Egypt. J. Chem. **Vol. 64,** No. 8 pp. 4689 - 4696 (2021)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Antimicrobial and antioxidant effects of *Cichorium intybus* aerial parts and Chemical profile

Khaled Rashed[a*], Monica Butnariu [b]

[a] *Pharmacognosy Department, National Research Centre, 33 El-Bohouth St.-Dokki, Giza, P.O.12622, EGYPT.*

[b] *Chemistry and Vegetal Biochemistry, Banat's University of Agricultural Sciences and Veterinary Medicine "King Michael I of Romania" from Timisoara, 300645, Calea Aradului 119, Timis, Romania*

Abstract

This work proved antioxidant and antimicrobial effects and chemical content of *Cichorium intybus* L. Methanol extract of *C. intybus* L. aerial parts were tested for antimicrobial activity, and for antioxidant effect. The results showed that the extract has a significant antimicrobial activity, it inhibited the growth of the Gram-negative bacteria and Fungi (has registered against various). The extract has a good antioxidant activity reported to Vitamin C (IC50=61.57±0.75 µg/mL; Vitamin C=5.78±0.08 µg/mL). Phytochemical evaluation has shown that the plant has flavonoids, triterpenes and others, and further phytochemical proved the identification of *β*-sitosterol, apigenin, kaempferol, apigenin 7-O-β-glucoside, kaempferol 3-O-α-rhamnoside, kaempferol-3-O-*β*-glucoside). In conclusion, *C. intybus* can be a new promising antioxidant and antimicrobial agents.

Key words: *Cichorium intybus* L., aerial parts, antimicrobial activity, antioxidant activity, chemical content.

1. Introduction

Traditional medicine has continued as the major reasonable and simply available source of treatment in the primary health care system [1]. Natural products have played a substantial portion in treating and preventing human diseases and as a favorable additive in foods [2]. Recently, investigation of natural products for the discovery of active compounds has also developed in finding naturally occurring antioxidants for use in foods to replace synthetic antioxidants and antimicrobial agents due to their carcinogenicity [3]. *C. intybus* L. is commonly known as chicory. *C. intybus* is an important plant in Eurasia and Africa. Important phytochemicals are distributed throughout the plant, the major contents are found in the root [4]. It contained sesquiterpene lactones, caffeic acid derivatives, inulin, sugars, proteins, hydroxycoumarins, flavonoids, alkaloids, steroids, terpenoids, oils, volatile compounds, coumarins, vitamins and polyynes [5]. Mechanism of pharmacological action of active compounds in C. intybus plants is determined by the presence of the following classes of compounds fat, inulin (which along with oligofructose are considered dietary fibers), latex, mannitol, minerals, sesquiterpene lactones (eudesmanolides, germacranolides and guaianolides) [6]. and vitamins. Among the specific chemical compounds biosynthesized by the mevalonate-farnesyl diphosphate-germacradiene pathway (via mevalonate) [7] of C. intybus plants have been identified 2, 3, 4, 9-tetrahydro-1H-pyrido-(3,4-b)indole-3-carboxylic acid, alpha-amyrin, baurenyl acetate, beta-sitosterol, taraxerone and inulooligosaccharides (IOS). It has antiallergic effects, anti-inflammatory effects, can have calcium homeostasis activity, cytochrome P450 activity [8] fecal bulking properties, hypoglycemic effect with dietary inulin-type fructans ($C_{6n}H_{10n}+2O_{5n}+1$) may modulate the production of peptides, such as incretins, by endocrine cells present in the intestinal mucosa and It is involved in managing weight problems, obesity and diabetes (ability to stimulate secretion of endogenous gastrointestinal peptides entangled in appetite adjusting) [9]. He

**Corresponding author: Khaled Rashed, Email: khalednabih2015@yahoo.co.uk

Receive Date: 04 July 2021, Revise Date: 17 July 2021, Accept Date: 26 July 2021

DOI: 10.21608/EJCHEM.2021.83913.4112

also has immunostimulatory activity, mutagenic properties and even prebiotic effect [10]. Till now, there are no reports on chemical composition and antioxidant and antimicrobial activities of *C. intybus* aerial parts and for this reason, this research article was done.

2.Experimental

2.1.Materials and Methods

UV/VIS: Shimadzu UV-visible recording spectrophotometer model-UV 240 (NRC, Egypt). 1H-NMR spectra and 13C-NMR spectra: Varian Unity Inova 400 Varian Unity (Graz University, Austria). MS (Finnigan MAT SSQ 7000, 70 ev). Silica gel (0.063-0.200 mm for column chromatography) and Sephadex LH-20 (Pharmacia Fine Chemicals). Thin layer chromatography (TLC) F254 plates. Solvent mixtures, BAW (n-butanol:acetic acid:water 4:1:5 upper phase, 15% acetic acid: water: glacial acetic acid: 85:15). Paper Chromatography (PC) Whatman No.1 (Whatman Led.Maid Stone, Kent, England) sheets for qualitative detection of flavonoids and sugars.

2.2. Plant material

Aerial parts of *C. intybus* L. were collected from Agricultural Research Center, Giza, Egypt in April 2019. The plant was identified by Mrs. Tereez Labib Consultant of Plant Taxonomy at the Ministry of Agriculture and director of Orman botanical garden, Giza, Egypt.

2.3. Preparation of the extract

Air dried powder of the aerial parts of *C. intybus* (860 g) was extracted with methanol 80% at room temperature several times until exhaustion. The extract was concentrated under reduced pressure to give 54 g of crude extract.

2.4.Qualitative Phytochemical Analysis:

The extract was tested for the presence of bioactive compounds by using following standard tests (Molisch 's test for carbohydrates, Shinoda test for flavonoids, forth test for saponins, Salkowski 's for terpenes and sterols, $FeCl_3$ and Mayer's reagents for detecting of tannins and alkaloids, respectively [11, 12, 13].

2.5.Isolation of the bioactive compounds from methanol extract of *C. intybus*

52 of the crude extract of C. intybus was defatted with n-hexane and the extract residue 38.5 g which was subjected to silica gel column chromatography eluting with dichloromethane, ethyl acetate and methanol gradually. Five main fractions were collected and each fraction was further fractionated to sub-fractions and the isolated compounds (*β*-sitosterol, apigenin, kaempferol, apigenin 7-O-β-glucoside, kaempferol 3-O-α-rhamnoside, kaempferol-3-O-β-glucoside) were purified over sephdex LH-20.

2.6. Acid hydrolysis of flavonoids

Solutions of 5 mg of compounds 4, 5, and 6 in 5 ml 10 % HCl were heated for 5h. The reaction mixture was extracted with Ethyl acetate. The Ethyl acetate fraction (aglycone) and the aqueous fraction (sugars) were concentrated for identification. The sugars were identified by TLC (acetonitrile-water 85:15) by comparison with authentic samples.

Structure Elucidation of the isolated compounds

β-sitosterol (1): 17 mg, white needles. 1H-NMR (CDCl3, 400 MHz): δ ppm 5.37 (IH, m, H-6), 3.52 (IH, m, H-3) , 1.09 (3H, s, CH3-19), 0.98 (3H, d, J= 6.5, CH3-21), 0.92 (3H, t, J= 7.4, CH3-29), 0.85 (3H, d, J= 6.7Hz, CH3-26), 0.81 (3H, d, J= 6.7Hz, CH3-27), 0.75 (3H, s, CH3-18). 13C-NMR(CDCl3,100 MHz): δ ppm 140.46 (C-5), 121.52 (C-6), 71.64 (C-3), 57.25 (C-17), 56.48 (C-14), 50.35 (C-9), 46.38 (C-24), 42,82 (C-13, 4), 39.88 (C-12), 37.64 (C-1), 36.75 (C-10), 35.92 (C-20), 34.24 (C-22), 31.78 (C-8, 7), 31.45 (C-2), 29.24 (C-25), 28.46 (C-16), 26.24 (C-23), 24.54 (C-15), 23.48 (C-28), 21.14 (C-11), 19.82 (C-26), 19.58 (C-19), 19.24 (C-27), 18.68 (C-21).

Apigenin (2): 27 mg, yellow powder. 1H-NMR (CD3OD, 500 MHz): δ ppm 7.85 (2H, d, J = 8.5 Hz, H -2', H 6'), 6.95 (2H, d, J =8.5 Hz, H-3', H-5'), 6.54 (1H, s, H-3), 6.42 (1H, s, H-8), 6.28 (1H, s, H-6). EI-MS: m/z 270.

Kaempferol (3): 8 mg, yellow powder. 1H-NMR (DMSO-d6, 400 MHz): δ ppm 8.12 (2H, d, J = 8 Hz, H-2', 6'), 6.96 (2H, d, J = 8 Hz, H-3', 5'), 6.47 (1H, d, J = 2 Hz, H-8), 6.19 (1H, d, J= 2 Hz, H-6). (+) ESI-MS: m/z 287 [M+H]+.

Apigenin 7-O-β-glucoside (4): 24 mg, yellow powder. UV λmax (MeOH): 269, 332, MeOH/NaOMe: 272, 387 A1C13: 277, 299, 346, 383, A1C13/HCI: 277, 298, 342, 383, NaOAc:268,338 NaOAc/H3BO3: 268, 335. 1H-NMR (DMSO-d6, 300 MHz): δ ppm 7.94 (2H, d, J= 8.5Hz, H-2′, H-6′), δ 6.92 (2H, d, J= 8.5 Hz, H-3′, H-5′), δ 6.87 (1H, s, H-3), δ 6.84 (1H, d, J= 2.0Hz, H-8), δ 6.42 (1H, d, J= 2.0Hz, H-6), δ 5.08 (1H, d, J= 7.2 Hz, H-1″), δ 3.1-4 (rest of sugar protons, H-2″ to H-6″). 13C-NMR: (DMSO-d6,100 MHz): δ ppm 182.2 (C-4), 164.5 (C-2), 163.8 (C-7), 162.6 (C-5), 161.4 (C-4'), 157.5 (C-9), 129.4 (C-2',6'), 121.6 (C-1'), 116.8 (C-3',5'), 105.6 (C-10), 103.7 (C-3), 100.6 (C-1"), 100.2 (C-6), 95.8 (C-8), 77.6 (C-5"), 76.9 (C-3"), 73.8 (C-2"), 70.4 (C-4"), 61.2 (C-6").

Kaempferol 3-O-α-rhamnoside (5): 22 mg, yellow powder. 1H-NMR (CD3OD, 400 MHz): δ ppm 7.74 (2H, d, J=8.2 Hz, H-2', 6). 6.92 (2H, d, J=8.2 Hz, H-3', 5'). 6.44 (1H, d, J= 2.2 Hz, H-8), 6.24 (1H, d, J= 2.2 Hz, H-6). 5.42 (1H, d, J=2.4 Hz, H-1"), 0.94 (CH3, d, J =6.2 Hz). 13C-NMR (CD3OD, 100 MHz): δ ppm 179.85 (C-4), 166.25 (C-7), 161.84 (C-5), 159.56 (C-4'), 158.28 (C-2), 136.45 (C-9), 132.28 (C-3),122.94 (C-6'), 116.84 (C-2'), 116.24 (C-3'), 106.12 (C-1'), 103.75 (C-5'), 104.74 (C-10), 100.12 (C-1"), 95.14 (C-8), 94.92 (C-6), 73.14 (C-5"), 72.45 (C-3"), 72.34 (C-2"), 72.28 (C-4"), 17.92 (CH3-rhamnosyl).

Kaempferol 3-O-β-glucoside (6): 12 mg, yellow powder. UV λmax (MeOH): 266, 344; (NaOMe): 274, 327sh, 401; (AlCl3): 274, 302, 349, 396; (AlCl3/HCl): 274, 347, 394; (NaOAc): 274, 307, 391; (NaOAc/H3BO3): 267, 352. 1H–NMR (DMSO–d6, 500 MHz): δ ppm 8.12 (2H, d, J = 8.5 Hz, H–2', 6'), 6.92 (2H, d, J=8.5 Hz, H–3', 5'), 6.54 (1H, d, J = 2 Hz, H–8), 6.22 (1H, d, J = 2 Hz, H–6), 5.35 (1H, d, J=7.5, H–1``), 4–3.1 (5H, m, other sugar protons).

2.7. Antioxidant assay

The antioxidant activity of *C. intybus* extract on stable radical 1,1-diphenyl-2-picrylhydrazyl (DPPH) was determined by standard assay with some modifications. In the experiment, 2 mg of the extract was dissolved in methanol and applied by serial dilution technique which concentrations range from 1000 to 1.9531 µg/mL.

Two milliliters of a methanol solution of samples of each concentration were mixed with 3 mL DPPH-methanol solution (40 mg/L) and allowed to stand for 30 min. Then the absorbance was measured at 517 nm using an double optical spectrophotometer, model UV-VIS spectrophotometer (PG Instruments) and soft UV WIN 5.05 to measure the absorbances of reference solutions, and the absorbances of samples. All records were made in quartz cuvettes with a 1 mm optical path. As a reference, ethanol of spectroscopic purity was used in all cases. From these values, corresponding percentage of inhibitions were calculated by using following equation:

% inhibition = [1-(ABSsample/ ABScontrol)] x 100

Percent (%) scavenging of DPPH free radical was calculated as.

% Scavenging = 100 × (Ablank-Asample/ Ablank)

Where Ablank is absorbance of control, Asample is the absorbance of the test sample.

Then per cent inhibitions were plotted against respective concentrations. IC_{50} values were calculated as concentration of the extract required to give 50% DPPH radical scavenging activity from the graph (linear regression curve). Ascorbic acid and BHT (tert-butyl-1-hydroxytoluene) a potential antioxidant was used as positive control at concentration of 500 µg/mL-1.953 µg/mL. Investigation was performed triplicate and the results were expressed as mean ±SD with 95% confidence interval in every case.

2.8. Antimicrobial assay

Disc diffusion assay was used to test antimicrobial and antifungal strains against two gram positive, four-gram negative organisms and two fungi.

Bacterial and fungal strains used for experiment were collected as pure culture, because were among top most frequently isolated organisms based on recent update by National Healthcare Safety Network produced in the acquisition of non-radical DPPH-H by the reaction. The degree of discolouration demonstrates the scavenging possibility of the extract. [19]. Abbas Z. K. et al. [20] indicated the similar tendency in C. intybus demonstrate good free radical scavenging possibility due to higher DPPH radical inhibition. In *C. intybus* plant through the mevalonate-farnesyl diphosphate-germacradiene pathway are synthesized, sesquiterpene lactones, thus it was identified (+)-germacrene A synthase from aerial parts of C. intybus. According to Abbasa Z. K. and collaborators the chicory leaves extract may contain varying amounts of Tannins (0.59 ± 0.04 mg / g), Saponins (0.18 ± 0.06 mg / g) and Total

flavonoids (TF) (6.82 ± 0.07mg / g dry weight). (Abbas et al., 2015). These outcomes are a little in the accordance as reported by Shad et al. (2013), Tannins, the large molecular weight polyphenolic substances identified naturally in of aerial parts of *C. intybus* have been found to perform a protective role in plants against micro-organisms, damage by animals [21], and unfavourable climatic conditions [20]. In fact, polyphenolic compounds have the property of forming multiple hydrogen bonds with carboxylic assemble of dietary proteins and proteolytic enzymes in the gastrointestinal tract which leads to attenuated digestibility of proteins and ultimately the interruption of living animal organisms evolution [22]. The saponins are the glycosidic substances identified of aerial parts of *C. intybus* with a bitter taste and foaming features. Some researchers notified that the saponins can have antifungal activity and anti-carcinogenic [23]. The extracts have antibacterial activities against Gram positive bacteria (*Staphylococcus aureus, Streptococcus pneumoniae, Enterococcus faecium, Listeria monocytogenes, Clostridium botulinum*) but also against Gram negative bacteria (*Pseudomonas aureus and different strains of E. coli),* and *Fungi (Candida albicans, Aspergillus niger, and Sacharomyces cerevaceae*) [24]. The extract used in this study displayed antibacterial activity, and there were no cases of resisted against, as (NHSN) surveillance of antimicrobial-resistant pathogens associated with healthcare-associated infections reports. Test samples (6 mg) were made by dissolving in calculated volumes of solvents separately and applied to discs (6 mm diameter) at a concentration of 400 µg/disc and carefully dried to evaporate residual solvents. Discs containing test material were placed on nutrient agar medium uniformly seeded with test microorganisms. Standard antibiotic chloramphenicol (2 µg/disc) discs and blank discs (impregnated with solvents) were used as a positive and negative control respectively. Antimicrobial activity of test agent was determined by measuring the diameter of the zone of inhibition expressed in millimeter.

3. Results and Discussion

Antioxidant activity of the aerial parts of *C. intybus* extracts with different Concentration was evaluated. The outcomes exhibit that methanol extract of aerial parts of *C. intybus* as advantageous wellspring of phenolic compounds such a natural bio compounds with 15 carbons from the category SLs. The DPPH test is a widely used procedure to appreciate the free radical scavenging ability of methanol extract of aerial parts of *C. intybus*. SLs from was *C. intybus* are a diverse and huge group of bio-active constituents with promising antioxidant character. The present investigation strived at identifying and screening of antibacterial activity of a mixture of sesquiterpene lactones SLs obtained from the methanol extract of aerial parts of C. intybus. The tested extract showed antibacterial activity, the methanol extracts a presented the good Antibacterial activity. Methanol extract inhibits Fungi, Gram negative bacteria and *Enterococcus faecium, Listeria monocytogenes, Clostridium botulinum more than Staphylococcus aureus and Streptococcus pneumonia.*

Flavonoids and Sesquiterpene Lactones are the major compounds of aerial parts of *C. intybus*. *C. intybus* leaf extracts proved antibacterial and antioxidant activity and these effects are related to kaempferol [17]. Apigenin was isolated from aerial part of P. oleracea showed a potent antibacterial property [18]. The Sesquiterpene Lactones isolated from chicory are 11-β,13-Dihydro-lactucin; 8-Deoxy-lactucin; Dihydro-8-deoxy-lactucin; Dihydro-lactucopicrin; Dihydro-lactucopicrin; Lactucin; Lactucopicrin; Lactuside C (jaquinellin glucoside) ; Santonin. Due to high triterpenes, flavonoids, coumarins, tannins and saponins content, the C. intybus has comparatively propitious reducing power and DPPH radical scavenging ability. DPPH procedure is established on the reduction of methanolic DPPH solution in the attendance of antioxidant produced in the acquisition of non-radical DPPH-H by the reaction. The degree of discolouration demonstrates the scavenging possibility of the extract [19]. (Abbas Z. K. et al. [20] indicated the similar tendency in C. intybus demonstrate good free radical scavenging possibility due to higher DPPH radical inhibition. In C. intybus plants through the mevalonate-farnesyl diphosphate-germacradiene pathway are synthesized, sesquiterpene lactones, thus it was identified (+)-germacrene A synthase from aerial parts of C. intybus. According to Abbasa Z. K. and collaborators the chicory leaves extract may contain varying amounts of Tannins (0.59 ± 0.04 mg / g), Saponins (0.18 ± 0.06 mg / g) and Total flavonoids (TF) (6.82 ± 0.07mg / g dry weight) [25]. These outcomes are a little in the accordance as reported by Shad et al. [21], Tannins, the large molecular weight polyphenolic substances identified naturally in of aerial parts of *C. intybus*. and have been found to perform a protective role in plants against micro-organisms, damage by animals [21], and unfavourable climatic conditions [20]. In fact, polyphenolic compounds

have the property of forming multiple hydrogen bonds with carboxylic assemble of dietary proteins and proteolytic enzymes in the gastrointestinal tract which leads to attenuated digestibility of proteins and ultimately the interruption of living animal organisms evolution [22]. The saponins are the glycosidic substances identified in of aerial parts of C. intybus. with a bitter taste and foaming features. Some researchers notified that the saponins can have antifungal activity and anti-carcinogenic [23]. The extracts have antibacterial activities against Gram positive bacteria (Staphylococcus aureus, Streptococcus pneumoniae, Enterococcus faecium, Listeria monocytogenes, Clostridium botulinum) but also against Gram negative bacteria (Pseudomonas aureus and different strains of E. coli), and Fungi (Candida albicans, Aspergillus niger, and Sacharomyces cerevaceae) [24]. The extract used in this study displayed antibacterial activity, and there were no cases of resisted against, as other studies show for example the research performed by Liu and collab [25]. Chicoric acid or cichoric acid is a hydroxycinnamic acid, an natural organic substances of the phenylpropanoid group and is biosintetised in a variety of plant species as is C. intybus. The two polyphenolic acids specific to aerial parts of C. intybus plants cause special properties that could greatly enhance the therapeutic applications and nutritional qualities of C. intybus plants [26]. CA (dicaffeyltartic acid) is Inhibitors of HIV integrase, an enzyme necessary for incorporation of viral DNA into cellular DNA. CA is a phenolic substance present in C. intybus plants with a mixed spectrum of biological qualities acquainted from antioxidant, to antiviral, to immunostimulatory attributes. CAF that is non-flavanoid phenolic compound has a good bioavailability, this molecule is responsible for the yellowish-gold color, and from a biochemical point of view it is synthesized when caffeic acid and tartaric acid undergo esterification (during fermentation, CAF is oxidized into its principal components).

The qualitative chemical composition of aerial parts of *C. intybus* is highlighted in table 1.

Table 1: Phytochemical analysis of *C. intybus* L. *extrac*t

Constituents	methanol extract
Triterpenes and /or Sterols	+
Carbohydrates and/or glycosides	+
Flavonoids	+
Coumarins	+
Alkaloids and/or nitrogenous compounds	+
Tannins	+
Saponins	-
+ presence of constituents, - absence of constituents	

Table 2. DPPH scavenging activity of *C. intybus* L. extract

Concentration Dose (µg/mL)	Concentration Log (µg/mL)	C. intybus L. extract	Ascorbic Acid (ASA)	BHT
1000	3.0	77.49±0.36	-	-
500	2.698	69.07±0.25	96.49±0.16	93.38±0.34
250	2.397	65.18±0.53	94.05±0.25	88.72±0.25
125	2.096	58.13±0.29	93.77±0.34	71.94±0.34
62.5	1.8	50.08±0.25	93.05±0.25	59.88±0.25
31.25	1.49	32.26±0.88	77.83±0.33	50.83±0.16
15.625	1.19	24.28±0.53	70.33±0.50	45.78±0.58
7.8125	0.89	15.08±0.78	56.05±0.41	37.33±0.44
3.9062	0.591	12.09±0.16	42.44±0.53	30.66±0.16
1.9531	0.290	12.03±0.27	39.66±0.57	26.33±0.60
IC50 Value (µg/mL)		61.57±0.75	5.78±0.08	28.06±0.32
ASA = Ascorbic acid, BHT = tert-butyl-1-hydroxytoluene, Mean ±SD, P<0.05 of independent sample T-test.				

Table 3. Antimicrobial activity of *C. intybus* L. extract (400 µg/disc) and chloramphenicol (CHP) (2 µg/disc)

Test microorganisms		*C. intybus* L. extract (mm)	CHP (mm)
Gram positive bacteria	*Staphylococcus aureus*	15	45
	Streptococcus pneumoniae	15	46
	Enterococcus faecium	18	46
	Listeria monocytogenes	18	45
	Clostridium botulinum	16	45
Gram negative bacteria	*Pseudomonas aureus*	18	46
	E. coli E24377A (O139:H28. Enterotoxigenic)	18	46
	E. coli 55989 (O128:H2. Enteroaggressive)	18	46
	E. coli SE15 (O150:H5. Commensal)	17	45
	E. coli E2348/69 (O127:H6. Enteropathogenic)	18	46
	E. coli UMN026 (O17:K52:H18. Extracellular pathogenic)	15	45
	E. coli (O19:H34. Extracellular pathogenic)	16	46
	E. coli (O7:K1. Extracellular pathogenic)	16	46
Fungi	*Candida albicans*	18	45
	Aspergillus niger	18	46
	Sacharomyces cerevaceae	18	45

Chromatographic separation Indicated the identification of compound 1 (β-sitosterol) and its spectral data was in accordance to that reported by Pateh et al. [14]. Compound 2 (apigenin) and compound 3 (kaempferol) were identified and their spectral data were in agreement with that of Said et al. [15]. Compounds 4, 5 and 6 were identified and their spectral data were very similar to that described by Amal et al. [16]. The specialty polyphenols that were identified, in *C. intybus* more precisely it is about substances as cinnamates (hydroxycinnamic acids), such as chicoric acid and caftaric acid.

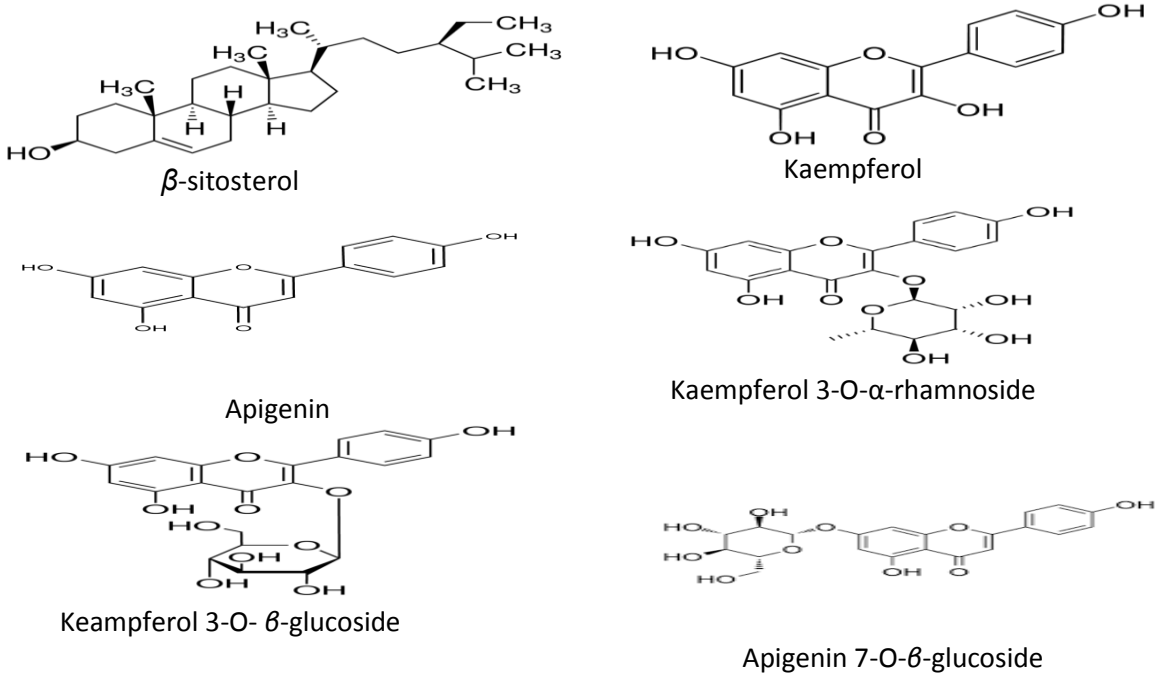

Figure 1. Compounds isolated from *C. intybus* extract

Conclusion

The extract of *Cichorium intybus* aerial parts had a good antioxidant effect and also it has a very good antibacterial effect, which is determined and potentiated by the unique chemical composition of chicory plants. The substantial background documented in of aerial parts of *C. intybus*. heightens this economical renewable raw material of interest for the pharmaceutical and food industries.

Conflicts of interest

There are no conflicts of interest to declare

References

[1] Shahid Akbar. *Cichorium intybus* L. (Asteraceae/Compositae), Handbook of 200 Medicinal Plants, 10.1007/978-3-030-16807-0, (2020); 609-621.

[2] Safarpoor Dehkordi, F., Tirgir, F. and Valizadeh, Y. Effects of Guajol® ointment synthesized from medicinal smoke condensate of jennet feces on burn wound healing on Wistar rat. Vet. Res. Forum., 8, (2017) 215-221

[3] Odeja, O., Ogwuche, C. E., Elemike, E. E., & Obi, G. Phytochemical screening, antioxidant and antimicrobial activities of Acalypha ciliata plant. Clinical Phytoscience, 2(1), (2016) 12.

[4] Bais HP, Ravishankar GA. Cichorium intybus L. Cultivation, processing, utility, value addition and biotechnology, with an emphasis on current status and future prospects. Journal of the Science of Food and Agriculture.;81(5) (2001) 467–484.

[5] Finke, B., Stahl, B., Pritschet, M., Facius, D., Wolfgang, J., and Boehm, G. Preparative continuous annular chromatography (P-CAC) enables the large-scale fractionation of fructans J Agric Food Chem 17; (2002); 4743-4748.

[6] Foster, J. G., Clapham, W. M., Belesky, D. P., Labreveux, M., Hall, M. H., & Sanderson, M. A. Influence of cultivation site on sesquiterpene lactone composition of forage chicory (Cichorium intybus L.). Journal of agricultural and food chemistry, 54(5), (2006) 1772–1778.

[7] De Kraker, J. W., Franssen, M. C., de Groot, A., Konig, W. A., and Bouwmeester, H. J. (+)-Germacrene A biosynthesis . The committed step in the biosynthesis of bitter sesquiterpene lactones in chicory. Plant Physiol;117(4); (1998) 1381-1392.

[8] De Kraker, J. W., Franssen, M. C., Dalm, M. C., de Groot, A., and Bouwmeester, H. J. Biosynthesis of germacrene A carboxylic acid in chicory roots. Demonstration of a cytochrome P450 (+)-germacrene a hydroxylase and NADP+-dependent sesquiterpenoid dehydrogenase(s) involved in sesquiterpene lactone biosynthesis. Plant Physiol;125(4): (2001)1930-1940.

[9] Flamm, G., Glinsmann, W., Kritchevsky, D., Prosky, L., and Roberfroid, M. Inulin and oligofructose as dietary fiber: a review of the evidence. Crit Rev Food Sci Nutr 2001;41(5):353-362.

[10] Perović, J., Tumbas Šaponjac, V., Kojić, J., Krulj, J., Moreno, D. A., García-Viguera, C., Bodroža-Solarov, M., & Ilić, N. (2020). Chicory (Cichorium intybus L.) as a food ingredient - Nutritional composition, bioactivity, safety, and health claims: A review. Food chemistry, 336, 127676.

[11] Sofowra A. Medicinal Plants And traditional Medicine in Africa. Spectrum Books Ltd., Ibadan, Nigeria (1993)191-289.

[12] Trease GE and Evans WC. Pharmacology, 11th ed., Bailliere Tindall, London (1989) 45-50.

[13] Harborne JB. Phytochemical Methods. Chapman and Hall. Ltd., London (1973) 49-188.

[14] Pateh UU, Haruna AK, Garba M, Iliya IM, Riyam Sabeeh Jasim, 2018. Antioxidant, Antimicrobial Activities and Phytochemical Constituents of Cichorium intybus L. Aerial Parts. International Journal of Botany, 14: 24-29.)

[15] Said A, Usama WH, El-Shenawy S, Salwa M. N, Khaled R.. Flavonoids and some biological activities of Ailanthus excelsa leaves. IUFS J Biol Res;69(1): (2010) 41-55.

[16] Amal MYM, Ahmed IK, Mahmoud AS. Isolation, structural elucidation of flavonoid constituents from Leptadenia pyrotechnica and intybus L.) leaves, Saudi J. Biol. Sci.; 22(3); (2015) 322–326.

[17] Teffo L.S. , M.A.Aderog ba J.N. Eloff.. Antibacterial and antioxidant activities of four kaempferol methyl ethers isolated from Dodonaea viscosa Jacq. var. angustifolia leaf extracts. South African Journal of Botany 76(1) (2010) 25-29

[18] Hanumantappa B. Nayaka, Ramesh L. Londonkar, Madire K. Umesh, and Asha Tukappa. Antibacterial Attributes of Apigenin, Isolated from Portulaca oleracea L. nternational Journal of Bacteriology. Volume 2014, Article ID 175851, (2014) 8 pages.

[19] De Andrade EF, de Souza Leone R, Ellendersen LN, Masson ML. Phenolic profile and antioxidant activity of extracts of leaves and flowers of yacon (Smallanthus sonchifolius). Ind Crops Prod 62: (2014) 499–506.

[20] Abbas, Z. K. Saggu, S. Sakeran, M. I. Zidan, N. Rehman, H. Ansari, A. A. Phytochemical,

antioxidant and mineral composition of hydroalcoholic extract of chicory (Cichorium evaluation of their toxicity and anti-tumor activity. Pharma Biol; 47(6) (2009) 539–552.
[21] Shad, M.A. Nawaz, H. Rehman, T. Ikram, N. Determionation of some biochemicals, phytochemicals and antioxidant properties of different parts of Cichorium intybus L: a comparative study, J. Anim. Plant Sci., 23 (4) (2013) 1060-1066.
[22] Barua N., Ibn Aziz M.A., Tareq A.M., Sayeed M.A., Alam N., Alam N.U., Uddin M.A., Lyzu C., Emran T.B. In vivo and in vitro evaluation of pharmacological activities of Adenia trilobata (Roxb.), Biochemistry and Biophysics Reports, Volume 23, (2020) 212-218.
[23] Riyam Sabeeh Jasim,. Antioxidant, Antimicrobial Activities and Phytochemical Constituents of Cichorium intybus L. Aerial Parts. International Journal of Botany, 14: (2018) 24-29.
[24] Mohamed, T. A., Hegazy, M. F., Abd El Aty, A. A., Ghabbour, H. A., Alsaid, M. S., Shahat, A. A., & Paré, P. W. Antimicrobial sesquiterpene lactones from Artemisia sieberi. Journal of Asian natural products research, 19(11), (2017) 1093–1101.
[25] Liu, H., Wang, Q., Liu, Y., Chen, G., & Cui, J. Antimicrobial and antioxidant activities of Cichorium intybus root extract using orthogonal matrix design. Journal of food science, 78(2), (2013) M258–M263.
[26] Innocenti M, Gallori S, Giaccherini C, Ieri F, Vincieri FF, Mulinacci N. Evaluation of the phenolic content in the aerial parts of different varieties of *Cichorium intybus* L. J Agric Food Chem. 53(16): (2005) 6497-502.