

Research Article

Phytochemical Constituents and Biological Activities of *Jasonia glutinosa* L.: The First Report for the Plant Growing in North Africa

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Received 21 August 2022; Revised 29 November 2022; Accepted 1 December 2022; Published 9 December 2022

Academic Editor: Eulogio J. Llorent Mart nez

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Jasonia glutinosa (rock tea), also known as *Chiliadenus glutinosa* Cass., is a medicinal plant growing in the Mediterranean Basin. It is used for the treatment of depression, gastrointestinal complaints, inflammations, appendicitis, colds, and respiratory disorders. The current study is the first report for the plant species growing in Libya and aims to investigate the phytochemical constituents, antioxidant, cytotoxic, and antimicrobial activities of the plant's aqueous ethanolic extract. The phytochemical investigation was conducted by the spectrophotometric quantitative assay and the LC-MS analysis. The analysis revealed the presence of 14.67 and 46.72 mg/g of the total phenolics and flavonoids equivalent to gallic acid and rutin, respectively. A total of thirty compounds of phenolic acids and flavonoids were identified by the LC-MS analysis, with a total relative percentage of 18.69%. The analysis revealed the dominance of methoxylated flavonoids and cinnamic acid derivatives, including caffeoylquinic acids. The in vitro antioxidant assays showed 265.55, 513.32, and 27.10 μ M Trolox eq/mg of extract in the ABTS, ORAC, and FRAP assays, respectively. Cancer cell growth inhibitions of 9.23, 11.42, and 34.01% at a concentration of 100 μ g/mL against MCF-7, HepG2, and PANC-1 cell lines were obtained, which is considered a weak cytotoxic effect when compared to the standard anticancer agent, doxorubicin (DOX). No antimicrobial activity was noticed for the plant extract against all tested microorganisms, i.e., *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus*, *Salmonella typhimurium*, *Candida albicans*, and *Saccharomyces cerevisiae*. The weak antimicrobial effect of the plant did not support the claim of traditional use of the plant as an antimicrobial agent.

1. Introduction

Production of reactive oxygen radicals is a physiological process in the human body and is essential for several normal cellular activities, including signal transduction, immunity functions, and normal aging of the cells [1, 2]. Overproduction of reactive oxygen species (ROS) is considered a pathological pathway associated with the development of several diseases, including cancer, atherosclerosis, neurodegenerative disorders, and liver and kidney

malfunctions [3, 4]. The environmental pollution, infections, crowdedness, and exhausts of various industries, in addition to certain human lifestyles and diets, are also stress factors affecting the body's soft tissues, including the liver, kidney, and brain [5–7]. All these diseases are linked to the serious degenerative effect of ROS on the body's macromolecules, such as DNA, nucleic acids, proteins, lipids, and carbohydrates [3, 8]. Cancers and infectious diseases are serious medical conditions that affect human life and impede the continuous improvement of people's living standards

around the world [9, 10], and their complications have been linked to oxidative stress and higher production of ROS [11].

The primary role of vegetables and fruits in the prevention of oxidative stress-related diseases is well understood by the public and the scientific community. The role of these natural ingredients in the treatment of liver dysfunction, cardiovascular diseases, central nervous system degeneration, and other soft tissue illnesses, which are initiated, progressed, and exaggerated by ROS, has been reported [12, 13].

The worldwide-spreading family, is one of the largest families of flowering plants. The family comprises about 1600 genera and 25,000 species, which approximates 10% of the global flora [14]. *Chiliadenus* Cass. has been described in the nineteenth century as a small genus that belongs to the family Asteraceae, and includes only ten species distributed in the Mediterranean and adjacent areas [15–17]. In Libya, only two species of the genus *Chiliadenus* have been identified [18]. These species were previously classified as members of the genera *Jasonia* and *Varthemia*, but Brullo, classified them as members of the genus *Chiliadenus* based on taxonomic characteristics [19]. *Jasonia glutinosa* or *Chiliadenus glutinosa* Cass. commonly known as rock tea, is a medicinal plant present in the Mediterranean Basin. It is considered an aromatic plant that grows in rocky crevices and limestone landings with an altitudinal range of 250 to 1800 m. They bloom in the summer, from July to September [20].

The phytochemical examination of *Jasonia* has led to the isolation and identification of numerous bioactive phytoconstituents of diverse chemical classes, e.g., sesquiterpenes, flavonoids, monoterpenes, and diterpenes [15]. The simultaneous estimation of *C. glutinosa* revealed the presence of sesquiterpene, lucinone and glutinone [21, 22], and sesquiterpene alcohol (eudesmane alcohol) [23]. Several phenolics and flavonoids have also been detected in the aerial parts of the plant [24, 25]. Other research showed that the most abundant phenolic acid was dicaffeoylquinic acid [26]. In addition, flavonoid methyl derivatives, e.g., patuletin, quercetin glucopyranosides, and kaempferol glucuronopyranosides, were also identified in the plant [24, 25]. In addition, *C. glutinosa* is an aromatic plant, and its essential constituents have been identified from the plant species growing in different areas [27, 28]. The overall analysis of the essential oil constituents of *C. glutinosa* indicated that camphor and borneol were the major constituents in the plant [27, 28].

In both folk and modern traditional medicine, *Jasonia glutinosa* is an important species and a popular stomachic herb. The plant is also used as a component in preparations showing gastrointestinal beneficial effects, e.g., antispasmodic and digestant, and as an anti-inflammatory drug [29]. Other traditional uses include treating appendicitis, cold, and respiratory diseases, as well as treating depression [20]. Several studies on the biological properties of *C. glutinosa* have been previously published and showed antioxidant [30], anti-inflammatory [22], and antimicrobial activities [31]. Moreover, the acetone extracts obtained from aerial parts of the plant exerted an antiparasitic effect [32].

Furthermore, ethnobotanical studies have revealed that this plant is not only used where it grows but can also be

found in some traditional taverns, restaurants, pharmacies, and herbal remedy shops [33].

The current study investigated the phytochemical constituents of *Jasonia glutinosa* by spectrophotometric analysis and the spectroscopic technique, LC-MS. The biological activities, i.e., antioxidant, cytotoxic, and antimicrobial activities, were also investigated for the plant extract. The growing area where *Jasonia glutinosa* was collected is part of what makes our work novel, as there have been no previous studies for the plant species growing in Libya. The study also emphasized the biological activity and phenolic components of *Jasonia glutinosa*, the plant that is immensely popular in the North African and Mediterranean countries and has a long history of usage in traditional medicine.

2. Materials and Methods

2.1. Plant Materials, Collection, Identification, and Extraction Procedure. The plant was collected in February 2022 from El-Jabal Al Akhdar area in Libya. The identification of the plant sample was precisely confirmed by the herbarium of Benghazi University's Faculty of Science, Botany department, Benghazi, Libya. 250 gm of the plant was chipped into small pieces, homogenized in a mixer, and extracted with methanol 70% using Soxhlet apparatus until complete exhaustion. The obtained extract was concentrated by removing the solvent under vacuum using a rotary evaporator. The resulting residues were weighed and kept in desiccators.

2.2. Total Phenolic and Total Flavonoid Contents. The total contents of phenols (TPC) were estimated using Folin–Ciocalteu reagent and by using a UV-vis spectrophotometer, according to the method of Attard 2013 [34]. The technique involved mixing 10 μ L of the sample/standard with 100 μ L of the Folin–Ciocalteu reagent previously diluted 1 : 10 with distilled water and 80 μ L of 1M Na₂CO₃ in a 96-well microplate. The plate was incubated at room temperature in the dark for 20 minutes. The intensity of the resulted blue color was measured at 630 nm against a blank consists of all ingredients except the sample. The standard calibration curve was plotted using the absorbance of various concentrations of gallic acid. The results were calculated from triplicate measurements and expressed as mg gallic acid equivalents/g of the weight of the dry extract (mg GAE/g) [35].

The total flavonoids content was evaluated in microplates by conducting the aluminum chloride reagent method as described by Kiranmai et al. [36]. The analysis was conducted on a Beckman DU-650 spectrophotometer in a 96-well microplate, whereas 15 μ L of the sample/standard was mixed with 175 μ L of methanol, 30 μ L of 1.25% AlCl₃, and 30 μ L of 0.125 M C₂H₃NaO₂ and incubated for 5 minutes. The color was measured at 420 nm against a blank methanol solution. The average of absorbance values of rutin at different concentrations (5, 10, 20, 40, 80, 100, 120, and 160 μ g/mL in methanol) were employed to plot the calibration curve. The TFC in the extract was expressed as

milligrams of the standard rutin equivalent per gram of the dried extract (mg RE/g).

2.3. LC-MS Analysis. All solvent used in the LC-MS analysis were of analytical grade. Shimadzu ExionLC (Shimadzu, Kyoto, Japan) equipped with a TurboIonSpray, SCIEX X500 R QTOF (SCIEX, Framingham, MA, USA) was used for the extract scanning. Accurately, 1 mg of the extract was dissolved in 2 ml of DMSO and centrifuged at 5000 rpm for 2.0 min. Accurately, 1.0 ml of the clear solution was transferred to the autosampler, and the injection volume was adjusted to 3.0 μ L. The instrument was operated using ion source gas 1 (psi): 50 and ion source gas 2 (psi): 50, and ion funnel electrospray source. The instrument parameters were adjusted as follows: capillary voltage (negative, -4000 V), nebulizer gas (2.0 bar), nitrogen flow (8 L/min), and dry temperature (200°C). The mass accuracy was <1 ppm, the mass resolution was 50,000 FSR (full sensitivity resolution), and the TOF repetition rate was up to 20 kHz. The chromatographic separation was performed on C18 reverse-phase (RP) column, 100 \times 2.1 mm, 3.0 μ m from GL-Science (Japan) at 50°C, autosampler temperature 8.0°C, with a flow rate of 0.35 mL/min, and total run time of 40 min using the gradient elution. The eluents consisted of as follows: mobile phase A: 0.1% formic acid in water and mobile phase B: 100% acetonitrile.

2.4. Antioxidant Assays

2.4.1. ABTS. The ABTS radical cation decolorization analysis was employed to investigate the free radical scavenging capacity of the extracts. The analysis was performed in microplates following the technique outlined by Arnao et al [37], with little modifications. A 192 mg of ABTS were dissolved in deionized water and transferred to a 50 mL volumetric flask, and the final volume was made with the addition of distilled water. Accurately, 1 mL of the prior solution was mixed with 17 μ L of 140 mM potassium persulphate and stored for 24 hours in a dark place. The reaction mixture was then diluted to 50 mL using methanol to attain the final ABTS dilution utilized in the experiment. In a 96-well plate ($n = 6$), 190 μ L of freshly produced ABTS reagent was combined with 10 μ L of the sample/standard, and the reaction was placed in an incubator for 30 minutes in a dark chamber with temperature control set at room temperature (22°C). At the end of the incubation time, the drop in the intensity of ABTS color was measured at 734 nm. The results were recorded using FluoStar Omega microplate reader (BMG Labtech, Ortenberg, Germany).

2.4.2. ORAC. The oxygen radical absorbance capacity (ORAC) assay was performed using the technique of Liang et al. [38], with little modifications; 10 μ L of the prepared sample was incubated with 30 μ L fluorescein (100 nM) for 10 minutes at 37°C. For background detection, the measurements of fluorescence (485 EX, 520 EM, nm) were conducted for three rounds (90 sec each). Following that,

70 μ L of newly prepared 2,2'-azobis(2-amidinopropane) dihydrochloride (AAPH) (300 mM) was immediately added to each well. The temperatures must be set at some higher point to ensure that azide decomposition temperature in the wells is reached. The measurements of florescent (485 EX, 520 EM, nm) was proceeded for 60 min (40 cycles, each 90 sec) by using FluoStar Omega microplate reader (BMG Labtech, Ortenberg, Germany).

2.4.3. FRAP. The test was carried out in microplates according to the technique described by Benzie and Strain with little modifications [39]. A newly produced TPTZ reagent (300 mM acetate buffer (PH 3.6), 10 mM TPTZ in 40 mM HCl, and 20 mM FeCl₃, in a ratio of 10:1:1 v/v/v, respectively). In a 96-well plate, 190 μ L of freshly made TPTZ reagent were combined with 10 μ L of sample, and the reactions were kept at ambient temperature for 30 minutes in a dark chamber. At the end of the incubation time, the resultant blue color was detected at 593 nm by FluoStar Omega microplate reader equipment (BMG Labtech, Ortenberg, Germany), and the activity of the extract was calculated as mg Trolox equivalent per gram of the plant's dried extract using the FRAP-Trolox calibration curve.

2.5. Antiproliferative Assay. The sulforhodamine B (SRB) assay was applied to assess cell viability in the presence of *J. glutinosa*. Three cell lines were chosen for the cytotoxic evaluation of the plant extract, i.e., breast adenocarcinoma (MCF-7), hepatocellular carcinoma (HepG2), and pancreatic cancer (PANC-1) cell lines. Aliquots of 100 μ L suspension of the cells (5×10^3 cells) were seeded into 96-well plates and kept incubated for 24 hours. Another aliquot of 100 μ L media containing *J. glutinosa* extract at various concentrations (from 0.001 to 100 μ g/mL) was delivered to the cells. Following 72 h of cells exposure to the *J. glutinosa* extract, cells were maintained by substituting the media with 150 μ L of 10% trichloroacetic acid (TCA) and kept in an incubator at 4°C for one hour. After discarding the TCA solution, the cells were rinsed five times with deionized water. Aliquots of 70 μ L SRB solution (0.4% w/v) were inserted and allowed to stand at ambient temperature for 10 min in a dark chamber. Then, 1% acetic acid was used to wash the plates. After that, 150 μ L of TRIS (10 mM) was applied to dissolve the protein-bound SRB stain. BMG LABTECH®- FLUOstar Omega microplate reader (BMG Labtech, Ortenberg, Germany) was used to measure the absorbance at 540 nm [40, 41].

2.6. Antimicrobial Assay. The antibacterial activity was assessed using a modified Kirby-Bauer disk diffusion susceptibility test procedure [42]. Paper disks containing the methanolic plant extract (50 μ L of *J. glutinosa* at 100 mg/mL) were prepared and attached on the surface of agar plates inoculated with the bacteria (*Escherichia coli* ATCC 8739, *Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 29213, *Salmonella typhimurium* ATCC 14028, *Candida albicans* ATCC 10231, and *Saccharomyces cerevisiae* ATCC

9763). The negative control was made of the same volume of DMSO, while the positive control was standard disks of antibacterial agents. The plates were kept inverted in the incubator for one day at 37°C. After incubation, the plates were inspected to measure the zones of inhibition. Diameters less than 5 mm were considered as no effect. The experiment was carried out three times.

2.7. Statistical Analysis. Results were presented as mean \pm standard deviation (SD). Statistical analysis was conducted by applying Student's *t*-test and *P* values less than 0.05 was recorded as significant. Correlations between acquired data were analyzed using the correlation coefficient statistical tool in the MS Excel software.

3. Results and Discussion

3.1. Spectrophotometric Analysis of Plant Constituents. The total contents of phenolics and flavonoids were measured quantitatively as gallic acid (GAE) and rutin (RE) equivalents per gram of the plant extract. The results (Table 1) revealed the presence of 14.67 ± 0.67 GAE and 46.42 ± 3.12 RE of the phenolics and flavonoids, respectively, in mg/g of the extract. Environmental conditions and soil content have been reported as intrinsic factors affecting plant constituents [43, 44]. The total phenolics and flavonoids of *J. glutinosa* growing in other areas have been reported. For instance, the phenolic contents have been measured for the commercial plant samples collected from local markets in Spain [26]. The methanol and water extracts of the plant have been shown to contain significantly higher levels of the phenolics compared to the current result, with 155.2 and 163.3 mg GAE/g of the extracts, respectively [26]. The large difference in phenolic content between Libyan and Spanish growing species could be attributed to the effects of environmental conditions and soil contents on the levels of the plant's phenolic constituents. However, the higher significant differences in phenolic contents between Libyan and Spanish species of the plant could be attributed in part to variations and conditions of the phenolic determination protocols, as well as the presence of other constituents other than phenolics capable of reducing the Folin-Ciocalteu reagent, such as reducing sugars and ascorbic acid, as previously reported [45].

3.2. Spectroscopic Analysis of Plant Constituents. The individual phenolics and flavonoids in the *Jasonia glutinosa* extract were tentatively identified by the LC-MS spectroscopic analysis. The molecular ions and related mass fragments of the identified compounds were detected in the negative and positive mass ion modes of analysis. Out of dozens of peaks in both positive and negative chromatograms, only thirty compounds related to the phenolic acid and flavonoid classes were tentatively identified (Table 2). The *m/z* of the molecular ions in the negative modes along with the *m/z* for the mass fragments and molecular formula of the identified compounds were all represented in Table 2 and arranged according to their retention times. The total relative

percentages of the identified compounds were calculated at 18.69% based on individual percentage of each identified peak in relation to the total peaks in the negative mode chromatogram. The identification of the compounds was established based on the mass fragments and molecular ion peaks of each compound in relation to the literature and also on the available literature of the phenolic and flavonoid constituents of the plant. The mass fragments of the sugar moieties and aglycones have also been used in the confirmation of the compound's tentative identity (Figure 1). For example, the presence of the aglycone fragment after the subtraction of 162 atomic mass unit (amu) indicated the hexoside nature of the sugar [60]. However, the presence of the fragment at *m/z* 191 amu indicates the removal of the quinic acid from its glycosidal forms. The quinic acid as a cyclitol sugar moiety has been identified in four compounds (3-caffeoylquinic acid (1), 1-caffeoylquinic acid (8), 1,3-dicaffeoylquinic acid (9), and 1,5-O-dicaffeoylquinic acid (10)) due to the presence of its *m/z* mass fragment unit at 191 in the negative mode spectra of these compounds. Furthermore, the aglycone part in these four compounds, 1, 8, 9, and 10, was identified due to the presence of a fragment at 179 amu assigned for the caffeic acid in the negative ion mode fragment spectra. The sugar moiety, glucuronide, was detected in two of the identified compounds, i.e., quercetin-3-O-glucuronide (5) and mearnssetin-O-glucuronide (7), by the presence of the aglycones mass units at *m/z* 301 and 331, indicating the loss of 176 amu from the molecular masses $[M-H]^-$ at *m/z* 477 and 507, respectively. In addition, a loss of 162 amu was assigned for the removal of hexose units, which are mainly considered as glucosides. Losses of 162 amu were found in the mass fragmentation spectra of quercetin-3-glucoside (4) (463 $[M-H]^-$ to the 301 $[M-H-glu]^-$), mearnssetin-O-hexoside (6) (493 $[M-H]^-$ to the 331 $[M-H-glu]^-$), kaempferol-3-O-glucoside (11) (447 $[M-H]^-$ to the 285 $[M-H-glu]^-$), and medioresinol-O-hexoside (13) (549 $[M-H]^-$ to the 387 $[M-H-glu]^-$). Furthermore, two acetyl glycosylated compounds, i.e., quercetin-3-acetylhexoside (12) (505 $[M-H]^-$ to the 301 $[M-H-glu-acetyl]^-$) and kaempferol-acetylglucoside (14) (489 $[M-H]^-$ to the 285 $[M-H-glu-acetyl]^-$) were marked by the removal of 204 amu from both compounds, which were assigned for the removal of hexosyl and acetyl residues.

The flavonoid aglycones, i.e., taxifolin (2), quercetin (15), luteolin (16), gallo catechin (24), and chrysin (26) were assigned based on their molecular masses in the negative mode mass analysis and the presence of specific fragments for each of them according to the literature [47, 51, 57]. The identified methoxylated flavonoids, i.e., isorhamnetin (17), trimethoxy dihydroflavonoid (18), rhamnetin (20), 4'-hydroxylwogonin (21), 5,7,2'-trihydroxy-6-methoxyflavone (25), 3'-O-methylorobol (methoxylated isoflavone) (28), trimethoxy flavonoid (29), and calycosin (methoxylated isoflavone) (30) were also assigned based on their mass fragmentation patterns, which were consistently reported, besides the losses of 15 amu for their molecular masses which have been assigned to the detached methyl group.

The overall analysis of the LC-MS spectral results confirmed the presence of phenolics and flavonoids in considerable amounts in the plant extract and revealed the

TABLE 1: Quantitative measurements of the phenolics, flavonoids, and antioxidant activity of *Jasonia glutinosa*.

Test	TPC	TFC	ABTS	ORAC	FRAP
Units	mg/g GAE	mg/g RE		μM Trolox eq/mg extract	
Results	$14.67 \pm 0.67^*$	$46.42 \pm 3.12^*$	$265.55 \pm 7.77^*$	$513.32 \pm 23.07^*$	$27.10 \pm 2.97^*$

*Data represented as mean of three measurements \pm SD; TPC, total phenolic contents; TFC, total flavonoid contents; ABTS, 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); ORAC, oxygen radical absorbance capacity; FRAP, ferric reducing antioxidant power.

TABLE 2: Phytochemical profiling of *J. glutinosa* extract.

No	Rt	Name	Molecular formula	m/z [M-H]-	Calculated exact mass	Relative %	Fragments
1	7.85	3-Caffeoylquinic acid (neochlorogenic acid)	C16H18O9	353.0968	353.0872	0.20	191.06, 85.03 [46]
2	9.02	Medioresinol	C21H24O7	387.1746	387.1443	0.08	163.11, 207.10, 367.03 [26]
3	10.65	Taxifolin	C15H12O7	303.0595	303.0504	0.08	125.02, 217.05 [47]
4	10.97	Quercetin-3-glucoside	C21H20O12	463.0994	463.0876	0.32	301.04 [48]
5	10.97	Quercetin-3-O-glucuronide (miquelianin)	C21H18O13	477.0789	477.0669	0.62	301.04, 151.00 [46]
6	11.04	Mearnsetin-O-hexoside	C22H22O13	493.1100	493.0982	0.14	331.05, 302.04, 288.03 [26]
7	11.10	Mearnsetin-O-glucuronide	C22H20O14	507.0892	507.0774	0.20	301.04, 316.03, 331.05 [26]
8	11.40	1-Caffeoylquinic acid		353.0972	353.0872	0.15	191.06, 179.03 [46]
9	11.41	1,3-Dicaffeoylquinic acid	C25H24O12	515.1304	515.1189	2.96	191.05, 179.03 353.09 [46]
10	11.41	1,5-O-Dicaffeoylquinic acid	C25H24O12	515.1293	515.1189	0.31	179.03, 191.06, 353.09 [49]
11	11.51	Kaempferol-3-O-glucoside	C21H20O11	447.1046	447.0927	0.05	285.04, 284.03, 255.03, 227.04 [46]
12	11.69	Quercetin-3-acetylhexoside	C23H22O13	505.1109	505.0982	0.27	301.03, 300.03, 271.03, 173.04 [50]
13	11.88	Medioresinol-O-hexoside	C27H34O12	549.2095	549.1972	0.09	387.17, 161.02 [26]
14	12.38	Kaempferol-acetylglucoside	C23H22O12	489.1153	489.1033	0.07	285.04, 284.04, 255.03 [48]
15	13.21	Quercetin	C15H10O7	301.0435	301.0348	0.45	285.04, 151.00 [51]
16	13.24	Luteolin	C15H10O6	285.0480	285.0399	0.53	217.05, 179.00, 151.00, 133.03 [51]
17	13.40	Isorhamnetin (methoxyflavonol)	C16H12O7	315.0592	315.0504	0.17	300.03, 285.04, 151.00 [46]
18	13.74	Trimethoxy dihydroflavonoid	C18H18O7	345.0694	345.0974	0.26	330.04, 315.02, 278.02 [26]
19	13.82	Honokiol (phenol)	C18H18O2	265.1516	265.1228	0.75	247.14, 221.15, 137.10 [52]
20	14.52	Rhamnetin (methoxyflavonol)	C16H12O7	315.0593	315.0504	0.14	300.03, 284.03, 255.03, 227.04 [53]
21	14.64	4'-Hydroxylwogonin (methoxy flavone)	C16H12O6	299.0637	299.0555	0.68	284, 255.03, 227.04 [54]
22	14.87	3,3'-Di-O-methylelagic acid	C16H10O8	329.0740	329.0297	3.52	299.02, 271.02 [55]
23	14.68	Glucogallin (phenolic glycoside)	C13H16O10	331.0810	331.0665	0.11	314.09, 299.02, 271.02 [56]
24	15.12	Gallocatechin	C15H14O7	305.1005	305.0661	0.10	304.91, 274.14, 163.11, 137.10 [57]
25	15.41	5,7,2'-Trihydroxy-6-methoxyflavone	C16H12O6	299.0639	299.0555	0.12	284.04, 165.02 [54]
26	15.85	Chrysin	C15H10O4	253.1804	253.0500	0.26	251.16, 207.18, 191.14
27	15.12	3,4-Dihydroxy-5-prenyl cinnamic acid	C14H16O4	247.1386	247.0970	4.66	203.14, 187.11, 163.11, 517.26 [58]
28	16.03	3'-O-Methylorobol (O-methylated isoflavone)	C16H12O6	299.0265	299.0555	0.19	271.03, 251.17 [59]
29	16.15	Trimethoxy flavonoid	C18H16O7	343.0896	343.0817	0.96	328.06, 313.04, 298, 270.02 [26]
30	16.58	Calycosin (O-methylated isoflavone)	C16H12O5	283.0675	283.0606	0.25	268.04 [59]
Total percentages of the identified compounds							18.69%

presence of 12.83% of the phenolic acid derivatives, including 3.82% of the phenolic glycosides. The analysis also revealed the presence of 5.86% flavonoids, of which 1.67% were glycosylated flavonoids, 4.19% were flavonoid aglycones, 3.11% were methoxylated flavonoids, and 0.44% were isoflavonoids. The analysis also revealed the dominance of

the cinnamic acid derivatives, including the caffeoylquinic acids and the methoxylated flavonoids, which is consistent with the reported LC-MS analysis for the plant species growing in Spain [26].

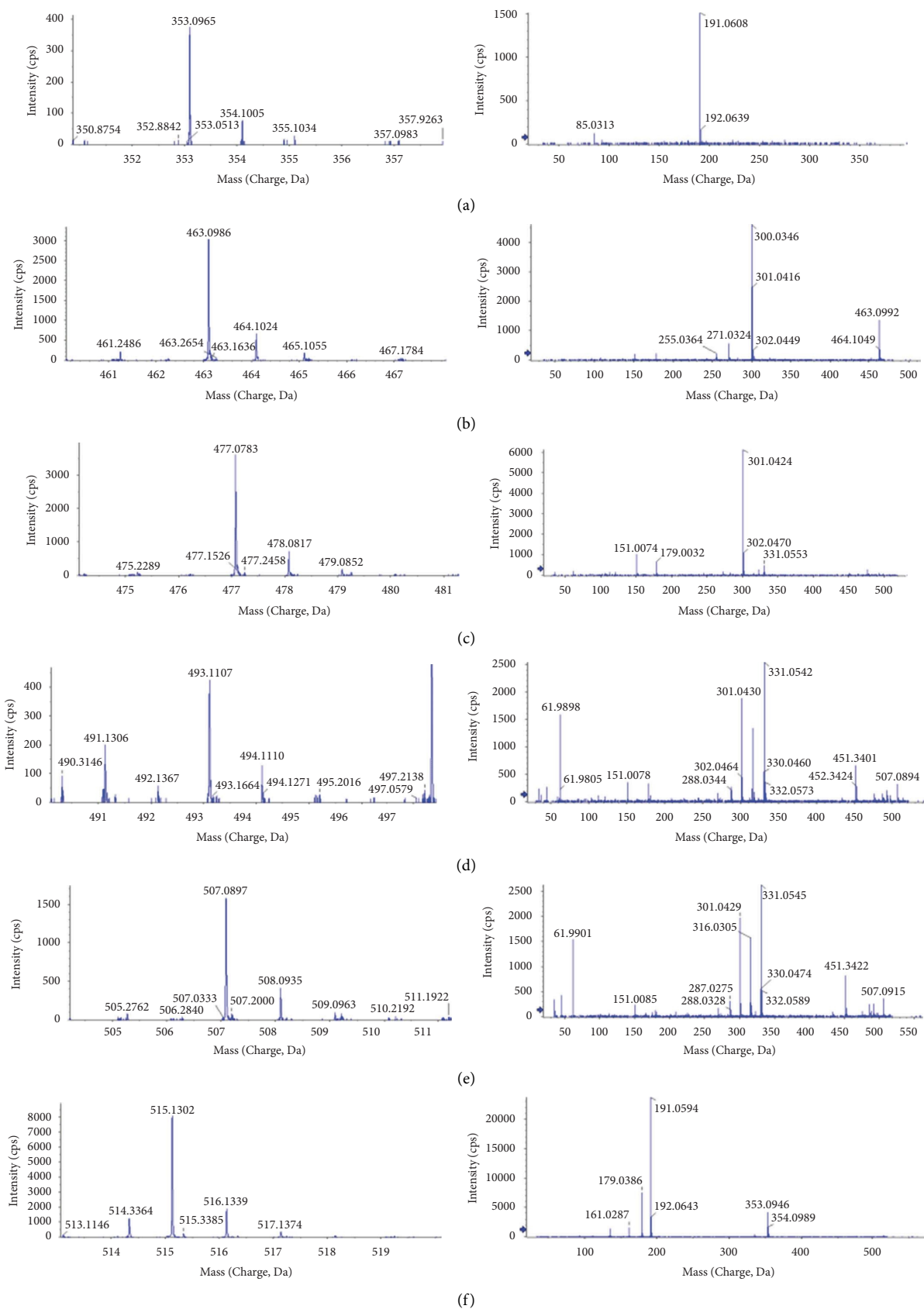


FIGURE 1: Mass fragmentations of the major phenolics and flavonoids in *J. glutinosa* extract. (a) 3-caffeoylquinic acid, (b) quercetin-3-glucoside, (c) quercetin-3-O-glucuronide, (d) mearnssetin-O-hexoside, (e) mearnssetin-O-glucuronide, and (f) 1,3-dicaffeoylquinic acid.

TABLE 3: Cell viability percentages at 100 $\mu\text{g/mL}$ *J. glutinosa* extract and doxorubicin.

Cell lines	MCF-7	HepG2	PANC-1
	Cell viability percentages (%)		
<i>J. glutinosa</i> extract	90.77 ± 3.37	88.58 ± 2.80	65.99 ± 1.94
DOX	26.95 ± 0.72	23.02 ± 0.31	18.93 ± 0.36

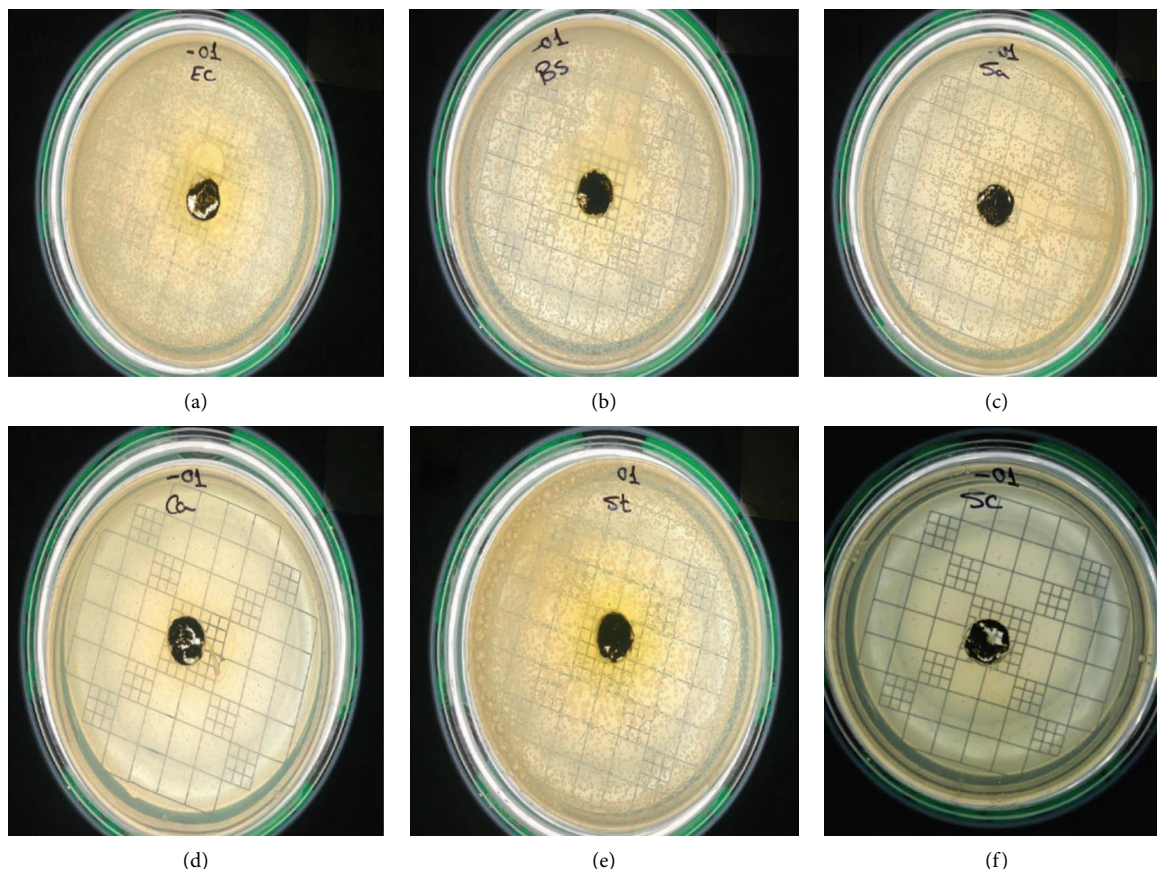


FIGURE 2: Results of disk diffusion susceptibility test of *J. glutinosa* (100 mg/mL) against (a) *Escherichia coli* ATCC 8739, (b) *Bacillus subtilis* ATCC 6633, (c) *Staphylococcus aureus* ATCC 29213, (d) *Candida albicans* ATCC 10231, (e) *Salmonella typhimurium* ATCC 14028, and (f) *Saccharomyces cerevisiae* ATCC 9763.

3.3. Antioxidant Activity of *J. glutinosa*. The antioxidant activity of *J. glutinosa* has been reported for plant species growing in different locations other than Libya [20, 26]. The current results also revealed the remarked antioxidant activity for the plant, which was assessed by three different assays, i.e., ABTS, ORAC, and FRAP (Table 1). These methods are common in vitro assays used to measure the free radical scavenging (ABTS and ORAC) and reducing power (FRAP) of plant extracts and biological samples. The current results are consistent with the findings of the spectrophotometric (TPC and TFC) and spectroscopical analysis (LC-MS) of the plant ethanolic extract, which revealed the presence of a considerable amount of the phenolic constituents measured at 18.69% of the total plant constituents that appeared in the LC-MS chromatogram. In addition, the antioxidant effect of polyphenols specially, flavonoids are well-known in literature [61, 62]. The results showed 265.55, 513.32, and 27.10 μM Trolox eq/mg of

extract in the ABTS, ORAC, and FRAP assays, respectively (Table 1). Compared to the reported antioxidant activity of the plant, our results demonstrated significantly higher activity compared to the plant species growing in Spain, which has been shown to have an ABTS power of 15.3 μM Trolox eq/100 g of the plant extract [26]. Furthermore, the same species inhibited the DPPH free radical with 17.4 μM Trolox eq/mg extract [26]. The ORAC and FRAP activities of the plant extract have been reported for the species growing in Spain and showed 2.72 μM Trolox eq/mg extract and 52.09 $\mu\text{mol Fe}^{2+}$ /g of extract, respectively [63]. These reported results also revealed the higher antioxidant content of the Libyan species, which exhibited 188x activity in the ORAC compared to the result reported for the Spanish species [63]. To the best of our knowledge, the current report is the first to discuss the antioxidant activity of the plant, *J. glutinosa*, from the African northern species. The results, when compared to the available reported of

antioxidant activity, also revealed the effect of environmental conditions on the plant constituents and their biological activities. In addition, the antioxidant activity of the plant is reflecting its benefit and safety for the human use as part of the traditional medicine system in the north Africa.

3.4. Antiproliferative Activity of *J. glutinosa*. Table 3 shows the antiproliferative activity of *J. glutinosa* extract, which demonstrated weak cytotoxic activity, with cell growth inhibition of 9.23, 11.42, and 34.01% at a concentration of 100 g/mL against tested cancer cells, namely MCF-7, HepG2, and PANC-1, when compared to the standard anticancer agent, DOX.

The current study's findings for *J. glutinosa* extract could be a sign of the safety of the plant for mammalian cells and be consistent with previous findings for the plant, which showed no cytotoxicity against the mouse embryonic fibroblast cell line, 3T3-L1 cells, until the concentration of 200 μ g/mL; however, the plant extract showed beneficial effects in the prevention of obesity, diabetes, and related metabolic complications [63]. A conflict between the current results of the weak cytotoxic effect and the presence of several constituents known for their cytotoxic and anticancer activities is a point of contention that needs to be explained. For instance, quercetin, taxifolin, luteolin, chrysin, kaempferol, and their glycosides, which were detected in the plant extract by the LC-MS analysis, have been reported for their cytotoxic activities [64–66]. In addition, caffeoylquinic acid derivatives, which were represented in the plant extract at \approx 3.6%, are also responsible for the remarkable antiproliferative activity in plants [67]. The presence of flavonoids and phenolic mixture might be the reason for the weak cytotoxic activity of the plant due to some mechanistic interference, which needs further studies to be clearly demonstrated. The results also reflect the safety of the plant, as it is consumed as food and in traditional medicine.

3.5. Antimicrobial Activity of *J. glutinosa*. The antimicrobial test of *J. glutinosa* has been conducted against six microorganisms using the common assay, the agar well diffusion method. In the test, two Gram negative bacteria, *E. coli*, *Salmonella typhimurium*; two Gram positive bacteria, *Bacillus subtilis*, *Staphylococcus aureus*; and two yeasts, *Candida albicans* and *Saccharomyces cerevisiae*, were used to provide ideas about the antimicrobial activity of *J. glutinosa*. The results clearly demonstrated no antimicrobial activity for the plant extract against all mentioned microorganisms at the tested dose of 100 mg/mL (Figure 2). The plant, *J. glutinosa*, has been listed as one of the plants employed in the Mediterranean area as an antimicrobial agent, particularly for intestinal infection [68]. However, other report has indicated very weak antimicrobial activity for *J. glutinosa*. For instance, different types of extracts obtained from the plant exhibited very weak antifungal activity against *Rhizopus stolonifer*, whereas dichloromethane extract showed a minimum inhibitory concentration above 1000 μ g/mL. However, ethyl acetate and methanol extracts have been shown to have no activity against *Rhizopus stolonifer* [30]. The current result for

the antimicrobial activity of the plant did not support the claim of traditional use of the plant as antimicrobial agent [69].

4. Conclusion

The phytochemical and biological investigations of *J. glutinosa* growing in Libya were reported here for the first time. The findings support the former reports, which confirm the presence and abundance of phenolics and flavonoids in the plant. The results also demonstrated considerable antioxidant activity and weak cytotoxic effect of the plant extract, which might reflect the safety of the plant, as it is consumed as food and is used in traditional medicine for curing several ailments. The results also supported the previous findings for the safety of the plant towards normal cells and its beneficial effects in the prevention of obesity, diabetes, and related metabolic complications. According to current results, the plant could be potential source for the phenolics and flavonoids with antioxidant activity. The findings of the antimicrobial assay for the plant extract showed no action, contradicting the assertion that it has historically been used as an antibacterial agent. However, the antimicrobial assay of the plant should be repeated against a wide variety of microorganisms and at a higher concentration of the plant extract than that used in the current study. The plant's nonpolar constituents may be more effective as antibacterial agents; hence, nonpolar extracts of the plant should also be investigated, which is part of our future plan.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

The researchers would like to thank the Deanship of Scientific Research, Qassim University, for funding the publication of this project.

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