakamura et al. 2016). This explained the highest value of TPC, TFC and TFLC in EA.F and B.F as compared to other solvents. Thus, EA.F and B.F has a better extraction potency in extraction of phenolics than other organic solvents like chloroform.

Antioxidant capacity

Polyphenolic compounds are the major constituents that present in the plant and mostly possess as potent antioxidants (Elufioye et al. 2019). Hence, the antioxidant activities of the plant samples were evaluated via four complementary techniques instead of a single method which were DPPH, ABTS, galvinoxyl and phenanthroline assays. This is because to give better conclusive results of the antioxidant properties of the extracts (Sacchetti et al. 2005; Houghton et al. 2007). Among them, DPPH assay is the most used method in evaluating antioxidant capacity by evaluating the radical scavenging activity. The antioxidant potential of the different samples was reported in Table 1 and the results were expressed as IC_{50} and $A_{0.5}$ values.

Generally, the extracts/fractions of SO displayed the scavenging abilities in concentration-dependent manner. Among the extracts/fractions, EA.F and B.F showed the highest DPPH and galvinoxyl scavenging activities and had the strongest ability of inhibiting the hydroxyl radical as measured in phenanthroline assay. However, EA.F was more efficient in scavenging the free radical of DPPH and GOX than the B.F. Interestingly, EA.F exhibited almost the same capability in scavenging DPPH as α-tocopherol and BHT. The results also revealed EA.F and B.F fractions that possessed the highest TPC value favoured to show stronger DPPH radical scavenging activity. Similarly, the study by Nakamura et al. (2016) showed that EA.F gave the highest DPPH activity. In contrast, the DPPH activity of methanol extract of *S. asper* from Pakistan was higher than in EA.F (Rahmat et al. 2012). According to Thavamoney et al. (2018), the radical scavenging activity was greatly affected by the presence of the hydroxyl group in the C-3 position. Therefore, stronger DPPH fractions might contain a lot of phenolic compounds that are structurally effective for scavenging the DPPH radicals (Nakamura et al. 2016).

In ABTS•+ assay, TAE was the most powerful in the reduction of ABTS•+ radical as compared to other extracts/fractions. Moreover, it was comparable to the control BHT and BHA where no significant difference was observed. Otherwise, C.F was found to be the weakest in ABTS•+ scavenging activity. On the other hand, EA.F and B.F showed the highest antioxidant activities among all fractions in GOR and phenanthroline tests which were firstly reported in this plant. This were in accordance with their high phenolic, flavonoid and flavonol contents. TAE showed strong ABTS•+ scavenging activity due to the presence of reducing molecules that may inhibit the potassium persulfate activity and hence reduced the production of ABTS•+. Wang et al. (1999) found that some compounds which had ABTS•+ scavenging activity did not showed DPPH· scavenging activity. The non-active phenolic compounds, which were not detected in the DPPH radical scavenging assay, reacted in the ABTS radical assay, and therefore lowered its values.

The difference in antioxidant activity might be due to the composition of phenolic compound in the samples that contained a high number of hydroxyl groups. This groups were responsible for a high antioxidant activity (Arabshahi-D et al. 2007). Besides that, the method and conditions of extraction (temperature and time) also affected these activities (Robards. 2003). The difference in the stoichiometry of reactions between the antioxidant compounds in the samples and the various radicals might also be inferred as a reason for the difference in their scavenging potential (Wang et al. 1999). Factors like stereo selectivity of the radicals or the solubility of the samples in different testing systems had been reported to affect the capacity of samples to react and quench different radicals (Wang et al. 1999).

AChE activity

Different samples of SO were tested to determine their ability as AChE inhibitors and the results were depicted in Table 2. M.E exhibited the most potent inhibitory activity of AChE, followed by C.F, EA.F, B.F, E.E, HAE, TAE and MAE. It was important to note that in spite of the lowest

Table 2 The inhibitory activity of AChE in different extracts/fractions of SO

Samples	% Acetylcholinesterase inhibitory activity
M.E	27.07 ± 1.86^{c}
C.F	39.62 ± 13.79^{bc}
EA.F	48.51 ± 4.43^{bc}
B.F	69.71 ± 4.62^{abc}
AP.F	66.60 ± 1.64^{abc}
MAE	139.38 ± 4.27^{a}
HAE	79.34 ± 1.001^{abc}
E.E	76.62 ± 3.43^{abc}
TAE	109.49 ± 2.32^{ab}
Gal*	6.27 ± 1.15^{c}

The values were expressed in mean ± S.D of biological triplicates

*Compound used as positive control

[a–c] Results with different superscript letters were significantly different

content of phenolic, flavonoid and flavonol compounds in C.F; this fraction was good in inhibiting AChE. On the other hand, literature data of the inhibitory effect of SO against AChE were insufficient. In this work, M.E exhibited the lowest IC_{50} (27.07 µg/mL) in inhibiting AChE activity, which was more powerful than the methanolic extract of *S. asper* (IC_{50}: 65 µg/mL) from Pakistan (Khan et al. 2012). Previous study also showed that methanolic extract gave good inhibitory activity against AChE, followed by ethyl acetate fraction, suggesting that the active constituents could be a cocktail of polar compounds in inhibiting AChE (Elufioye et al. 2019). However, in another research, hexanic extract was the most effective extraction against AChE (Ayaz et al. 2014). These suggested that the organic solvents were able to effectively extract the molecules which inhibited the enzyme at the best.

Phytochemical compounds in the plant extracts/fractions

In order to evaluate the compounds that were responsible for the various bioactivities as examined above, the samples with the best antioxidant activity (EA.F and B.F) and enzyme inhibition (M.E) were subjected to compound analysis using LC–MS/QTOF. The identification of the compounds was presented in Table 3 and illustrated in Fig. 4. Their retention time and mass spectrometry obtained by MS/QTOF were compared with the reported data in the literature. M.E, EA.F and B.F contained a total of 10, 17, and 12 compounds respectively. Among them, 14 compounds were phenolic acid derivatives while the rest was composed of sesquiterpene lactones and phenylpropanoid derivatives. Quininic acid was the main compound in the M.E while gallic acid was the main compound in EA.F and B.F. Quininic acid was detected at (1.07 min) in the ESI-QTOF positive ion mode. It gave $[M–H]^+$ ion at m/z 204.0669 in accordance with the molecular formula $C_{11}H_9NO_3$. Gallic acid was found in the EA.F and B.F at the same retention times (4.86 min) and it gave $[M–H]^+$ ion at m/z 171.0285 with the molecular formula $C_7H_6O_5$ respectively.

The results were consistent with previous studies on the leaves and aerial parts of SO and other species of the same genus (Abhijeet et al. 2018; Li and Yang 2018). Aesculin and quininic acid was found in the crude extract, which were comparable with the results cited by Xu et al. (2008). Sonchusides A-D and macrocliniside A had been previously isolated and identified in the whole methanolic extract from SO (Miyase and Fukushima 1987). Meanwhile, 15-O-β-D-glucopyranosyl-11β,13-dihydro urospermal A had not only characterised in the whole plant of *S. asper* and roots of SO in Egypt (Helal et al. 2000; Elkhayat 2009), but it was also found in SO plant originated from Algerian as observed in this study.

Flavonoids are another important group of phenolic compounds that are widely found in Sowthistle (Abhijeet et al. 2018). Among these, gallic acid, catechol and apigenin-7-O-ß-D-glucuronide methyl ester were cited in the literature (Li and Yang 2018) and all of them were found and identified in the EA.F and B.F. Other flavonoids that were found in the fractions were luteolin 7-β-D-glucosiduronic acid, apigenin, sinapinic acid, 3-hydroxyflavone and ascorbic acid. Besides, 15-O-β-glucopyranosyl-11β,13-dihydrourospermal A, corchoionoside C and sonchuside H had been found in the M.E and EA.F. They were isolated previously for the first time from SO, *S. erzincanicus* and *S. arvensis* (Bondarenko et al. 1978; Elkhayat 2009; Ozgen et al. 2010). Interestingly, the EA.F which contained the highest amount of phytochemical contents (phenols, flavonoids and flavonols) exhibited the highest number of compounds as compared to the B.F and M.E.

From the pharmacological point of view, the presence of loliolid, quinic acid, luteolin 7-β-D-glucosiduronic acid and sinapinic acid especially in the potent EA.F are very important since they are well-known to have strong antioxidant activities and may have been responsible for the observed activity (Inbathamizh and Padmini 2013; Nićiforović and Abramovič 2014; Malgorzata et al. 2015; Ma et al. 2018). In addition, apigenin-7-O-ß-D-glucuronide methyl ester, 3-hydroxyflavone and ascorbic acid were only identified in the B.F which they had effective scavenging activity against DPPH radical (Nayak et al. 2014; Wąsik and Antkiewicz-Michaluk 2017; Kamalakararao et al. 2018). The sesquiterpene lactone melampolide (costunolide) was only present in the M.E and is known for its neuroprotective effect (Ham et al. 2012). The EA.F and B.F also showed an efficient AChE inhibitory activity that might be due to gallic acid, catechol, apigenin, sinapic acid and ascorbic acid as reported by the other studies (Nićiforović and Abramovič 2014; Badhani et al. 2015; Wąsik and Antkiewicz-Michaluk 2017; Wang et al. 2018). Thus, this study showed good antioxidant and AChE properties of the polar fractions which are good sources of phenolic compounds and can be used in the management of AD.

Conclusion

To the best of our knowledge, this was the first report that directly compared the biological activities, as well as the phytoconstituents of seven different extraction solvents of SO. This study showed that the EA.F and the B.F demonstrated the highest activity in DPPH, galvinoxyl and phenanthroline scavenging assays as well as total phenolic, flavonoid and flavonol contents. The TAE showed high ABTS activity and the M.E exhibited the highest activity in inhibiting AChE. Coupling with LC–MS/QTOF allowed

Table 3 Identification of compounds in three active extracts/fractions of SO using LC–MS/QTOF

Samples	Peak	R.T. (min)	M-H$^+$ (m/z)	Mass	Compound name	Molecular formula
M.E	1	1.070	204.0669	203.0606	Quininic acid	$C_{11}H_9NO_3$
	2	1.187	379.0409	340.0744	Aesculin	$C_{15}H_{16}O_9$
	3	7.417	321.1326	298.1437	3-(acetyl-oxy)-1-methoxy-1-(3,4,5-trimethoxyphenyl) propane	$C_{15}H_{22}O_6$
	4	9.308	409.1837	386.1952	Corchoionoside C	$C_{19}H_{30}O_8$
	5	9.962	453.2086	430.2201	Sonchuside H	$C_{21}H_{34}O_9$
	6	14.440	197.1164	196.1098	Loliolid	$C_{11}H_{16}O_3$
	7	21.990	255.1353	232.1458	Melampolide	$C_{15}H_{20}O_2$
	8	27.270	481.1455	442.1804	15-O-β-D-glucopyranosyl-11β,13-dihydro urospermal A	$C_{21}H_{30}O_{10}$
	9	27.335	287.1265	264.1372	Tanacetin	$C_{15}H_{20}O_4$
	10	33.047	463.1354	424.1691	Macrocliniside A	$C_{21}H_{28}O_9$
EA.F	11	0.976	298.0736	594.1421	2-(3,4-dihydroxyphenyl)-2-{[2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3,4-dihydro-2H-chromen-3-yl]oxy}-3,4,5,7-chromanetetrol	$C_{30}H_{26}O_{13}$
	12	4.866	171.0285	170.0211	Gallic acid	$C_7H_6O_5$
	13	4.869	463.0905	462.0853	Luteolin 7- β -D-glucosiduronic acid	$C_{21}H_{18}O_{12}$
	14	4.880	263.0335	224.0701	Sinapinic acid	$C_{11}H_{12}O_5$
	3	7.300	321.1313	298.1416	3-(acetyl-oxy)-1-methoxy-1-(3,4,5-trimethoxyphenyl)propane	$C_{15}H_{22}O_6$
	4	9.153	409.1833	386.1938	Corchoionoside C	$C_{19}H_{30}O_8$
	5	9.801	453.2114	430.2211	Sonchuside H	$C_{21}H_{34}O_9$
	15	13.712	111.0449	110.0373	Catechol	$C_6H_6O_2$
	6	14.240	197.1172	196.1106	Loliolid	$C_{11}H_{16}O_3$
	16	14.942	461.1049	460.1012	Apigenin-7-O-ß-D-glucuronide methyl ester	$C_{22}H_{20}O_{11}$
	17	16.797	271.0581	270.0493	Apigenin	$C_{15}H_{10}O_5$
	18	20.148	269.1751	268.1665	15-hydroxy-4β,15,11β,13- tetrahydroreynosin	$C_{15}H_{24}O_4$
	19	20.361	265.105	242.1169	3-hydroxy-1-(4-hydroxy-3,5-di methoxyphenyl)-1-methoxypropane	$C_{12}H_{18}O_5$
	20	22.471	183.0872	182.0786	D-(-)-mannitol	$C_6H_{14}O_6$
	8	27.145	443.1882	442.1798	15-O- β-D-glucopyranosyl-11 β,13-dihydro urospermal A	$C_{21}H_{30}O_{10}$
	21	33.642	309.2771	308.2723	Ethyl linoleate	$C_{20}H_{36}O_2$
	22	35.045	365.1097	728.211	Quinic acid	$C_{39}H_{36}O_{14}$
B.F	23	0.859	177.042	176.036	Vitamic C	$C_6H_8O_6$
	12	4.863	171.0284	170.0205	Gallic acid	$C_7H_6O_5$
	3	7.281	321.1328	298.1439	3-(acetyl-oxy)-1-methoxy-1-(3,4,5-trimethoxyphenyl)propane	$C_{15}H_{22}O_6$
	4	9.119	409.1826	386.1923	Corchoionoside C	$C_{19}H_{30}O_8$
	5	9.755	453.2067	430.2179	Sonchuside H	$C_{21}H_{34}O_9$
	15	13.652	111.0448	110.0376	Catechol	$C_6H_6O_2$
	6	14.163	197.1177	196.1109	Loliolid	$C_{11}H_{16}O_3$
	16	14.899	461.1084	460.1016	Apigenin-7-O-ß-D-glucuronide methyl ester	$C_{22}H_{20}O_{11}$
	24	18.544	261.0517	238.0632	3-hydroxyflavone	$C_{15}H_{10}O_3$
	18	20.044	269.1771	268.1698	15-hydroxy-4β, 15,11 β, 13-tetrahydroreynosin	$C_{15}H_{24}O_4$
	20	22.408	183.0867	182.078	D-(-)-mannitol	$C_6H_{14}O_6$
	21	33.645	309.2801	308.2751	Ethyl linoleate	$C_{20}H_{36}O_2$

R.T: retention time, M-H + (m/z): mass spectral data, M.E: methanolic extract, EA.F: ethyl acetate fraction and B.F: butanolic fraction

us to identify 24 compounds in the three active extracts; mainly phenolics, flavonoids and sesquiterpene lactones which were responsible for their biological activities. This study gave initial insight of the effective extraction for a promising treatment of AD.

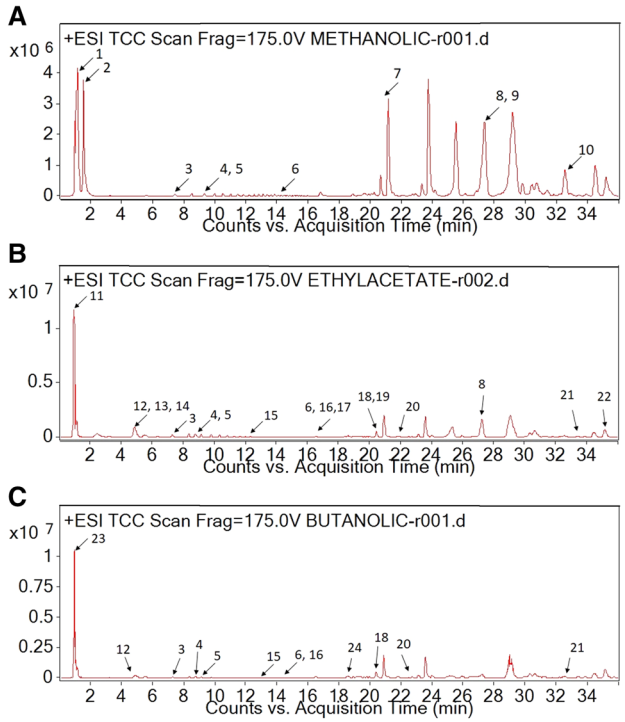

Fig. 4 Base peak chromatograms data detected in the aerial parts of SO by LC–MS/QTOF in positive ionization mode. The compounds in the three samples: (a) M.E, (b) EA.F and (c) B.F were characterized, numbered and presented as in Table 3. 1: Quininic acid; 2: Aesculin; 3: 3-(acetyl-oxy)-1-methoxy-1-(3,4,5-trimethoxyphenyl) propane; 4: Corchoionoside C; 5: Sonchuside H; 6: Loliolid; 7: Melampolide; 8: 15-O-β-D-glucopyranosyl-11β,13-dihydro urospermal A; 9: Tanacetin; 10: Macrocliniside A; 11: 2-(3,4-dihydroxyphenyl)-2-{[2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3,4-dihydro-2H-chromen-3-yl]oxy}-3,4,5,7-chromanetetrol; 12: Gallic acid; 13: Luteolin 7- β -D-glucosiduronic acid; 14: Sinapinic acid; 15: Catechol; 16: Apigenin-7-O-ß-D-glucuronide methyl ester; 17: Apigenin; 18: 15-hydroxy-4β,15,11β,13-tetrahydroreynosin; 19: 3-hydroxy-1-(4-hydroxy-3,5-di methoxyphenyl)-1-methoxypropane; 20: D-(-)-mannitol; 21: Ethyl linoleate; 22: Quinic acid; 23: Vitamin C; 24: 3-hydroxyflavone

Acknowledgements The authors would like to thank Integrative Pharmacogenomics Institute (iPROMISE), UiTM for providing facilities to carry out related research work.

Author contributions FA conducted the experimental work, collected the data, and wrote the draft of manuscript. NG, CB, AB and TLK conceived and designed the experiment, and furnished the designated work. HA and MHMI checked the experimental results, analysed the data, and critically reviewed the manuscript. All authors had read and approved the final manuscript.

Funding This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability All data supporting the findings in this work are adequately contained within the manuscript.

Compliance with ethical standards

Ethical statement The current work did not involve animals and human. The authors also would like to declare that the present manuscript and data have not been published and are not currently under review for publication elsewhere.

Conflict of interest Fatine Aissani has no conflict of interest. Nedjoud Grara has no conflict of interest. Chawki Bensouici has no conflict of interest. Aissam Bousbia has no conflict of interest. Hayette Ayed has no conflict of interest. Muhd Hanis Md Idris has no conflict of interest. Lay Kek Teh has no conflict of interest.

Informed consent Not applicable.

Code availability Not applicable.

References

Abhijeet VP, Prakash DK, Yunus NA (2018) A review on ethnomedicinal, pharmacological and a review on ethnomedicinal, pharmacological and phytochemical aspects of Sonchus oleraceus Linn. (Asteraceae). Int J Pharm Biol Sci 8(3):1–9

Abubakar EM, Misau S, Modibbo S, Lamaran Bala G (2017) Percentage yield and acute toxicity of the plant extracts of *Ceiba pentandra* grown in Bauchi State, North Eastern Nigeria. J Pharmacogn Phytochem 6(5):1777–1779

Ajayi AM, de Martins DTO, Balogun SO, de Oliveira RG, Ascêncio SD, Soares IM, dos Barbosa RS, Ademowo OG (2017) Ocimum gratissimum L. leaf flavonoid-rich fraction suppress LPS-induced inflammatory response in RAW 264.7 macrophages and peritonitis in mice. J Ethnopharmacol 204:169–178

Alva G, Cummings JL (2008) Relative tolerability of Alzheimer's disease treatments. Psychiatry (Edgmont) 5(11):27–36

Arabshahi-D S, Vishalakshi Devi AU, Urooj A (2007) Evaluation of antioxidant activity of some plant extracts and their heat, pH and storage stability. Food Chem 100(3):1100–1105

Ayaz M, Junaid M, Ahmed J, Ullah F, Sadiq A, Ahmad S, Imran M (2014) Phenolic contents, antioxidant and anticholinesterase potentials of crude extract, subsequent fractions and crude saponins from *Polygonum hydropiper* L. BMC Complement. Altern Med 14(1):1–9

Baatouche S, Cheriet T, Sarri D, Mekkiou R, Boumaza O, Benayache S, Benayache F, Brouard I, León F, Seghiri R (2019) Centaurea microcarpa Coss. & Dur. (Asteraceae) extracts: new cyanogenic glucoside and other constituents. Nat Prod Res 33(21):3070–3076

Badhani B, Sharma N, Kakkar R (2015) Gallic acid: A versatile antioxidant with promising therapeutic and industrial applications. RSC Adv 5:27540–27557

Blois MS (1958) Antioxidant determinations by the use of a stable free radical. Nature 4617(181):1119–1200

Bondarenko VG, Glyzin VI, Shelyuto VL (1978) Sonchoside - A new flavonoid glycoside from *Sonchus arvensis*. Chem Nat Compd 14:340

Castellani RJ, Rolston RK, Smith MA (2010) Alzheimer disease. Dis Mon 56(9):484–546

Dehmlow EV, Guntenhöner M, Van Ree T (1999) A novel alkaloid from *Fluggea virosa*: 14,15-epoxynorsecurinine. Phytochemistry 52(8):1715–1716

Dhanani T, Shah S, Gajbhiye NA, Kumar S (2017) Effect of extraction methods on yield, phytochemical constituents and antioxidant activity of Withania somnifera. Arab J Chem 10:S1193–S1199

Dos Santos FSM, Bezerra JWA, Kamdem JP, Boligon AA, Anraku MM, Da Silva ARP, Fidelis KR, Leite NF, Pinho AI, Coutinho HDM, dos Santos JEG (2019) Polyphenolic composition, antibacterial, modulator and neuroprotective activity of Tarenaya spinosa (Jacq.) Raf. (Cleomaceae). Asian Pac J Trop Biomed 9(1):12–17

Elkhayat ES (2009) Cytotoxic and antibacterial constituents from the roots of *Sonchus oleraceus* L. growing in Egypt. Phcog Mag 5(20):324–328

Ellman GL, Courtney KD, Andres V, Featherstone RM (1961) A new and rapid colorimetric determination of acetylcholinesterase activity. Biochem Pharmacol 7:88–95

Elufioye TO, Chinaka CG, Oyedeji AO (2019) Antioxidant and anticholinesterase activities of *Macrosphyra longistyla* (DC) Hiern relevant in the management of Alzheimer's disease. Antioxidants 8(400):1–5

Feng Y, Wang X (2012) Antioxidant therapies for Alzheimer's disease. Oxid Med Cell Longev 2012:472932

Ferreira A, Proença C, Serralheiro MLM, Araújo MEM (2006) The in vitro screening for acetylcholinesterase inhibition and antioxidant activity of medicinal plants from Portugal. J Ethnopharmacol 108:31–37

Guarrera P, Lucchese F, Medori S (2008) Ethnophytotherapeutical research in the high Molise region (Central-Southern Italy). J Ethnobiol Ethnomed 4:7

Guil-Guerrero JL, Giménez-Giménez A, Rodríguez-García I, Torija-Isasa ME (1998) Nutritional composition of Sonchus species (*S. asper* L., *S. oleraceus* L. and *S. tenerrimus* L.). J Sci Food Agric 76:628–632

Gutzmann H, Hadler D (1998) Sustained efficacy and safety of idebenone in the treatment of Alzheimer's disease: Update on a 2-year double-blind multicentre study. J Neural Transm Suppl 54:301–310

Ham A, Lee SJ, Shin J, Kim KH, Mar W (2012) Regulatory effects of costunolide on dopamine metabolism-associated genes inhibit dopamine-induced apoptosis in human dopaminergic SH-SY5Y cells. Neurosci Lett 507(2):101–105

Hayouni EA, Abedrabba M, Bouix M, Hamdi M (2007) The effects of solvents and extraction method on the phenolic contents and biological activities in vitro of Tunisian *Quercus coccifera* L. and *Juniperus phoenicea* L. fruit extracts. Food Chem 105:1126–1134

Helal AM, Nakamura N, El-askary H, Masao H (2000) Sesquiterpene lactone glucosides from *Sonchus asper*. Phytochemistry 53(4):473–477

Hossain MA, Shah MD (2015) A study on the total phenols content and antioxidant activity of essential oil and different solvent extracts of endemic plant *Merremia borneensis*. Arab J Chem 8(1):66–71

Houghton PJ, Howes MJ, Lee CC, Steventon G (2007) Uses and abuses of in vitro tests in ethnopharmacology: Visualizing an elephant. J Ethnopharmacol 110(3):391–400

Inbathamizh L, Padmini E (2013) Quinic acid as a potent drug candidate for prostate cancer: a comparative pharmacokinetic approach. Asian J Pharm Clin Res 6(4):106–112

Jacotet-Navarro M, Laguerre M, Fabiano-Tixier AS, Tenon M, Feuillère N, Bily A, Chemat F (2018) What is the best ethanol-water ratio for the extraction of antioxidants from rosemary? Impact of the solvent on yield, composition, and activity of the extracts. Electrophoresis 39:1946–1956

Jan S, Khan MR, Rashid U, Bokhari J (2013) Assessment of antioxidant potential, total phenolics and flavonoids of different solvent fractions of *Monotheca buxifolia* fruit. Osong Publ Heal Res Perspect 4(5):246–254

Kamalakararao K, Gopalakrishnan VK, Zenebe H, Govinda-Rao D, Padal SB, Krishna-Chaithanya K (2018) Anti-inflammatory activity of bioactive flavonoid apigenin-7-O-β-D-glucuronide methyl ester from ethyl acetate leaf extract of *Manilkara zapota* on lipopolysaccharide-induced pro-inflammatory mediators nitric oxide (NO), prostaglandin E2 (PGE2) in RAW 264.7 cells. Drug Invent Today 10(4):531–535

Khan RA, Khan MR, Sahreen S (2012) Brain antioxidant markers, cognitive performance and acetylcholinesterase activity of rats: efficiency of *Sonchus asper*. Behav Brain Funct 8(21):1–7

Kumaran A, Joel Karunakaran R (2007) In vitro antioxidant activities of methanol extracts of five Phyllanthus species from India. LWT Food Sci Technol 40(2):344–352

Lane RM, Potkin SG, Enz A (2006) Targeting acetylcholinesterase and butyrylcholinesterase in dementia. Int J Neuropsychopharmacol 9:101–124

Li Q, Dong DD, Huang QP, Li J, Du YY, Li B, Li HQ, Huyan T (2017) The anti-inflammatory effect of Sonchus oleraceus aqueous extract on lipopolysaccharide stimulated RAW 2647 cells and mice. Pharm Biol 55(1):799–809

Li XM, Yang PL (2018) Research progress of Sonchus species. Int J Food Prop 21(1):147–157

Lovell MA, Markesbery WR (2007) Oxidative DNA damage in mild cognitive impairment and late-stage Alzheimer's disease. Nucl Acids Res 35(22):7497–7504

Ma Q, Jiang J, Zhang X, Zhu W (2018) Identification of luteolin 7-O-β-D-glucuronide from *Cirsium japonicum* and its anti-inflammatory mechanism. J Funct Foods 46:521–528

Malgorzata G, Katarzyna W, Wanda M, Potaniec B, Miroslaw A (2015) Loliolide: the most ubiquitous lactone. Folia Biol Oecologica Carbon 11:1–8

Miyase T, Fukushima L (1987) Studies on sesquiterpene glycosides from *Sonchus oleraceus* L. Chem Pharm Bull 35(7):2869–2874

Müller L, Gnoyke S, Popken AM, Böhm V (2010) Antioxidant capacity and related parameters of different fruit formulations. LWT Food Sci Technol 43(6):992–999

Nakamura M, Ra J, Jee Y, Kim J (2016) Impact of different partitioned solvents on chemical composition and bioavailability of *Sasa quelpaertensis* Nakai leaf extract. J Food Drug Anal 25(2):316–326

Nayak Y, Venkatachalam H, Daroji VK, Mathew G, Jayashree BS, Unnikrishnan MK (2014) Antidiabetic activity of 3-hydroxyflavone analogues in high fructose fed insulin resistant rats. EXCLI J 13:1055–1074

Nićiforović N, Abramovič H (2014) Sinapic acid and its derivatives: Natural sources and bioactivity. Compr Rev Food Sci Food Saf 13:34–51

Nunomura A, Perry G, Aliev G, Hirai K, Takeda A, Balraj EK, Jones PK, Ghanbari H, Wataya H, Shimohama S, Chiba S, Atwood CS, Petersen RB, Smith MA (2001) Oxidative damage is the earliest event in Alzheimer disease. J Neuropathol Exp Neurol 60(8):759–767

Oken BS, Storzbach DM, Kaye JA (1998) The efficacy of *Ginkgo biloba* on cognitive function in Alzheimer disease. Arch Neurol 55(11):1409–1415

Ozgen U, Sevindik H, Kazaz C, Yigit D, Kandemir A, Secen H, Calis I (2010) A new sulfated α-ionone glycoside from *Sonchus erzincanicus* Matthews. Molecules 15(4):2593–2599

Pellegrini N, Colombi B, Salvatore S, Brenna OV, Galaverna G, Del Rio D, Bianchi M, Bennett RN, Brighenti F (2007) Evaluation of antioxidant capacity of some fruit and vegetable foods: Efficiency of extraction of a sequence of solvents. J Sci Food Agric 87:103–111

Piechocka J, Szulc P, Dziedziński M, Kobus-Cisowska J, Szczepaniak O, Szymanowska-Powałowska D (2020) Antioxidant potential of various solvent extract from *Morus alba* fruits and its major polyphenols composition. Cienc Rural 50(1):e20190371

Rahmat A, Khan MR, Sumaira S, Mushtaq A (2012) Evaluation of phenolic contents and antioxidant activity of various solvent extracts of *Sonchus asper* (L.) Hill. Chem Cent J 6(12):1–7

Re R, Pellegrini N, Proteggente A, Pannala A, Yang M, Rice-Evans C (1999) Antioxidant activity applying an improved ABTS radical cation decolorization assay. Free Radic Biol Med 26(9–10):1231–1237

Robards K (2003) Strategies for the determination of bioactive phenols in plants, fruit and vegetables. J Chromatogr A 1000:657–691

Sacchetti G, Maietti S, Muzzoli M, Scaglianti M, Manfredini S, Radice M, Bruni R (2005) Comparative evaluation of 11 essential oils of different origin as functional antioxidants, antiradicals and antimicrobials in foods. Food Chem 91(4):621–632

Schaffer S, Schmitt-Schillig S, Müller WE, Eckert GP (2005) Antioxidant properties of Mediterranean food plant extracts: Geographical differences. J Physiol Pharmacol 56(Suppl 1):115–124

Shi H, Noguchi N, Niki E (2001) Galvinoxyl method for standardizing electron and proton donation activity. Methods Enzymol 335:66–157

Singleton VL, Rossi J (1965) Colorimetry of total phenolics with phosphomolybdic-phophotungstic. Am J Enol Vitic 16:144–158

Smach MA, Hafsa J, Charfeddine B, Dridi H, Limem K (2015) Effects of sage extract on memory performance in mice and acetylcholinesterase activity. Ann Pharm Fr 73(4):281–288

Szydłowska-Czerniak A, Dianoczki C, Recseg K, Karlovits G, Szłyk E (2008) Determination of antioxidant capacities of vegetable oils by ferric-ion spectrophotometric methods. Talanta 76:899–905

Teugwa CM, Mejiato PC, Zofou D, Tchinda BT, Boyom FF (2013) Antioxidant and antidiabetic profiles of two African medicinal plants: *Picralima nitida* (Apocynaceae) and *Sonchus oleraceus* (Asteraceae). BMC Complement Altern Med 13:175

Thakur N, Arya V (2012) Preliminary phytochemical analysis of the extracts of Psidium leaves. J Pharmacogn Phytochem 1(1):1–4

Thavamoney N, Sivanadian L, Hong L, Hock T, Khoo E (2018) Extraction and recovery of phytochemical components and antioxidative properties in fruit parts of *Dacryodes rostrata* influenced by different solvents. J Food Sci Technol 55(7):2534–2543

Topçu G, Ay M, Bilici A, Sarikürkcü C, Öztürk M, Ulubelen A (2007) A new flavone from antioxidant extracts of *Pistacia terebinthus*. Food Chem 103:816–822

Vieira BS, Barreto RW (2006) First record of *Bremia lactucae* infecting *Sonchus oleraceus* and *Sonchus asper* in Brazil and its infectivity to lettuce. J Phytopathol 154:84–87

Wang M, Shao Y, Li J, Zhu N, Rangarajan M, Lavoie EJ (1999) Antioxidative phenolic glycosides from sage (*Salvia officinalis*). J Nat Prod 62(3):454–456

Wang TY, Li Q, Bi KS (2018) Bioactive flavonoids in medicinal plants: Structure, activity and biological fate. Asian J Pharm Sci 13(1):12–23

Wąsik A, Antkiewicz-Michaluk L (2017) The mechanism of neuroprotective action of natural compounds. Pharmacol Rep 69(5):851–860

Whittaker VP (1990) The contribution of drugs and toxins to understanding of cholinergic function. Trends Pharmacol Sci 11(1):8–13

Xia DZ, Yu XF, Zhu ZY, Zou ZD (2011) Antioxidant and antibacterial activity of six edible wild plants (Sonchus spp) in China. Nat Prod Res 25(20):1893–1901

Xu YJ, Sun SB, Sun LM, Qiu DF, Liu XJ, Jiang ZB (2008) Quinic acid esters and sesquiterpenes from *Sonchus arvensis*. Food Chem 111:92–97

Yin J, Kwon G, Wang M (2007) The antioxidant and cytotoxic activities of Sonchus oleraceus L extracts. Nutr Res Pract 1(3):189–194