**Tropical Journal of Natural Product Research** 

Available online at https://www.tjnpr.org

**Original Research Article** 



### Phenolic Constituents, Antioxidant and Antimicrobial Activities of Globe Artichoke (Cynara scolymus L.) Aqueous Extracts

Mohamed A. Ali<sup>1</sup>, Magdy A. Shallan<sup>1</sup>, Walaa A. Meshrf<sup>1</sup>, Diaa A. Marrez<sup>2</sup>\*

<sup>1</sup>Biochemistry Department, Faculty of Agriculture, Cairo University, Giza, Egypt <sup>2</sup>Food Toxicology and Contaminants Department, National Research Centre, Dokki, Cairo, Egypt

## ARTICLE INFO ABSTRACT

Article history: Received 16 September 2021 Revised 17 October 2021 Accepted 25 November 2021 Published online 05 December 2021

**Copyright:** © 2021 Ali *et al.* This is an open-access article distributed under the terms of the <u>Creative</u> <u>Commons</u> Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Globe artichoke (Cynara scolymus L.) is a promising herbal plant, rich in bioactive compounds. The present study aimed to determine the phenolic profile, antioxidants and antimicrobial activities of globe artichoke bracts and receptacles aqueous extracts. Phenolic compounds in artichoke bracts and receptacles aqueous extracts were determined by high performance liquid chromatography (HPLC). The antioxidant activity was assayed using the 2,2-diphenyl-1picrylhydrazyl (DPPH), 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) radical scavenging and ferric ion reducing antioxidant power (FRAP), and the antimicrobial activity was determined using disc-diffusion assay. The total phenolic and flavonoid contents of the bracts extract (24.04  $\mu$ g GAE mg<sup>-1</sup> and 194.07  $\mu$ g QE mg<sup>-1</sup>, respectively) were higher than in the receptacles (15.1  $\mu$ g GAE mg<sup>-1</sup> and 52.07  $\mu$ g QE mg<sup>-1</sup>, respectively). The bracts extract contained ten phenolic compounds, of which the major one was p-hydroxybenzoic (9.88 mg g<sup>-1</sup>), while the receptacles extract contained five compounds, with Gentisic acid ( $6.36 \text{ mg g}^{-1}$ ) as the major compound. The bracts extract showed higher antioxidant activity (26.05% and 20.21% at 10ppm for DPPH and ABTS, and 14.05 µmol/L at 100 ppm for FRAP) compared to that of the receptacles. The aqueous extracts of bracts and receptacles showed antimicrobial activity against all tested foodborne pathogenic bacteria and mycotoxigenic fungi with inhibition zone diameters ranging from 7.2 to 11.2 mm and minimum inhibitory concentration (MIC) values ranging between 0.04 and 4.2 mg mL<sup>-1</sup>. The results revealed that globe artichoke bracts and receptacles could possess important antioxidant and antimicrobial properties that may improve its quality as a functional food.

Keywords: Globe artichoke, aqueous extract, phenolic profile, antimicrobial, antioxidant.

#### Introduction

Functional foods or nutraceuticals are relatively recent concepts; in the last few decades, which have garnered a growing interest in coining a certain category of foods or nutrients that contain bioactive compounds and have possible health values or pharmaceutical applications.<sup>1,2</sup> Globe artichoke (*Cynara scolymus* L.) is one of the largest functional foods. It contains many bioactive compounds and is used as medicines and for nutraceutical application.<sup>3</sup> It is a vegetable crop native to the Mediterranean basin which contributes significantly to the local agricultural economy, grown mainly for its immature flower buds, and it is a perennial plant belonging to Asteraceae family. It is one of the most suitable plants growing organically.<sup>4</sup> Italy ranks first for its production (about 377,000 t annually) followed by Spain (224,000 t) and Egypt (180,000 t).<sup>5</sup> During the harvesting process of artichoke, a large amount of waste biomass about 80-85% which is unsuitable for human consumption such as bracts and stems are discarded.<sup>1,2</sup> Francavilla et al.<sup>8</sup> found that the waste of artichoke crop that were discarded after the harvesting was about 33 tons dry weight per hectare.

\*Corresponding author. E mail: <u>diaamm80@hotmail.com</u> Tel: +201019621995

Citation: Ali MA, Shallan MA, Meshrf WA, Marrez DA. Phenolic Constituents, Antioxidant and Antimicrobial Activities of Globe Artichoke (*Cynara scolymus* L.) Aqueous Extracts. Trop J Nat Prod Res. 2021; 5(11):1986-1994. doi.org/10.26538/tjnpr/v5i11.16

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

Sihem *et al.*<sup>9</sup> and Fratianni *et al.*<sup>10</sup> reported that the phenolic composition of artichoke wastes, and artichoke edible parts are the same. Globe artichoke is considered a healthy food, due to its nutritional and phytochemical composition. It contains proteins, minerals, low amount of lipids, dietary fiber and a high proportion of phenolics.<sup>11</sup>

Artichoke is rich in polyphenols including flavonoids, phenolic acids, hydroxycinnamic acid derivatives, and lignans with a wide spectrum of medical applications in nearly all parts of the plants.<sup>12-16</sup> Artichoke has many polyphenols groups, the major ones being cynarin, chlorogenic acid (5-*O*-caffeoylquinic acid), and caffeic acid. Beside the wide range of chlorogenic acid and caffeic acid derivatives which were observed in leaves and heads of artichoke, other compounds such as; flavonoids luteolin & apigenin, and different derivatives of cyanidin caffeoylglucoside were found.<sup>17-19</sup> Aqueous and organic extracts of edible part of artichoke contain flavones, glycosidic flavones, and phenolic acids.<sup>20</sup> Artichoke is growing in the Mediterranean region, considered an edible plant and used for its antioxidant, antibacterial, antifungal, and anticancer activities.<sup>21</sup>

Artichoke has an ability to scavenge free radicals (as antioxidant) and this antioxidant activity is related to their content of caffeic acid.<sup>22</sup> The aqueous leaf extracts of artichoke reduced the total viable counts and total coliform as a result of their antimicrobial activity during the process of marination and storage of *Sardinella aurita*. In this study, the phenolic profile, phenolic burden, antioxidant, and antibacterial activity were investigated. The main objective of this study was to determine the phenolic profile of globe artichoke bracts and receptacles aqueous extracts using HPLC as well as to determine the antioxidant activity against foodborne pathogenic bacteria and mycotoxigenic fungi.

#### **Materials and Methods**

#### Collection and extraction of plant material

The artichoke (Cynara scolymus L.) was purchased from Abu El Matamir, Beheria Governorate, Egypt, during February to April 2019. Plant materials were identified by Dr. Abdelhalem Mohamed (Flora and Plant Classification Research Department, Horticultural Research institute, ARC, Egypt). A voucher specimen was deposited at the herbarium of Agriculture Research Center with number M317. The plant parts were separated into its botanical parts; receptacles and bracts, then washed with distilled water and dried in National Research Centre Dokki, Cairo, Egypt using solar dryer. The dried parts were grinded using Braun Multiquick Mixer (4250 Original, Germany) and the successive extraction technique was performed for 100 g from receptacles and bracts using four solvents, hexane, diethyl ether (anhydrous), ethanol, and double distilled water, with continuous mixing in a reciprocating shaker (MP-7552, hsiHefer, Sanfrancisco). The residual was separated by filtration and the filtrate of each extract was dried using rotary evaporator (heidoph, North America) at 50°C.

#### Determination of the total phenolic content (TPC)

Total phenolic content was determined in both receptacles and bracts aqueous extracts using Folin-Ciocalteu reagent.<sup>23</sup> All determinations were performed in triplicate. The absorbance of the developed blue color was measured at 650 nm against a blank using spectrophotometer (UV mini-1240, SHIMADZU, Nakagyo-Ku, Kyoto, Japan). Gallic acid was used as a standard in concentrations ranging from 10-100 ppm. Total phenolic content was expressed in  $\mu g$  of Gallic acid equivalent per mg of dry extract ( $\mu g$  of GAE /mg of dry extract) according to the equation of the calibration curve of gallic acid solution.

#### Determination of the total flavonoid content (TFC)

Flavonoids contents were determined in globe artichoke aqueous extract according to the aluminium chloride colorimetric method.<sup>24</sup> All determinations were performed in triplicate. The absorbance was measured at 510 nm against a blank using spectrophotometer. Quercetin was used as a standard in concentrations ranging from 10-100 ppm. Total flavonoid content was expressed in  $\mu$ g of quercetin equivalent per mg of dry extract ( $\mu$ g of QC /mg of dry extract) according to the equation of the calibration curve of quercetin solution.

#### Determinations of phenolic profile using HPLC

The phenolic profile of aqueous extracts of bracts and receptacles globe artichoke was determined using HPLC. HPLC analysis was carried out according to Kim *et al.*<sup>25</sup> using Agilent Technologies 1100 series liquid chromatograph equipped with an auto sampler and a diode-array detector. The analytical column was an Eclipse XDB-C18 (150 X 4.6  $\mu$ m; 5  $\mu$ m) with a C18 guard column (Phenomenex, Torrance, CA). The mobile phase consisted of acetonitrile (solvent A) and 2% acetic acid in water (v/v) (solvent B). The flow rate was kept at 0.8 mL/min for a total run time of 60 min and the gradient programme was as follows: 100% B to 85% B in 30 min, 85% B to 50% B in 20 min, 50% B to 0% B in 5 min and 0% B to 100% B in 5 min. The injection volume was 50  $\mu$ L and peaks were monitored simultaneously at 280, 320, and 360 nm for benzoic acid and cinnamic acid derivatives and flavonoids, respectively. The column temperature was set during the separation process to 35°C.

# Antioxidant activity of globe artichoke aqueous extract (2,2-Diphenyl-1-picrylhydrazyl) radical scavenging

2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging performance of aqueous extract was determined according to the procedure mentioned by Chandrasekar *et al.*<sup>26</sup> The receptacles and bracts aqueous extracts were prepared by dissolving 4 mg of sample in 4 mL double distilled water. DPPH (0.1 mM, 500  $\mu$ L) was mixed with different concentrations of receptacles and bracts aqueous extracts (10, 50, 100, 200, and 400 ppm). The reaction mixture was vortexed and kept in the dark at room temperature (25.2°C) for 30

min. After incubation, absorbance was measured by spectrophotometer at 517nm. Butylated hydroxytoluene (BHT) was used as a reference standard at concentration 100 ppm. The DPPH scavenging activity was calculated using the following formula:

DPPH scavenging activity (% inhibition) =  $\frac{A_0 - A_1}{A_0} \times 100$ 

 $A_0$  is the negative control absorption and  $A_1$  is the sample absorption.

#### ABTS radical scavenging

ABTS radical scavenging study was performed as explained by Re *et*  $al.^{27}$  ABTS stock solutions were prepared by mixing 7 mM ABTS solution and 2.45 mM of K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> (Potassium per-sulphate) solution, then the mixture incubated for 12 h at room temperature (25.2°C). Working solution was diluted by ethanol until the absorbance gives 0.708±0.002 at 734 nm. The receptacles and bracts aqueous extracts were prepared by dissolving 4mg of sample in 4mL double distilled water. Different concentrations of receptacles and bracts aqueous extracts (10, 20, 40, and 80 ppm) reacted with 2 mL of ABTS<sup>+</sup> solution. After 30 min of incubation, absorbance was measured at 734 nm, at 25°C. ABTS<sup>+</sup> scavenging capacity was compared with BHT and calculated as follows:

% ABTS radical scavenging activity  $= \frac{A_0 - A_1}{A_0} \times 100$ 

Where A<sub>0</sub>: the absorbance of ethanolic ABTS and A<sub>1</sub>: the absorbance of ABTS radical with sample extract or standard.

#### Ferric ion reducing antioxidant power (FRAP)

FRAP assay was carried out for receptacles and bracts aqueous extracts according to Pulido *et al.*<sup>28</sup> The stock solutions included 300 mM acetate buffer (pH 3.6), 10 mM TPTZ (Mwt: 312.3) solution in 40 mM HCl and 20 mM FeCl<sub>3</sub> (Mwt: 270). FRAP reagent for samples (acetate buffer: TPTZ: FeCl<sub>3</sub>) was prepared in 10:1:1 respectively and the reagent for standard curve with FeSO<sub>4</sub>·7H<sub>2</sub>O (acetate buffer: TPTZ: Dis.deionzed water) in 10:1:1 respectively. Using the stock standard solution of 1 mM FeSO<sub>4</sub>·7H<sub>2</sub>O (positive control), different concentrations of tested samples (100, 200, 400, and 800) and standard were allowed to react with 2 mL FRAP solution for 30 min at room temperature (25.2°C) in the dark. The activated samples against FRAP reagent (forming blue colored product, ferrous tripyridyltriazine complex), was estimated by measuring the absorbance at 593 nm by spectrophotometer. The FRAP value was calculated according to the results of standard curve of standard solution of ascorbic acid by using the FRAP value formula:

$$FRAP \text{ value of extract } (\mu \text{ mol/L}) \\ = \frac{Abs. \text{ of extract } X \text{ FRAP value of standard } (\mu \text{ mol/L})}{Abs. \text{ of standard}}$$

Antimicrobial activity of globe artichoke aqueous extract Tested microorganisms

The inhibitory effect of globe artichoke aqueous extract was performed on seven strains of foodborne pathogenic bacteria. Three Gram-positive bacteria; *Bacillus cereus* EMCC 1080, *Staphylococcus aureus* ATCC 13565, *Staphylococcus sciuri* 2-6 and four Gramnegative bacteria; *Salmonella enterica* SA19992307, *Salmonella typhi* ATCC 25566, *Escherichia coli* 0157 H7 ATCC 51659, and *Pseudomonas aeruginosa* NRRL B-272. The stock cultures were grown on nutrient agar slant at 37°C for 24 h and then kept in refrigerator till use. Eight fungal strains were used for antifungal assay; *Aspergillus flavus* NRR 3357, *Aspergillus ochraceus* ITAL 14, *Aspergillus niger* IMI288550, *Aspergillus westerdijikia* CCT 6795, *Fusarium proliferatum* MPVP 328, *Aspergillus carbonarius* ITAL 204, *Aspergillus parasiticus* SSWT 2999, and *Penicillium verucosum* BFE 500. The stock cultures were grown on potato dextrose agar slant at 25°C for 5 days and then kept in refrigerator till use.

#### Disc diffusion technique

The sensitivity test of globe artichoke aqueous extract was determined with different bacterial cultures using disc diffusion method by Kirby-Bauer technique.<sup>29,30</sup> DMSO represented a negative control and

#### ISSN 2616-0684 (Print) ISSN 2616-0692 (Electronic)

tetracycline (500 µg/mL) was used as a positive control. Thereafter, the inoculated plates were incubated at 37°C for 24 h. At the end of the incubation period, inhibition zones (mm) were measured and expressed as the diameter of clear zone including the diameter of the paper disc.

The fungal strains were plated onto potato dextrose agar (PDA) and incubated for 5 days at 25°C. The spore suspension of each fungus (2 x  $10^8$  CFU/mL) was prepared in 0.01% Tween 80 solution. Negative control was prepared by using DMSO and the commercial fungicide Nystatin (1000 Unit/mL) was used as a positive control. The inoculated plates were incubated at 25°C for 24-48 h. At the end of the period, antifungal activity was evaluated by measuring the zone of inhibition (mm) against the tested fungus.<sup>31</sup>

#### Determination of minimum inhibitory concentration (MIC)

Minimum inhibitory concentration for globe artichoke receptacles and bracts aqueous extracts was determined using the microbroth dilution method according to Andrews.<sup>32</sup> Two-fold serial dilutions of receptacles and bracts aqueous extracts ranging from 10 to 0.02 mg/mL were used. Equal volumes of tested bacteria ( $10^5$  CFU/mL) were added to each well. MIC values were taken as the lowest concentration of the antimicrobial agent that inhibited bacterial growth after 24 h incubation at 37°C. MIC against fungi was performed by using the technique of Sokmen *et al.*<sup>33</sup> and Marrez and Sultan.<sup>34</sup> Globe artichoke aqueous extract at different concentrations were separately dissolved in 0.5 mL of 0.1% Tween 80, then mixed with 9.5 mL of melting, 45°C, PDA and poured into Petri dish (6 cm). The prepared plates were centrally inoculated with 3µL of fungal suspension ( $10^8$  CFU/mL; 0.5 McFarland standard). The plates were incubated at 25°C for 24-48 h. At the end of the incubation period, mycelial growth was monitored, and MIC was determined.

#### Statistical analysis

All tests were processed in triplicate and the data was represented by the Standard Error of mean (SE). "WASP-Web Agri Stat Package at ICAR: Central Coastal Agricultural Research Institute" was applied for statistical analysis. One-way, "Two-way" analysis of variation (ANOVA) were used to analyze the difference between groups by applying the least significant difference (LSD) test with 5% level of significance (P<0.05).

#### **Results and discussion**

#### Total phenolic and flavonoid contents

The total phenolic content (TPC) and total flavonoid content (TFC) of bracts and receptacles aqueous extracts from globe artichoke were determined as shown in Table 1. The results showed that the phenolic content of bracts aqueous extract (expressed in GAE) was higher than the total phenolic content of receptacles aqueous extract with 24.04 and 15.1 µg GAE/mg, respectively. Also, the total flavonoid content of bracts aqueous extract (expressed in Quercetin equivalents) was higher than the total flavonoid content of receptacles aqueous extract with 194.07 and 52.07 µg QC/mg, respectively. Also, Ben Salem *et al.*<sup>35</sup> revealed that the leaves aqueous extract of artichoke had high amount of total phenolic and total flavonoid (about 49.49 mg Gallic/g DW and 9.49 mg Catechin/g DW, respectively). One of the most important secondary metabolites in plants are phenolic compounds which are considered a defense mechanism against microbial infection,<sup>36</sup> and they were developed to obtain active compounds "natural antioxidants" that the removing of toxic agents is basically attributed to the phenolic compounds.<sup>37</sup> Zan *et al.*<sup>38</sup> investigated that the leaves aqueous extract of *Cynara cardunculus var. scolymus* L. contained phenolic and flavonoid compounds.

#### Phenolic profile in globe artichoke aqueous extracts

Phenolic compounds profile in globe artichoke receptacles and bracts aqueous extracts were identified and quantified using HPLC (Table 2). The HPLC analysis of globe artichoke showed ten phenolic compounds in bracts aqueous extract and five compounds in receptacles aqueous extract. The prevailing compounds in bracts extract were *p*-hydroxybenzoic with 9.88 mg g<sup>-1</sup>, Chlorogenic with 5.21 mg g<sup>-1</sup>, and Apigenin with 5.18 mg g<sup>-1</sup>. On the other hand, the major compounds found in receptacles aqueous extract were Gentisic with 6.36 mg g<sup>-1</sup>, Qurecetin with 2.78 mg g<sup>-1</sup> and Syringic with 1.95 mg g<sup>-1</sup>, while Protocatechuic, *p*-hydroxybenzoic, Chlorogenic, *p*-coumaric, and Apigenin were not detected in receptacles aqueous extract.

Polyphenolic compounds are widely studied for its biological activities, as they extensively were found in plants and their content differentiate according to several factors such as; climate, plant type, and season of harvest. The bioactivity of phenolic compounds is figured out by their chemical structure, proportion, and interaction with other compounds. In folk remedy, the leaves of shrubs and fruit trees were used to treat several diseases, and with time it's have been forgotten but their benefits are now being rediscovered.<sup>39</sup>

**Table 1:** TPC and TFC values of globe artichoke obtained from aqueous extract of receptacles and bracts

Aqueous extracts	TPC μg GAC/mg and TFC μg QC/mg			
	TPC	TFC		
Receptacles	$15.1 \pm 0.52^{b}$	$52.07 \pm 1.33^{b}$		
Bracts	$24.04\pm1.05^{\mathrm{a}}$	$194.07\pm2.9^{a}$		

n = 3, \*SE: standard error, different superscripts within column are significantly different at 5%

Compound	RT (Min.)	<b>Concentration</b> (mg/g extract)		
Compound	KI (MIII.)	Bracts aqueous extract	Receptacles aqueous extract	
Protocatechuic	7.7	5.01	ND	
p-hydroxybenzoic	12.1	9.88	ND	
Gentisic	12	2.86	6.36	
Chlorogenic	16.5	5.21	ND	
Syringic	19.3	1.58	1.95	
<i>p</i> -coumaric	35	4.82	ND	
Qurecetin	49.5	2.36	2.78	
Apigenin	55.2	5.18	ND	
Kaempferol	55.9	0.35	1.02	
Chrysin	59	4.81	0.52	

Table 2: Phenolic compounds in globe artichoke bracts and receptacles aqueous extracts

ND: Not detected

Petropoulos *et al.*<sup>19</sup> identified thirteen phenolic compounds in cardoon, nine being categorized as phenolic acids and other were characterized as flavonoids. Also, Borgognone *et al.*<sup>40</sup> reported that the chlorogenic acid and cynarin contents in cardoon leaves were higher than the flavonoids. Also, the results which were obtained by Santana-Gálvez *et al.*<sup>41</sup> stated that these compounds have a beneficial usage, they could be used as a food additive and as pharmaceutical agents. The syringic and quinic acids showed different biological activity such as; antioxidant, antimicrobial, anti-inflammatory, anti-hyperglycemic, and neuroprotective activities.<sup>42-47</sup> Zan *et al.*<sup>38</sup> reported that the aqueous extract of artichoke contained phenolic acids; chlorogenic acid, gallic acid, caffeic acid, and Rosmarinic acid and flavonoids such as; hyperoside, sakuranetin, isoquercetrin, quercetin, and *rutin.* According to the previous studies by Noldin *et al.*,<sup>48</sup> Wang *et al.*,<sup>49</sup> Schutz *et al.*,<sup>50</sup> the polyphenolics and flavonoids are frequently components of artichoke.

#### Antioxidant activity

### DPPH and ABTS radical scavenging activity of bracts and receptacles aqueous extracts

The useful effects of phenolic compounds on health as antioxidants were observed in a number of studies.<sup>51,52</sup> Artichoke leaves extract had showed a vigorous free radical scavenging activity because of the presence of chlorogenic acid, apigenin, caffeic acid, and scolymoside cynaroside.<sup>49,53,54</sup> DPPH and ABTS methods are usually used to assess the antioxidant capacities. These two methods are considered spectrophotometric techniques and colorimetric assay based on electron transfer reaction. The antioxidant activities were evaluated by these methods through measuring the change of color which occurred when the radicals bind to antioxidant compounds (hydrogen donors), as the different degrees of color change is related to the amount and type of antioxidant compounds inside the cell.

The data in Table 3 showed the free radical scavenging activity of globe artichoke bracts and receptacles aqueous extracts. All extracts

had an antioxidant activity at different concentrations and there was a dose-response relationship that the activity increased as the concentration increased. The results revealed that the bracts had higher antioxidant activity than receptacles against DPPH radical. The DPPH scavenging free radical activity of bracts aqueous extract ranged from 26.05% at 10 ppm to 79.52% at 400 ppm, on the other hand the DPPH scavenging free radical activity of receptacles aqueous extract ranged from 23.5% at 10 ppm to 49.55% 400 ppm. The hydromethanolic extracts of heads, leaf blades, midribs and petioles, and seeds of *Cynara cardunculus* L. var. *altilis* DC showed antioxidant activity for DPPH assay.<sup>19</sup> The results of Zan *et al.*<sup>38</sup> reported that the aqueous leaves extract of artichoke showed a DPPH scavenging activity (4.52% at 10 ppm, 15.12% at 100 ppm, and 70.62% at 1000 ppm), and these previous results showed a relation between the concentration of the extract and the DPPH scavenging ability.

The results in Table 4 showed the ABTS free radical scavenging activity of globe artichoke bracts and receptacles aqueous extracts. The ABTS free radical scavenging of bracts aqueous extract ranged from 20.21% at 10 ppm to 47.01% at 80 ppm, while the ABTS scavenging free radical activity of receptacles aqueous extract ranged from 16.11% at 10 ppm to 35.60% at 80 ppm. Yang et al.<sup>37</sup> reported that the water fraction of artichoke showed antioxidant activity for DPPH and ABTS. Dabbou *et al.*<sup>55</sup> observed that the 'Violet d'Hyéres' cultivar showed the highest antioxidant activity by ABTS assay. Turkiewicz et al.<sup>56</sup> revealed that the internal bracts of aqueous methanol extracts of Cultivar "Blanca de Tudela" and cv. "Calico" showed antioxidant activity as ABTS (ranged between 12.49 to 20.74 mmol Trolox /100 g) and the Cultivar "Blanca de Tudela" was the highest compared with cv. "Calico". Biel et al.<sup>57</sup> investigated that the water artichoke leaf extract showed antioxidant activity by using ABTS and DPPH assay that the radical scavenging activity was 79.74% with ABTS but in case of DPPH the radical scavenging activity was lower 44%.

		Sca	wenging free radical	s %		
Aqueous extracts	Concentration (ppm)					
	10	50	100	200	400	
Receptacles	$23.5 \pm 0.1^{j}$	$26.83\pm0.12^{\rm h}$	$30.93\pm0.1^{\text{g}}$	$40.03\pm0.27^{\rm f}$	$49.55 \pm 0.23^{d}$	
Bracts	$26.05\pm0.1^i$	$45.22\pm0.1^{e}$	$71.82\pm0.2^{\text{c}}$	$72.82\pm0.29^{b}$	$79.52\pm0.17^a$	
BHT	$60.25\pm0.11^e$	$62.39\pm0.21^{d}$	$63.11\pm0.03^{c}$	$67.65\pm0.14^{b}$	$70.71\pm0.13^a$	

Table 3: DPPH	scavenging	activity of	of globe	artichoke	bracts and	receptacles a	queous extracts

Each value represents the mean  $\pm$  SE, n=3, BHT: Butylated hydroxytoluene, values with the same letter are not significantly different at (P $\leq$ 0.05), and the comparison is done according to concentrations.

Table 4: ABTS	scavenging activity	of globe artichoke of br	acts and receptacles aqueous extracts

		ABTS scavengin	g free radicals %		
Aqueous extracts	Concentration (ppm)				
-	10	20	40	50	
Receptacles	$16.11 \pm 0.45^{g}$	$18.03\pm0.19^{\rm f}$	$25.17\pm0.28^{\rm c}$	$35.60 \pm 0.56^{b}$	
Bracts	$20.21\pm0.23^{e}$	$23.93\pm0.24^{d}$	$35.13\pm0.0^{b}$	$47.01\pm0.24^a$	
BHT	$99\pm0.0^{a}$	$99\pm0.0^{a}$	$99\pm0.0^{\rm a}$	$99\pm0.0^{\rm a}$	

Each value represents the mean  $\pm$  SE, n=3, BHT: Butylated hydroxytoluene, values with the same letter are not significantly different at (P $\leq 0.05$ ), and the comparison is done according to concentrations.

Ferric reducing antioxidant power of bracts and receptacles aqueous extract

FRAP assay is a direct method which is used to determine the ability of plant extracts (as reductants) to reduce the ferric ions Fe<sup>3+</sup> to ferrous ions Fe<sup>2+</sup>. In this study the antioxidant property of aqueous extract of bracts and receptacles from globe artichoke was measured according to its possible ability into reduce 2, 4, 6-tripyridil-s-triazine ferric [TPTZ-Fe (III)] complex. The production of ferrous (Fe<sup>2+</sup>) was assessed by the formation of the blue-colored complex followed by the incubation of the reaction mixture.<sup>58</sup> According to the comparison between two parts of globe artichoke; bracts and receptacles, the aqueous extract of bracts showed the largest FRAP value. The FRAP values of bracts and receptacles aqueous extracts at 100 ppm were 14.05 and 1.38  $\mu$  mol/L, respectively. These values were increased to 59.81 and 15.97  $\mu$ mol/L at 800 ppm (Table 5). Contrary to this, the results that were obtained by Jiménez-Moreno *et al.*<sup>16</sup> showed the FRAP value of 60% methanol extracts was higher than water extracts. The results of antioxidant activity were coinciding with the results of phenolic burden values (total phenolic and total flavonoid) and chromatographic analysis (HPLC analysis) which showed that the bracts aqueous extract had the largest phenolic & flavonoids compounds, so the ability of bracts aqueous extract to reduce an oxidative damage or scavenge free radicals was higher than receptacles, and this ability may be related to their higher content of phenolics and flavonoids. Fritsche *et al.*<sup>59</sup> reported that chlorogenic acid, luteolin, and luteolin derivatives of artichoke leaf extracts had a vigorous antioxidant activity. As the results of antioxidant activity of artichoke, Kaymaz *et al.*<sup>60</sup> revealed that the leaves aqueous extract of artichoke decreased the level of MDA (Malondialdehyde) and caused a significant rise of SOD (Superoxide dismutase), CAT (Catalase), and GPx (Glutathione peroxidase) activity. Ben Salem *et al.*,<sup>35</sup> Oliveira *et al.*,<sup>61</sup> Kollia *et al.*,<sup>62</sup> Kollia *et al.*,<sup>63</sup> stated that the different methods such as; DPPH, ABTS, and FRAP which were used to assess the antioxidant activity showed that ethanolic and aqueous extracts of artichoke had a high radical scavenging potential.

#### Antimicrobial activity of globe artichoke aqueous extracts Antibacterial activity

As shown in Table 6, the antibacterial activity of artichoke bracts and receptacles aqueous extracts were assessed against seven strains of foodborne pathogenic bacteria. Bracts aqueous extract showed antibacterial activity against all tested bacteria with inhibition zone value ranged from 7.2 to 9.3 mm, while the antibacterial activity ranged between 7.3 and 9.5 mm in the case of receptacles extract. The highest antibacterial activity (9.3 mm) was recorded against *S. typhi* using bracts extract and the highest activity (9.5 mm) was recorded by receptacles extract against *S. enterica* followed by bracts extract against *Staph. aureus* with inhibition zone value of 8.8 mm. The

results showed non-significant difference between the effect of bracts and receptacles against the same strain.

Several serious diseases of bacterial foodborne had been occurred because of the antibiotics resistance, so many researchers tried to find another natural plant sources as antibacterial compound which could be used to overcome these diseases.<sup>64</sup> Secondary metabolites such as; phenolics, flavonoids, terpenoids, alkaloids, quinones, polyacetylenes, and tannins which have been produced by plants act as antimicrobial agents.<sup>65-67</sup> These compounds also called phytoalexins, as they were natural antimicrobials produced by plants as a mechanism of defence against phytopathogens such as; fungi, bacteria, and viruses.68 These biomolecules have a wide range of useful chemical characteristics including complex structures and unique scaffolds, which inhibit microorganisms.<sup>69,70</sup> Mejri et al.<sup>71</sup> reported that floral stems which were extracted by different organic solvents (butanol, ethyl acetate, and ethanol or methanol) showed an antimicrobial activity against Gram-negative and Gram-positive bacteria and the results showed that the most effective extract against all tested microorganisms was the methanolic extract.

Figure 1 illustrates the minimum inhibitory concentration (MIC) of artichoke bracts and receptacles aqueous extracts against seven strains of foodborne pathogenic bacteria. The highest antibacterial activity of bracts aqueous extract was observed against *B. cereus* with MIC value of 0.02 mg mL<sup>-1</sup> followed by *Staph. aureus* and *Staph. sciuri* with MIC value of 0.04 mg mL<sup>-1</sup> for both, while the lowest activity was showed against *P. aeruginosa* with MIC value of 1.33 mg mL<sup>-1</sup>. In case of receptacles, the highest activity was recorded against *B. cereus* with MIC value of 0.18 mg/mL followed by *Staph. aureus* and *S. enterica* with MIC value of 0.2 mg mL<sup>-1</sup> for both, while the highest MIC values (1.83 and 1.8 mg mL<sup>-1</sup>) were observed against *P. aeruginosa* and *Staph. sciuri*, respectively.

<b>Table 5:</b> FRAP value of globe artichoke of bracts and receptacles aqueous extract	Table 5:	: FRAP	value of	globe art	ichoke of	bracts and	receptacles a	queous extract
---	----------	--------	----------	-----------	-----------	------------	---------------	----------------

		FRAP	value µM	
Aqueous extracts		Concentra	ation (ppm)	
	100	200	400	500
Receptacles	$1.38\pm0.017^{\rm h}$	$3.22\pm0.048^{\text{g}}$	$8.11 \pm 0.023^{\rm f}$	$15.97 \pm 0.067^{d}$
Bracts	$14.05\pm0.12^{e}$	$19.97 \pm 0.099^{c}$	$36.63 \pm 0.13^b$	$59.81\pm0.32^{a}$
BHT	$72.80\pm0.29^{\rm d}$	$100.38\pm0.07^{c}$	$116.23\pm0.1^{b}$	$140.0\pm0.18^{a}$

Each value represents the mean  $\pm$  SE, n=3, values with the same letter are not significantly different at (P $\leq$ 0.05), and the comparison is done according to concentrations.

Table 6: Antibacterial activity of	of globe artichoke bracts and	receptacles aqueous extracts agains	t different bacterial strains
------------------------------------	-------------------------------	-------------------------------------	-------------------------------

Bacteria	Inhibition Zone (mm)					
	Negative control	Positive control	Bracts	Receptacles		
B. cereus	0	$27.2\pm1.89^{\rm a}$	$7.3\pm0.33^{\text{b}}$	$7.5\pm0.28^{\text{b}}$		
Staph. sciuri	0	$26.5\pm1.32^{\rm a}$	$8\pm0.16^{b}$	$7.8\pm0.16^{b}$		
Staph. aureus	0	$28.7\pm0.58^{a}$	$8.8\pm0.33^{b}$	$7.7\pm0.33^{b}$		
E. coli	0	$11.5\pm0.86^{a}$	$8\pm0.28^{b}$	$8.3\pm0.16^{b}$		
S. typhi	0	$25.2\pm2.52^{\rm a}$	$9.3\pm0.73^{b}$	$8.5\pm0.76^{b}$		
S. enterica	0	$24.8\pm1.15^{a}$	$8\pm0.0^{\rm b}$	$9.5\pm0.76^{b}$		
P. aeruginosa	0	$13.0\pm0.70^a$	$7.2\pm0.73^{b}$	$7.3\pm0.88^{b}$		

receptacles aqueous extracts against different foodborne pathogenic bacterial strains n = 3, \*SE: standard error, different superscripts within row are significantly different at 5% level, negative control: DMSO, positive control: tetracycline

#### Antifungal activity

As shown in Table 7, the antifungal activity of artichoke bracts and receptacles aqueous extracts were assessed against eight strains of mycotoxigenic fungi. Bracts aqueous extract showed antifungal activity against all tested fungi with inhibition zone value ranged from 8.0 to 11.2 mm, while the antifungal activity ranged between 8.7-9.8 mm in case of receptacles extract. The highest antifungal activity (11.2

and 9.8 mm) were recorded against *P. verrucosum* with bracts and receptacles extracts respectively, followed by bracts extract against *A. flavus* with inhibition zone value of 10.0 mm.

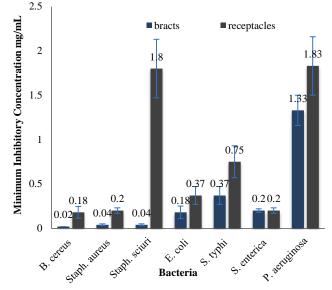
Figure 2 illustrates the minimum inhibitory concentration (MIC) of artichoke bracts and receptacles aqueous extracts against eight strains of mycotoxigenic fungi. In bracts extract the lowest MIC value (0.04 mg mL<sup>-1</sup>) was observed against *A. niger* followed by *A. parasiticus*, *A.* 

*carbonarius*, and *A. ochraceus* with MIC value of 0.1 mg mL<sup>-1</sup>, while the highest value was recorded against *F. proleferatum* with MIC value of 0.42 mg mL<sup>-1</sup>. For receptacles aqueous extract, the highest activity was recorded against *A. ochraceus* and *A. westerdijikia* with MIC value of 1.5 mg mL<sup>-1</sup> and the lowest activity was observed against *A. parasiticus* and *A. niger* with MIC value of 4.2 and 3.3 mg mL<sup>-1</sup>, respectively. According to the statistical analysis, the results revealed non-significant difference between the activity of bracts and the activity of receptacles on the same mycotoxigenic fungal strain. There was non-significant difference between the effect of bracts and receptacles and positive control (Nystatin) against mycotoxigenic fungal strains; *A. westerdijikia* and *F. proleferatum*.

According to the results of HPLC analysis which declared that the bracts and receptacles aqueous extracts contained different phenolic & flavonoid compounds such as; Qurecetin and Kaempferol. These results were in accordance with the antimicrobial results which investigated that the bracts and receptacles aqueous extract showed antimicrobial activity against all tested microorganisms and the bracts were the effective one, as the polyphenolic burden in bracts was higher than receptacles.

Xie et al.,<sup>72</sup> investigated that the special position of hydroxyl groups on the aromatic rings of flavonoids structure enhances their antimicrobial activity. The carbon skeleton of flavonoids (C6-C3-C6) consisting of three rings; two of them are phenyl rings (A & B), and the other one is a heterocyclic ring (C). The hydroxyl groups in ring A (at least one) on a position C-7 is considered vital for antibacterial activity, and this biological effect could increase with another site such as; C-5 and C-6.<sup>73</sup> Å number of studies stated that flavonoids can inhibit the growth of bacteria through several mechanisms include; inhibition the function of cytoplasmic membrane by effecting on the biofilm formation, permeability, porins, inhibition of synthesis of nucleic acid, and also through the interaction with some important enzymes.<sup>74-76</sup> Quercetin was found in bracts and receptacles aqueous extracts. Siriwong et al.77 reported that quercetin could inhibit the growth of Gram-positive bacteria by increasing the permeability of the cytoplasmic membrane. Also, Chen and Huang,78 stated that quercetin and kaempferol inhibit the interaction between DNA B helicase of K. *pneumoniae* and deoxynucleotide triphosphates (dNTPs). Additionally, Huang *et al.*<sup>79</sup> investigated that DNA PriA helicase of *S. aureus* was inhibited by kaempferol. The antimicrobial activity of artichoke leaf extract may be attributed to their phenolic burden which makes the nutrition factors such as; carbohydrates, vitamins, and minerals are not available for microorganisms through binding to them, also they may change the structure of the enzymes.<sup>80</sup> Lou et al.<sup>81</sup> revealed that the chlorogenic acid can inhibit large number of bacteria and fungi growth.

The present study looked at the efficiency of the receptacles and bracts aqueous extracts from the Egyptian cultivar of the globe artichoke (*Cynara cardunculus* var. *scolymus* L.). The results of study were positive towards the antimicrobial activity against specific Grampositive and Gram-negative foodborne pathogenic bacteria and also against mycotoxigenic fungi. They were also positive with the DPPH and ABTS radicals and also to reduce the Fe<sup>3+</sup> TPTZ complex. The previous findings may not translate to microbes or be chemically applicable in other parts of the world.



**Figure 1:** Minimum inhibitory concentration of globe artichoke bracts and receptacles aqueous extracts against tested bacteria.

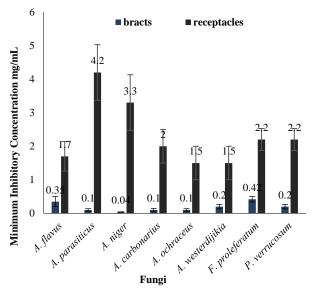


Figure 2: Minimum inhibitory concentration of globe artichoke bracts and receptacles aqueous extracts against mycotoxigenic fungi

Table 7: Antifungal activity of globe artichoke bracts an	nd receptacles aqueous extracts	against mycotoxigenic fungi

Fungi	Inhibition Zone (mm)					
	Negative control	<b>Positive control</b>	Bracts	Receptacles		
A. flavus	0	$22.0\pm1.50^{a}$	$10.0\pm0.76^{b}$	$8.8\pm0.166^{b}$		
A. parasiticus	0	$20.3\pm2.52^{a}$	$9.3\pm0.44^{b}$	$9.3\pm0.44^{b}$		
A. niger	0	$20.2\pm1.53^{a}$	$9.7\pm0.88^{b}$	$9.5\pm0.577^{b}$		
A. carbonarius	0	$15.3\pm2.01^{a}$	$8.0\pm0.28^{b}$	$9.7\pm0.44^{b}$		
A. ochraceus	0	$13.2\pm1.04^{\rm a}$	$9.7\pm0.166^{b}$	$9.5\pm0.28^{b}$		
A. westerdijikia	0	$12.0\pm0.28^{\rm a}$	$9.3\pm0.166^{\rm a}$	$8.7\pm0.44^{a}$		
F. proleferatum	0	$10.7\pm0.76^{a}$	$9.5\pm0.28^{\rm a}$	$9.2\pm0.166^a$		
P. verrucosum	00	$19.8\pm2.56^{\rm a}$	$11.2\pm0.73^{b}$	$9.8\pm0.44^{b}$		

n = 3, \*SE: standard error, different superscripts within row are significantly different at 5% level, negative control: DMSO, positive control: Nystatin.

#### Conclusion

The current research demonstrated that the aqueous extracts of artichoke bracts and receptacles are rich in total phenolic, total flavonoid and the TPC and TFC content in bracts were higher than receptacles. Also, the bracts aqueous extract contained the highest phenolics compared with receptacles. Furthermore, the bracts extract showed antioxidant and antimicrobial activity higher than receptacles aqueous extract. Finally, bracts is a discarded waste, so the aqueous extract of bracts may be a promising economic and ecological waste to be used in biological, pharmaceutical, and industrial applications.

#### **Conflict of Interest**

There are no conflicts of interest to declare

#### **Authors' Declaration**

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

#### Acknowledgements

This work was supported by the Science and Technology Development Fund (STDF) under grant No. 41535, and the National Research Centre, Cairo, Egypt. Principle Investigator Ahmed S. M Fouzy.

#### References

- Gul K, Singh A, Jabeen, R. Nutraceuticals and functional foods: The foods for the future world. Crit Rev Food Sci Nutr. 2016; 56(16): 2617-2627.
- Gutiérrez-del-Río I, Fernández J, Lombó F. Plant nutraceuticals as antimicrobial agents in food preservation: Terpenoids, polyphenols and thiols. Int J Antimicrob Agents. 2018; 52(3):309-315.
- Shallan MA, Ali MA, Meshrf WA, Marrez DA. *In vitro* antimicrobial, antioxidant and anticancer activities of globe artichoke (*Cynara cardunculus var. scolymus* L.) bracts and receptacles ethanolic extract. Biocatal Agric Biotechnol. 2020; 29(10):101774.
- Yildirim AB, Basay S, Turker AU. A comparison of organically and conventionally grown artichokes: phenolic constituents, antioxidant, and antibacterial activities. Acta Alimentaria. 2020; 49(1):69-75.
- FAOSTAT. The State of Food and Agriculture, moving forward on food loss and waste reduction. FAO, Rome. 2019. 156 p.
- Zuorro A, Maffei G, Lavecchia R. Reuse potential of artichoke (*Cynara scolimus* L.) waste for the recovery of phenolic compounds and bioenergy. J Clean Prod. 2016; 111(A):279-284.
- Rabelo RS, Machado MT, Martínez J, Hubinger MD. Ultrasound assisted extraction and nanofiltration of phenolic compounds from artichoke solid wastes. J Food Eng. 2016; 178(A6):170-180.
- Francavilla M, Marone M, Marasco P, Contillo F, Monteleone M. Artichoke biorefinery: from food to advanced technological applications. Foods. 2021; 10(1):112.
- Sihem D, Samia D, Gaetano P, Sara L, Giovanni M, Hassiba C, Laura G, Noureddine HA. *In vitro* antioxidant activities and phenolic content in crop residues of Tunisian globe artichoke. Sci Horticult. 2015; 190(2015):128-136.
- Fratianni F, Tucci M, De Palma M, Pepe R, Nazzaro F. Polyphenolic composition in different parts of some cultivars of globe artichoke (*Cynara cardunculus L. var. scolymus* (L.) Fiori). Food Chem. 2007; 104(3):1282-1286.

- Noriega-Rodríguez D, Soto-Maldonado C, Torres-Alarcón C, Pastrana-Castro L, Weinstein-Oppenheimer C, Zúñiga-Hansen M. Valorization of globe artichoke (*Cynara* scolymus) agro-industrial discards, obtaining an extract 189 with a selective effect on viability of cancer cell lines. Proc. 2020; 8(6):715.
- Abu-Reidah IM, Arráez-Román D, Segura-Carretero A, Fernández-Gutiérrez A. Extensive characterisation of bioactive phenolic constituents from globe artichoke (*Cynara scolymus* L.) by HPLC–DAD-ESI-QTOF-MS. Food Chem. 2013; 141(3): 2269-2277.
- Blanco E, Sabetta W, Danzi D, Negro D, Passeri V, Lisi AD, Paolocci F, Sonnante G. Isolation and characterization of the flavonol regulator CcMYB12 from the globe artichoke [*Cynara cardunculus* var. *scolymus* (L.) Fiori]. Front Plant Sci. 2018; 9(7): 941(1-16).
- Dabbou S, Dabbou S, Flamini G, Pandino G, Gasco L, Helal AN. Phytochemical compounds from the crop byproducts of Tunisian globe artichoke cultivars. Chem Biodivers. 2016; 13(11):1475-1483.
- Durazzo A, Foddai MS, Temperini A, Azzini E, Venneria E, Lucarini M, Finotti E, Maiani G, Crinò P, Saccardo F, Maiani G. Antioxidant properties of seeds from lines of artichoke, cultivated cardoon and wild cardoon. Antioxid. 2013; 2(2):52-61.
- Jiménez-Moreno N, Cimminelli M, Volpe F, Ansó R, Esparza I, Mármol I, Rodríguez-Yoldi M, Ancín-Azpilicueta C. Phenolic composition of artichoke waste and its antioxidant capacity on differentiated Caco-2 cells. Nutr. 2019; 11(8):1723.
- Rocchetti G, Giuberti G, Lucchini F, Lucini L. Polyphenols and sesquiterpene lactones from artichoke heads: Modulation of starch digestion, gut bioaccessibility, and bioavailability following *in vitro* digestion and large intestine fermentation. Antioxid. 2020; 9(4): 306.
- Lattanzio V, Kroon PA, Linsalata V, Cardinali A. Globe artichoke: A functional food and source of nutraceutical ingredients. J Funct Foods. 2009; 1(2):131-144.
- Petropoulos SA, Pereira C, Tzortzakis N, Barros L, Ferreira IC. Nutritional value and bioactive compounds characterization of plant parts from *Cynara cardunculus* L. (*Asteraceae*) cultivated in central Greece. Front Plant Sci. 2018; 9(4):459 (1-12).
- Elshamy AI, Abdallah HM, Farrag A, Riciputi Y, Pasini F, Taher RF, Hegazy ME. Artichoke phenolics confer protection against acute kidney injury. Rev Bras Farmacogn. 2020; 30(1):34-42.
- 21. Sokkar HH, Dena A, Mahana NA, Badr A. Artichoke extracts in cancer therapy: do the extraction conditions affect the anticancer activity? Future J Pharm Sci. 2020; 6(1):1-21.
- 22. Rejeb IB, Dhen N, Gargouri M, Boulila A. Chemical composition, antioxidant potential and enzymes inhibitory properties of Globe artichoke by-products. Chem Biodiver. 2020; 17(9): e2000073.
- Makkar HP. Effects and fate of tannins in ruminant animals, adaptation to tannins, and strategies to overcome detrimental effects of feeding tannin-rich feeds. Small Rum Res. 2003; 49(3):241-256.
- Zhishen J, Mengcheng T, Jianming W. The determination of flavonoid contents in mulberry and their scavenging effects on superoxide radicals. Food Chem. 1999; 64(4):555-559.
- Kim KH, Tsao R, Yang R, Cui SW. Phenolic acid profiles and antioxidant activities of wheat bran extracts and the effect of hydrolysis conditions. Food Chem. 2006; 95(3):466-473.
- Chandrasekar D, Madhusudhana K, Ramakrishna S, Diwan PV. Determination of DPPH free radical scavenging activity by reversed phase HPLC: a sensitive screening

method for polyherbal formulations. J Pharm Biomed Anal. 2006; 40(2):460-464.

- Re R, Pellegrini N, Proteggente A, Pannala A, Yang M, Rice-Evans C. Antioxidant activity applying an improved ABTS radical cation decolorization assay. Free Rad Biol Med. 1999; 26(9-10): 1231-1237.
- Pulido R, Bravo L, Saura-Calixto F. Antioxidant activity of dietary polyphenols as determined by a modified ferric reducing/antioxidant power assay. J Agric Food Chem. 2000; 48(8):3396-3402.
- Bauer A, Kirby W, Sheriss J, Turck M. Antibiotic susceptibility testing by standardized single method. Am J Clin Pathol. 1966; 45(4):493-496.
- Marrez DA, Naguib MM, Sultan YY, Higazy AM. Antimicrobial and anticancer activities of *Scenedesmus obliquus* metabolites. Heliyon. 2019; 5(3):e01404.
- 31. Medeiros M, Oliveira D, Rodrigues D, Freitas D. Prevalence and antimicrobial resistance of *Salmonella* in chicken carcasses at retail in 15 Brazilian cities. *Revista* Panamericana de Salud Pública. 2011; 30(6): 555-560.
- Andrews JM. Determination of minimum inhibitory concentrations. J Antimicrob Chemother. 2001; 48(1):5-16.
- 33. Sokmen A, Okmen A, Gulluce M, Akpulat H, Dafera D. The *in vitro* antimicrobial and antioxidant activities of the essential oils and methanol extracts of *endemic Thymus spathulifolius*. Food Contr. 2004; 15(8):627-634.
- Marrez DA and Sultan YY. Antifungal activity of the cyanobacterium *Microcystis aeruginosa* against mycotoxigenic fungi. J Appl Pharm Sci. 2016; 6(11):191-198.
- Ben Salem M, Affes H, Athmouni K, Ksouda K, Dhouibi R, Sahnoun Z, Zeghal KM. Chemicals Compositions, Antioxidant and Anti-Inlammatory Activity of *Cynara scolymus* Leaves Extracts, and Analysis of Major Bioactive Polyphenols by HPLC. Evid-Based Compl Altern Med. 2017; 2017 (4): 4951937 (1–14).
- 36. Chen GL, Zhang X, Chen SG, Han MD, Gao YQ. Antioxidant activities and contents of free, esterified and insoluble-bound phenolics in 14 subtropical fruit leaves collected from the south of China. J Funct Foods. 2017; 30(C):290-302.
- 37. Yang M, Ma Y, Wang Z, Khan A, Zhou W, Zhao T, Cao J, Cheng G, Cai S. Phenolic constituents, antioxidant and cytoprotective activities of crude extract and fractions from cultivated artichoke inflorescence. Ind Crops Prod. 2020; 143(1):111433 (1-11).
- Zan MA, Ferraz AB, Richter MF, Picada, JN, de Andrade HH, Lehmann M, Dihl, R, Nunes, E, Semedo J, Da Silva J. *In vivo* genotoxicity evaluation of an artichoke (*Cynara scolymus* L.) aqueous extract. J Food Sci. 2013; 78(2):T367-T371.
- Staszowska-Karkut M and Materska M. Phenolic composition, mineral content, and beneficial bioactivities of leaf extracts from black currant (*Ribes nigrum* L.), raspberry (*Rubus idaeus*), and aronia (*Aronia melanocarpa*). Nutr. 2020; 12(2): 463.
- 40. Borgognone D, Cardarelli M, Rea E, Lucini L, Colla G. Salinity source-induced changes in yield, mineral composition, phenolic acids and flavonoids in leaves of artichoke and cardoon grown in floating system. J Sci Food Agric. 2014; 94(6): 1231–1237.
- Santana-Gálvez J, Cisneros-Zevallos L, Jacobo-Velázquez DA. Chlorogenic acid: Recent advances on its dual role as a food additive and a nutraceutical against metabolic syndrome. Molecules. 2017; 22(3):358.
- 42. Cao Y, Zhang L, Sun S, Yi Z, Jiang X, Jia, D. Neuroprotective effects of syringic acid against OGD/Rinduced injury in cultured hippocampal neuronal cells. Int J Mol Med. 2016; 38(2):567-573.

- 43. Cikman O, Soylemez O, Ozkan OF, Kiraz HA, Sayar I, Ademoglu S, Taysi, S, Karaayvaz M. Antioxidant activity of syringic acid prevents oxidative stress in l-arginine– induced acute pancreatitis: An experimental study on rats. Int Surg. 2015; 100(5): 891-896.
- Sancak EB, Akbas A, Silan C, Cakir DU, Turkon H, Ozkanli SS. Protective effect of syringic acid on kidney ischemia-reperfusion injury. Ren Fail. 2016; 38(4):629-635.
- 45. Semaming Y, Pannengpetch P, Chattipakorn SC, Chattipakorn N. Pharmacological properties of protocatechuic acid and its potential roles as complementary medicine. Evid-Based Compl Altern Med. 2015; 593902(D):1-11.
- 46. Singh VK, Romaine PL, Newman VL, Seed TM. Medical countermeasures for unwanted CBRN exposures: part II radiological and nuclear threats with review of recent countermeasure patents. Expert Opin Ther Pathol. 2016; 26(12):1399-1408.
- Yakoub A, Abdehedi O, Jridi M, Elfalleh W, Nasri M, Ferchichi A. Flavonoids, phenols, antioxidant, and antimicrobial activities in various extracts from Tossa jute leave (*Corchorus olitorus* L.). Ind Crops Prod. 2018; 118(8):206-213.
- Noldin V, Cechinel Filho V, Monache F, Benassi J, Christmann I, Pedrosa R, Yunes R. Chemical composition and biological activities of the leaves of *Cynara scolymus* L. (alcachofra) cultivated in Brasil. New Chem. 2003; 26(3):331-334.
- Wang M, Simon JE, Aviles IF, He K, Zheng QY, Tadmor, Y. Analysis of antioxidative phenolic compounds in artichoke (*Cynara scolymus* L.). J Agric Food Chem. 2003; 51(3):601-608.
- Schütz K, Muks E, Carle R, Schieber A. Quantitative determination of phenolic compounds in artichoke-based dietary supplements and pharmaceuticals by highperformance liquid chromatography. J Agric Food Chem. 2006; 54(23):8812-8817.
- Zhang B, Deng Z, Ramdath DD, Tang Y, Chen PX, Liu R, Liu Q, Tsao R. Phenolic profiles of 20 Canadian lentil cultivars and their contribution to antioxidant activity and inhibitory effects on α-glucosidase and pancreatic lipase. Food Chem. 2015; 172(4):862-872.
- 52. Zhou J, Ma Y, Jia Y, Pang M, Cheng G, Cai S. Phenolic profiles, antioxidant activities and cytoprotective effects of different phenolic fractions from oil palm (*Elaeis guineensis* Jacq.) fruits treated by ultra-high pressure. Food Chem. 2019; 288(8):68-77.
- 53. Azzini E, Bugianesi R, Romano F, Di Venere D, Miccadei S, Durazzo A, Foddai MS, Catasta G, Linsalata V, Maiani G. Absorption and metabolism of bioactive molecules after oral consumption of cooked edible heads of *Cynara scolymus* L. (*cultivar Violetto di Provenza*) in human subjects: a pilot study. Br J Nutr. 2007; 97(5): 963-969.
- Löhr G, Deters A, Hensel A. *In vitro* investigations of *Cynara scolymus* L. extract on cell physiology of HepG2 liver cells. Br J Pharm Sci. 2009; 45(2):201-208.
- 55. Dabbou S, Dabbou S, Flamini G, Peiretti PG, Pandino G, Helal AN. Biochemical characterization and antioxidant activities of the edible part of globe artichoke cultivars grown in Tunisia. Int J Food Prop. 2017; 20(1):S810-S819.
- 56. Turkiewicz IP, Wojdyło A, Tkacz K, Nowicka P, Hernández F. Antidiabetic, anticholinesterase and antioxidant activity vs. terpenoids and phenolic compounds in selected new cultivars and hybrids of artichoke *Cynara scolymus* L. Molecules. 2019; 24(7):1222.
- Biel W, Witkowicz R, Piątkowska E, Podsiadło C. Proximate composition, minerals and antioxidant activity of artichoke leaf extracts. Biol Trace Elem Res. 2020; 194(2):589-595.
- 58. Sharma A and Cannoo DS. Effect of extraction solvents/techniques on polyphenolic contents and

antioxidant potential of the aerial parts of *Nepeta leucophylla* and the analysis of their phytoconstituents using RP-HPLC-DAD and GC-MS. RSC Adv. 2016; 6(81): 78151-78160.

- Fritsche J, Beindorff C, Dachtler M, Zhang H, Lammers J. Isolation, characterization and determination of minor artichoke (*Cynara scolymus* L.) leaf extract compounds. Eur Food Res Technol. 2002; 215(2):149-157.
- 60. Kaymaz M, Kandemir F, Pamukçu E, Eröksüz Y, Özdemir N. Effects of aqueous artichoke (*Cynara scolymus*) leaf extract on hepatic damage generated by alpha-amanitine. Kafkas Univ Vet Fak Derg. 2017; 23(1):155-160.
- Oliveira G, Oliveira F, Alencar M, Gomes Junior A, Souza A, Cavalcante, A, Freitas R. Evaluation of antioxidant capacity of the aqueous extract of *Cynara scolymus* L. (*Asteraceae*) *in vitro* and in *Saccharomyces cerevisiae*. Afr J Pharm Pharmacol. 2014; 8(5): 136-147.
- 62. Kollia E, Markaki P, Zoumpoulakis P, Proestos C. Comparison of different extraction methods for the determination of the antioxidant an antifungal activity of *Cynara scolymus* and *C. cardunculus* extracts and infusions. Nat Prod Commun. 2017; 12:423-426.
- Kollia E, Markaki P, Zoumpoulakis P, Proestos C. Antioxidant activity of *Cynara scolymus* L. and *Cynara cardunculus* L. extracts obtained by different extraction techniques. Nat Prod Res. 2017; 31(10):1163-1167.
- 64. Kim G, Gan R, Zhang D, Farha A, Habimana O, Mavumengwana V, Li H, Wang X, Corke H. Large-Scale Screening of 239 Traditional Chinese Medicinal Plant Extracts for Their Antibacterial Activities against Multidrug-Resistant *Staphylococcus aureus* and Cytotoxic Activities. Pathogens. 2020; 9(3):185.
- Noumi E, Snoussi M, Merghni A, Nazzaro F, Quindós G, Akdamar, G, Mastouri M, Al-Sieni A, Ceylan, O. Phytochemical composition, anti-biofilm and anti-quorum sensing potential of fruit, stem and leaves of *Salvadora persica* L. methanolic extracts. Microbial Path. 2017; 109(8):169-176.
- 66. Packiavathy I, Agilandeswari P, Musthafa K, Pandian S, Ravi A. Antibiofilm and quorum sensing inhibitory potential of *Cuminum cyminum* and its secondary metabolite methyl eugenol against Gram negative bacterial pathogens. Food Res Int. 2012; 45(1): 85-92.
- 67. Elisha IL, Botha FS, McGaw LJ, Eloff JN. The antibacterial activity of extracts of nine plant species with good activity against *Escherichia coli* against five other bacteria and cytotoxicity of extracts. BMC Compl Med Ther. 2017; 17(1):1-10.

- Lewis K and Ausubel FM. Prospects for plant-derived antibacterials. Nat Biotechnol. 2006; 24(12):1504-1507.
- 69. Gyawali R and Ibrahim S. Natural products as antimicrobial agents. Food control. 2014; 46:412-429.
- Silva LN, Zimmer KR, Macedo AJ, Trentin DS. Plant natural products targeting bacterial virulence factors. Chem Rev. 2016; 116(16): 9162-9236.
- Mejri F, Baati T, Martins A, Selmi S, Serralheiro ML, Falé PL, Hosni K. Phytochemical analysis and *in vitro* and *in vivo* evaluation of biological activities of artichoke (*Cynara scolymus* L.) floral stems: Towards the valorization of food by-products. Food Chem. 2020; 333(1-2):127506.
- 72. Xie Y, Yang W, Tang F, Chen X, Ren L. Antibacterial activities of flavonoids: structure-activity relationship and mechanism. Curr Med Chem. 2015; 22(1):132-149.
- Farhadi F, Khameneh B, Iranshahi M, Iranshahy M. Antibacterial activity of flavonoids and their structure– activity relationship: An update review. Phytother Res. 2019; 33(1):13-40.
- Barbieri R, Coppo E, Marchese A, Daglia M, Sobarzo-Sánchez E, Nabavi SF, Nabavi SM. Phytochemicals for human disease: An update on plant-derived compounds antibacterial activity. Microbiol Res. 2017; 196(Mar):44-68.
- Khameneh B, Iranshahy M, Soheili V, Bazzaz B. Review on plant antimicrobials: A mechanistic viewpoint. Antimicrob Resist Infect Contr. 2019; 8(1):1-28.
- Górniak I, Bartoszewski R, Króliczewski J. Comprehensive review of antimicrobial activities of plant flavonoids. Phytochem Rev. 2019; 18(1):241-272.
- Siriwong S, Thumanu K, Hengpratom T, Eumkeb G. Synergy and mode of action of ceftazidime plus quercetin or luteolin on *Streptococcus pyogenes*. Evid-Based Compl Altern Med. 2015; 759459(D):1-13.
- Chen CC and Huang CY. Inhibition of *Klebsiella* pneumoniae DnaB helicase by the flavonol galangin. The Protein J. 2011; 30(1): 59-65.
- 79. Huang Y, Huang C, Chen C, Yang K, Huang C. Inhibition of *Staphylococcus aureus* PriA helicase by flavonol kaempferol. The Protein J. 2015; 34(3):169-172.
- Essid I, Tajine S, Gharbi S, Bellagha S. Use of pomegranate peel and artichoke leaf extracts to improve the quality of marinated sardine (*Sardinella aurita*) fillets. J Food Sci Technol. 2020; 57(2):713-722.
- Lou Z, Wang H, Zhu S, Ma C and Wang Z. Antibacterial activity and mechanism of action of chlorogenic acid. J Food Sci. 2011; 76(6):398-403.