Comparative assessment of biological activities of different parts of halophytic plant Tamarix articulata (T. articulata) growing in Saudi Arabia

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Abstract

Owing to extremely high salinity and harsh environmental conditions, T. articulata is one of the most abundant wild plants growing in the deserts of Saudi Arabia. Such plants may contain novel compounds to display promising biological activities. Here, in this study, we evaluate the biological activities of methanolic extracts of fresh leaves, dry leaves, stem, and roots of T. articulata. The antioxidant activity was determined by 2, 2-diphenyl-1-picrylhydrazyl (DPPH) and total phenolic and flavonoid content were determined using standard colorimetric methods. Whereas antimicrobial and ant-proliferative activities were determined by standard well-diffusion and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) methods, respectively. Our results demonstrate that all methanolic extracts of T. articulata showed antioxidant activity, however, the methanolic extract of dry leaves exhibits promising antioxidant effect with IC₅₀ value 49.08 ± 1.98, which was strongly supported by total phenolic (409.92 ± 6.03 mg GAE/g DW) and flavonoid (177.71 mg QE/g DW) content. Although, antimicrobial activity was also exhibited by all the methanolic extracts, however, methanolic extract of dry leaves exhibits promising antimicrobial activity in Gram-positive bacteria Staphylococcus epidemidis. Furthermore, MTT assay revealed that all methanolic extracts exhibit antiproliferative activity in MCF-7 (breast cancer) and RKO (colorectal cancer) cells with IC₅₀ values ranges from 219 ± 5.112 µg/ml to 253 ± 5.231 µg/ml and 220 ± 4.330 µg/ml to 325 ± 6.213 µg/ml, respectively. However, the most promising antiproliferative effect was displayed by methanolic extract of dry leaves with IC₅₀ values 219 ± 5.112 µg/ml and 220 ± 4.330 µg/ml, respectively. In summary, these findings provide evidence that T. articulata has promising biological activities and can be used for many pharmaceutical activities in the future.

1. Introduction

Plants are excellent sources of secondary metabolites including alkaloids, terpenoids, tannins, polyphenols, and flavonoids. Due to these secondary metabolites, the medicinal plants have great significance in the modern world. More than 30% of drugs in the modern world are derived from a plant source or derived from plant products (de Fátima et al., 2014; Patwardhan, 2005; Rah et al., 2012; Rah et al., 2015b). These valuable secondary metabolites possess numerous pharmacological activities including antioxidant, antimicrobial, anti-depressant, anti-lipidemic, anti-inflammatory, antitumor and other biological activities which can be of immense significance in therapeutics against different medical ailments (Alnuqaydan et al., 2020; Iwara et al., 2014; Ksouri et al., 2009; Mubashir et al., 2017; Nascimento et al., 2000). Attributable to nature’s enormous diversity of plant species on this planet, these plants possess chemical substances and influence the biological processes of the human body because of their compatibility (Samy et al., 1999).

T. articulata is commonly called “Athal” in the Arabic region. It is a type of halophytic plant and grows much faster than other plants in extremely arid and harsh environmental conditions. T. articulata belongs to family Tamaricaceae. The plant is woody
and can reach a height of 50 feet and a width of 6 feet (Alnuqaydan and Rah, 2019). A long time ago the plant was used by a tribal population called Tafilet of the southeastern region of Morocco for its medicinal properties against various diseases such as heart disease, ulcers, hypertension, skin diseases, gastrointestinal disorders, and hair loss (Hebi and Eddouks, 2017; Hebi et al., 2017; Hebi et al., 2018; Tabet et al., 2018). Despite a few biological activities of T. articulata that have been reported from the Morocco region, but it is still not clear the phytochemical composition and the comprehensive analysis of biological activities of different parts of T. articulata. Therefore, the present study was conducted to evaluate the comparative analysis of biological activities of different methanolic extracts (fresh leaf, dry leaves, stem, and root) of T. articulata found in Saudi Arabia.

2. Material and methods

2.1. Plant material and preparation of methanolic extracts

T. articulata plant specimens were collected from the desert areas of the Qassim region of Saudi Arabia in August 2019 along with dried leaves from the floor.

Methanolic extracts were prepared as per standard protocol (Wannes et al., 2010). The different parts of T. articulata were completely air-dried; the fine powder was obtained after grinding 100 g of each plant part (fresh leaves, dry leaves, stem, and root) in a kitchen blender. 12 g of each part was weighed, dissolved in 100% methanol, and were constantly stirring at room temperature for 3 days. Mixtures obtained were filtered through Whatman filter paper in a clean autoclaved glass beaker. The solvent was evaporated completely to get a fine powder of residue. The residue powder was stored at 4 °C and dissolved in 90% methanol for further experiments to evaluate the biological activities of the various residues of different parts of T. articulata plant.

2.2. Chemicals

Folin–Ciocalteu reagent (FCR), 3-(4,5-dimethylthiazol-2-yl)-2,5'-diphenyltetrazolium bromide (MTT), gallic acid (GA), 1,1'-diphenyl-2-picrylhydrazyl (DPPH), quercetin (QE), aluminium chloride (AlCl₃), dimethyl sulfoxide (DMSO) and HPLC grade methanol were purchased from Sigma-Aldrich St. Louis, Mo., USA. Other analytical grade solvents and chemicals were procured locally.

2.3. Cell culture and treatments

MCF-7 (breast cancer) and RKO (colon cancer) cell lines were obtained from American Type Culture Collection (ATCC) and cultured in a humidified incubator with 5% CO₂. The cells were cultured in the Roswell Park Memorial Institute (RPMI)-1640 and Dulbeccco’s Minimal Essential Medium (DMEM) cell culture media respectively, which were supplemented with 10% fetal bovine serum (FBS) and 1% penicillin–streptomycin solution to avoid any bacterial contamination. Both the cell lines were free from Mycoplasma contamination.

2.4. Total phenolic content

The total phenolic content of all methanolic extracts of different parts of T. articulata was determined by FCR. GA was used as a reference phenolic compound for the determination of phenolic content in different methanolic extracts. As determined in previous studies (de Oliveira et al., 2009), 1.0 ml of FCR was mixed with 1.0 ml of methanolic extract from different parts of the plant having concentration (1.0 mg/mL). After proper mixing for at least 5 min, add 3.0 ml of 2% sodium carbonate solution and vortex the glass tubes to ensure complete mixing. Keep the glass tubes containing the mixture in the dark at room temperature for 3 h after proper mixing. Record the absorbance at 760 nm of each solution using a spectrophotometer. The absorbance recorded were analyzed and expressed the results in milligrams of QE equivalent per gram dry weight (mg QE/g DW).

2.5. Total flavonoid content

The total flavonoid content of methanolic extracts of different parts of T. articulata was determined by using the AlCl₃ method (Eberle et al., 2018). Briefly, 2.0 ml of methanolic extract of different parts of T. articulata with concentration (1.0 mg/mL) were added to 2.0 ml of 10% AlCl₃ solution and vortex the solution to ensure complete mixing. After 10 min of incubation, record the absorbance of different extracts at 430 nm. Quercetin (0–40 μg/mL) was used as a reference for establishing standard curve (y = ax + b) and quantification of the flavonoid content of methanolic extracts from different parts of T. articulata. The concentration of total flavonoid content was expressed in milligrams of QE equivalent per gram dry weight (mg QE/g DW).

2.6. DPPH antioxidant assay

To determine the antioxidant activity of methanolic extracts of various parts of T. articulata, the DPPH assay was performed to estimate the scavenging ability of various extracts by quenching DPPH. As previously determined by Brand-Williams et al., in 1995 (Brand-Williams et al., 1995), the assay was performed in triplicates with slight modifications, and the mean absorbance was calculated and noted. Briefly, freshly prepared DPPH solution (0.3 mM) was prepared in 95% methanol, stored in an amber color bottle at 4–8 °C. All the T. articulata were dissolved in 95% methanol and make various concentrations (1000–0.976 μg/mL) of an extract as well as ascorbic acid (positive control) by applying serial dilution method. Add 500 μl of (0.3 mM) of DPPH working solution to each serial diluted 500 μl of extract as well as ascorbic acid as positive control under restricted light. Additionally, 500 μl of DPPH is mixed with 500 μl of 95% methanol as a control without extract or ascorbic acid. The mixtures of DPPH working solution and extract, ascorbic acid (positive control), or control are mixed well and incubated in dark for 30 min. The absorbance of different extracts, positive control and blank were measured by spectrophotometer at 517 nm after adjusting zero for 95% methanol. The change in coloration from dark blue to yellowish color of DPPH was recorded and percent inhibition of DPPH radical exhibited by extract samples and ascorbic acid as a positive control was calculated by using formula % radical scavenging activity or (% inhibition) = \((\frac{A_b - A_e}{A_b}) \times 100\)

A₀ is the absorbance of blank, Aₑ is the absorbance of extract or ascorbic acid (positive control)

2.7. Antibacterial activity of plant extract

The antibacterial activity of various extracts of T. articulata was performed by Agar well diffusion method (Ahmad and Beg, 2001; Ramesh et al., 2002). Briefly, 0.1 ml of bacterial inoculum (10⁷ colony forming units (CFU)/ml), was inoculated with a sterile cotton swab on plates containing Muller Hinton agar. 8.0 mm wells were made by punching into the solidified agar medium plate and seal the bottom of well with sterile melted agar. Add 100 μl extract (2.5 and 5 mg/mL) in each well separately, along with solvent blank
(95% methanol) and positive controls (gentamycin and ampicillin). Incubate plates overnight at 37 °C. The next day the antibacterial activity was analyzed by measuring the zone of inhibition of different concentrations against the test organism. The entire set of experiments was conducted in triplicates.

2.8. Cell viability assay

The proliferation of cells was analyzed by MTT assay as per the standard protocol (Rah et al., 2012). Briefly, MCF-7 and RKO cells were processed for trypsinization and plated at a density of 5 × 10^5 cells per well of 96-well plate. The cells seeded in triplicates were treated with varying concentrations of different extracts of T. articulata (100–10000 μg/ml) and control DMSO for 24 h, incubated in an incubator containing 5% CO2. Subsequently, cells were saturated with MTT dye (2.5 mg/ml) for 3 h at 37 °C. The crystals formed of formazan were solubilized in DMSO, mixed properly by vortex and the optical density was measured at 570 nm by multi-plate reader. The percentage of cell proliferation was analyzed as the percent cell viability of treated cells compared with the control of DMSO cells.

2.9. Statistical analysis

All the experiments were accomplished for at least three independent times. The latest version of software Graph Pad Prism was used for statistical analysis of all independent unbiased experiments. The results obtained were denoted as the mean of ± SEM. Entire results were calculated by using the Student’s unpaired t-test, wherein a p-value of less than 0.05 was reflected significant (* means p < 0.05, ** p < 0.01, and *** p < 0.001).

3. Results

3.1. Methanolic extracts of T. articulata exhibit promising antioxidant activity and possess abundant flavonoid and phenolic content

To evaluate the antioxidant potential of methanolic extracts of different parts of T. articulata, we accomplish the scavenging activity of DPPH radicals exhibited by methanolic extracts of different parts of T. articulata along with the standard compound ascorbic acid. As summarized in (Fig. 1a–d and Table 1) the higher concentrations of all methanolic extracts of T. articulata displays a promising scavenging activity by donating electrons to the purple-colored solution of DPPH, that results in decolorization of the purple color of DPPH to yellowish color, due to trapping of electrons donated by solution of DPPH, that results in decolorization of the purple color. The total flavonoid content of methanolic extract of dry leaves of T. articulata displays highest antioxidant activity, and have abundant total polyphenolic and flavonoid content; however, methanolic extract of dry leaves displays highest antioxidant activity and demonstrates that polyphenolic and flavonoid content, indicates promising biochemical activities among all extracts.

3.2. Methanolic extracts of T. articulata exhibits promising antibacterial activity

The antibacterial activity of all methanolic extracts of T. articulata was determined by using a well-known diffusion method. As summarized in Table 3, the methanolic extracts of different parts of T. articulata were significantly active against both Gram-positive and Gram-negative bacterial species. The highest antimicrobial activity was exhibited by methanolic extract of dry leaves of T. articulata (5 mg/ml) against both Gram-negative bacteria exhibit zone of inhibition (20.1 ± 0.30 mm, 19.9 ± 0.18 mm, 18.1 ± 0.18 mm against P. aeruginosa, K. pneumonia, E. coli) and Gram-positive bacteria (22.7 ± 0.23 mm, 25.3 ± 0.34 mm, 19.4 ± 0.12 mm against S. aureus, E. epidermidis, S. pneumonia) respectively.

3.3. Methanolic extracts of T. articulata exhibits antiproliferative effect on cancer cells

To evaluate the antiproliferative effect of methanolic extracts of different parts of T. articulata, cancer cells (MCF-7 and RKO cells) were cultured in RPMI-1640 medium and exposed to increasing (100–10000 μM) concentrations of methanolic extracts of T. articulata for 24 h. As confirmed (Fig. 3a and b), all the four methanolic extracts of T. articulata reduces the cell viability of both MCF-7 and RKO cells as the concentrations increase above 100 μM and the effect is significant above 200 μM concentrations of T. articulata. Using GraphPad Prism the IC_{50} value of all the methanolic extracts of T. articulata on MCF-7 cells are (fresh leaves-220 ± 5.231 μg/ml, dry leaves-219 ± 5.112 μg/ml, stem-220 ± 5.643 μg/ml, root-253 ± 5.231 μg/ml) and RKO cells are (fresh leaves-225 ± 2.39 μg/ml, dry leaves-220 ± 4.330 μg/ml, stem-266 ± 5.120 μg/ml, root-325 ± 6.213 μg/ml). Although the results reveal that all the extracts show promising antiproliferative activity against tumor cells, however, the methanolic extract of dry leaves exhibit maximum antiproliferative activity against both breast cancer (MCF-7) and colorectal cancer (RKO) cells.

4. Discussion

Recent advancements in alternative medicine and ethnopharmacological findings revealed that medicinal plants play an important role in the modern health care system. In recent past, conservation of medicinal plants and their unrelenting supply is part of future global medical and health strategy (Sher et al., 2010). T. articulata is a halophytic, fork medicinal plant and has been used against various skin diseases in Saudi Arabia from long back. Although some biological activities including antidiabetic,
antiepileptic, anti-hair fall as well as antilipidemic activities have been reported from the southern region of Morocco (Hebi and Eddouks, 2017; Hebi et al., 2017; Hebi et al., 2018), however, it is yet to be evaluated and elucidated the biological activities of *T. articulata* plant of Saudi Arabian region. Therefore, the present study is based on the comparative analysis of biological activities of methanolic extracts of different parts of *T. articulata*.

Owing to environmental and other oxidative stress, plants produce secondary metabolites that decrease the production of free radicals and helps in the protection of cellular damage due to oxidative stress (Kasote et al., 2015). These secondary metabolites are most commonly polyphenolic compounds including flavonoids. The polyphenolic compounds exhibit antioxidant potential by reducing the level of reactive oxygen species and prevents lipid peroxidation (Ghasemzadeh and Ghasemzadeh, 2011). Previous studies revealed that the presence of polyphenolic compounds in plant extracts have promising antioxidant activity to neutralize free radicals (Alara et al., 2019; Kumaran, 2006; Rahmani et al., 2017).

**Fig. 1.** (a–d) Antioxidant effect of methanolic extracts of *T. articulata* by DPPH radical scavenging assay. The data represent the mean value ± SE of 3 independent experiments.

*p < 0.05.

**Table 1**
The scavenging activity of DPPH radicals of methanolic extracts of different parts of *T. articulata*.

| Concentration (µg/mL) | T. articulata (Fresh Leaves) | T. articulata (Dry Leaves) | T. articulata (Stem) | T. articulata (Root) | Quercetin |
|-----------------------|------------------------------|----------------------------|----------------------|----------------------|-----------|
| 0.97                  | 23.2 ± 1.38                  | 27.4 ± 1.40                | 29.6 ± 1.41          | 90.4 ± 1.74          |
| 1.95                  | 32.9 ± 1.35                  | 59.7 ± 1.28                | 71.7 ± 1.98          | 94.0 ± 1.62          |
| 3.90                  | 63.0 ± 1.72                  | 86.3 ± 1.47                | 91.2 ± 1.72          | 94.8 ± 1.71          |
| 7.81                  | 85.0 ± 1.43                  | 94.5 ± 1.56                | 94.1 ± 1.36          | 96.2 ± 1.32          |
| 15.62                 | 95.0 ± 1.58                  | 94.7 ± 1.93                | 95.0 ± 1.39          | 96.3 ± 1.34          |
| 31.25                 | 99.6 ± 1.65                  | 95.9 ± 1.81                | 96.0 ± 1.32          | 96.4 ± 1.51          |
| IC₅₀                   | 49.08 ± 1.98                 | 53.00 ± 1.08               | 49.13 ± 1.46         | 8.17 ± 1.11          |

**Table 2**
Total polyphenolic, and flavonoid content of all the four methanolic extracts of *T. articulata* collected from Qassim region of Saudi Arabia. Values represent the mean value ± SE of 3 independent experiments.

|                      | T. articulata (Fresh Leaves) | T. articulata (Dry Leaves) | T. articulata (Stem) | T. articulata (Root) |
|----------------------|------------------------------|-----------------------------|----------------------|----------------------|
| Total phenolic content (mg GAE/g DW) | 137.12 ± 5.01                | 409.92 ± 6.03               | 141.75 ± 4.21        | 387.08 ± 5.93        |
| Total flavonoid content (mg QE/g DW) | 80.66 ± 3.54                 | 177.71 ± 3.76               | 60.66 ± 2.88         | 45.23 ± 2.13         |
Antimicrobial activities of methanolic extracts of T. articulata, have been reported to be effective against multidrug-resistant microorganisms, including bacteria such as Staphylococcus aureus, Pseudomonas aeruginosa, and Klebsiella pneumoniae. However, methanolic extract of dry leaves of T. articulata exhibits promising activity. In the recent past, a methanolic extract of Euphoria terracina was reported to have high efficacy on cancer cells and minimal toxicity on normal cells. Still, there is a scope for more drugs with a high content of bioflavonoids and phenolic compounds, methanolic extracts of Hippophae rhamnoides exhibited promising activity against Gram-positive S. aureus and B. subtilis (Jeong et al., 2010; Kumar et al., 2013). Consistent with previous reports, all the four methanolic extracts of T. articulata shows the significant antibacterial activity as revealed by the zone of inhibition against both Gram-positive and Gram-negative bacteria when compared to positive control ampicillin and gentamycin respectively. However, methanolic extract of dry leaves of T. articulata exhibits maximum antibacterial activity against both Gram-positive and Gram-negative bacteria with zone of inhibition (20.1 ± 0.30 mm, 19.9 ± 0.18 mm, 18.1 ± 0.18 mm against P. aeruginosa, K. pneumoniae, E. coli) and Gram-positive bacteria (22.7 ± 0.23 mm, 25.3 ± 0.34 mm, 19.4 ± 0.12 mm against S. aureus, S. epidermidis, S. pneumoniae) respectively. These results demonstrate that T. articulata could be used as promising antibacterial agents in the future.

Naturally occurring plant extracts and compounds are an important source of drugs against many diseases including cancer. Almost half of the FDA approved pharmaceutical drugs are either derived from plant source directly or from plant derivatives (Patridge et al., 2016). Still, there is a scope for more drugs with high efficacy on cancer cells and minimal toxicity on normal cells. In the recent past, a methanolic extract of Euphoria terracina was reported to have high efficacy on cancer cells and minimal toxicity on normal cells.

Table 3
Antimicrobial activities of methanolic extracts of T. articulata. Values represent the mean value ± SE of 3 independent experiments.

| T. articulata | Gram Negative Bacteria Inhibition zone (mm) | Standard | Gram Positive Bacteria Inhibition zone (mm) | Standard |
|---------------|--------------------------------------------|----------|-------------------------------------------|----------|
| Extracts      | P. aeruginosa | K. pneumonia | E. coli | Gentamycin | S. aureus | S. epidermidis | S. pneumonia | Ampicillin |
| Fresh Leaves  | 5 mg/mL       |              |         |           |          |            |             |           |
| 2.5 mg/mL     | 18.6 ± 0.44   | 17.7 ± 0.19  | 15.3 ± 0.35 | 21.3 ± 0.25 | 19.2 ± 0.44 | 19.2 ± 0.25 | 16.1 ± 0.35 | 29.3 ± 0.30 |
| Dry Leaves    | 5 mg/mL       |              |         |           |          |            |             |           |
| 2.5 mg/mL     | 15.3 ± 0.35   | 11.3 ± 0.58  | 12.0 ± 0.19 | 16.0 ± 0.44 | 16.2 ± 0.19 | 11.9 ± 0.19 |           |           |
| Stem          | 5 mg/mL       |              |         |           |          |            |             |           |
| 2.5 mg/mL     | 20.1 ± 0.30   | 19.9 ± 0.18  | 16.1 ± 0.18 | 22.7 ± 0.23 | 25.3 ± 0.34 | 19.4 ± 0.12 |           |           |
| Root          | 5 mg/mL       |              |         |           |          |            |             |           |
| 2.5 mg/mL     | 15.9 ± 0.30   | 14.7 ± 0.37  | 14.7 ± 0.44 | 21.7 ± 0.21 | 20.2 ± 0.22 | 22.1 ± 0.34 | 17.2 ± 0.18 | 28.1 ± 0.40 |
|               | 16.2 ± 0.16   | 14.7 ± 0.22  | 13.8 ± 0.20 | 16.9 ± 0.23 | 17.3 ± 0.44 | 12.1 ± 0.19 |           |           |
exhibits a significant antiproliferative effect on hepatocellular carcinoma cell line (HepG2) (El Manawaty et al., 2013). Additionally, natural compounds and their derivatives isolated from medicinal plant extracts have shown promising antioxidant activities in vitro and preclinical studies (Chanda et al., 2012; Rah et al., 2015a; Zilla et al., 2014). Consistent with previous results, our findings revealed that T. articulata methanolic extracts display strong antiproliferative effect by reducing the cell viability of MCF-7 (breast cancer) and RKO (colorectal cancer) cells significantly; however, the most promising effect was exerted by methanolic extract of dry leaves of T. articulata with IC₅₀ values of 219 ± 5.112 μg/ml and 220 ± 4.330 μg/ml against MCF-7, and RKO cancer cells, respectively. These results indicate that T. articulata extracts exhibit a promising antiproliferative effects on cancer cells.

5. Conclusion

T. articulata is one of the most abundant wild plants growing in the deserts of Saudi Arabia. Our results demonstrated for the first time the biological activities of T. articulata and showed promising antioxidant activity, which was strongly supported by total phenolic and flavonoid content. The antimicrobial activity was also exhibited by all the methanolic extracts against both Gram-positive and Gram-negative bacteria significantly. Furthermore, all the methanolic extracts exhibit antiproliferative activity in MCF-7 (breast cancer) and RKO (colorectal cancer). In summary, these findings provide evidence that T. articulata has promising biological activities and can be used for many pharmaceutical activities in the future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors would like to thank the Research and Development Office at the ministry of education in Saudi Arabia for their partial support to study potential bioactivities of natural products.

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