Int. J. Morphol.,
42(2):362-367, 2024.

Phytochemical Screening and *in vitro* Anticancer Activity of Some Medicinal Plants Grown in the Kingdom of Saudi Arabia

Cribado Fitoquímico y Actividad Anticancerígena *in vitro* de Algunas Plantas Medicinales Cultivadas en el Reino de Arabia Saudita

Usama A. Mahalel[1,2]; Ibrahim B. Abdel-Farid[1,2]; Mohamed M. Rowezak[1]; Sabry A. El-Naggar[3]; Karim S. El-Said[4]; Diaa Massoud[1,5] & Arafa I. Hamed[2]

MAHALEL, U. A.; ABDEL-FARID, I. B.; ROWEZAK, M. M.; EL-NAGGAR, S. A.; EL-SAID, K. S.; MASSOUD, D. & HAMED, A. I. Phytochemical screening and *in vitro* anticancer activity of some medicinal plants grown in the Kingdom of Saudi Arabia. *Int. J. Morphol., 42(2)*:362-367, 2024.

SUMMARY: This study evaluated the phytochemical screening, antioxidant capacity, and *in vitro* anticancer activities of four plants namely, *Gypsophila capillaris*, *Anabasis lachnantha*, *Haloxylon salicornicum*, and *Horwoodia dicksoniae* which belong to four different families: *Caryophyllaceae, Amaranthaceae, Chenopodiaceae, Brassicaceae*, respectively. The total phenolics, anthocyanins, saponins, total antioxidant capacity (TAC), and DPPH assays were determined by spectrophotometer. *In vitro* anticancer activity was assessed using two human cancer cell lines; hepatocellular carcinoma (HepG-2) and breast adenocarcinoma (MCF-7) to estimate the inhibition concentration 50 % (IC_{50}). The results showed that *H. dicksoniae* has the highest concentrations of phenolics and saponins, while *H. salicornicum* has the highest DPPH. The highest concentration of TAC was found in *G. capillaries.* Among the tested extracts, *G. capillaries* and *H. salicornicum* have the potential activity against MCF-7 and HepG-2 cell lines *in vitro*. The content of polyphenols in *G. capillaries* was profiled by high-performance liquid chromatography (HPLC). The highest concentration among the phenolic compounds was chlorogenic (60.8 µg/ml) while the highest concentration among the flavonoid compounds was hesperidin (1444.92 µg/ml). In summary, *G. capillaries* and *H. salicornicum* extracts have potent anticancer activity against HepG-2 and MCF-7 cell lines.

KEY WORDS: Metabolomic screening, Antioxidant; Anticancer; HepG-2, MCF-7.

INTRODUCTION

Natural products showed several medicinal applications in different countries such as Egypt, Greece, China, and India (Hammond *et al*., 1997). A high percentage of the world population (80 %) relies on natural products as medicines to save their health needs (Bodeker & Kronenberg, 2002). Saudi Arabia's flora considers one of the most important examples of flora diversity in the world (Mandaville, 2013). The area is interesting for the probability of containment of some chemicals and the presence of compounds important by value therapeutic may help in the treatment against tumors or mitigation of the toxic effects of chemotherapy and radiation (Sher & Aldosari, 2012). In recent decades, it has been discovered several natural chemicals extracted from medicinal plants as anti-cancer compounds, such as taxol and vincristine, which are used medically around the world. In addition, several promising compounds may help alleviate the side effects of conventional treatments for tumors. Cancer cells are highly heterogeneous, and such heterogeneity gives the tumor an advantage to survive under drug treatments and developed resistance to the chemotherapy agent. Besides that, the chemotherapy treatment for cancer patients causes severe side effects including nephrotoxicity, electrolyte disturbances, myelosuppression, neurotoxicity, anaphylactic reactions, kidney damage, and hepatotoxicity (Srivastava *et al*., 2019).

[1] Biology Department, College of Science, Jouf University, Kingdom of Saudi Arabia.
[2] Botany Department, Faculty of Science, Aswan University, Aswan 81528, Egypt.
[3] Zoology Department, Faculty of Science, Tanta University, Tanta 3111, Egypt.
[4] Biochemistry Division, Chemistry Department, Faculty of Science, Tanta University, Tanta 3111, Egypt.
[5] Zoology Department, Faculty of Science, Fayoum University, Egypt.

Received: 2023-11-14 Accepted: 2023-12-24

Over the last few years, complementary and alternative medicine (CAM) has been used for cancer patients in different countries. The pre-clinical and clinical studies have shown that when CAM combined with chemotherapy can provide effective for cancer patients. CAM has demonstrated potential benefits in terms of improving the sensitivity of chemotherapy drugs and lowering the complications and adverse effects related to chemotherapy treatments (Mukherjee *et al*., 2001). For instance, curcumin, ginseng, ginger, and garlic have been found to decrease cancer progression and mitigate chemotherapy-induced complications (Vemuri *et al*., 2017).

Gypsophila capillaris (Forssk) C. Chr. is a glabrous, annual to perennial medicinal plant that belongs to family, Caryophyllaceae. This plant has been found to grow in the arid region of southwest Asia and recorded in Saudi Arabia and other countries as well. Studies on *G. capillaris* showed that it contains several chemical compounds such as triterpene saponins, sterols, flavonoids. Recently, it has been shown that the gypsogenic acid isolated from *G. trichotoma* roots showed cytotoxic activity *in vitro* (Krasteva *et al*., 2014). Generally, *Gypsophila* species have been described as anti-inflammatory, anti-angiogenic, anti-viral, antioxidant, antibacterial, anticancer agents, and immunomodulatory agents (Laszczyk, 2009). *Anabasis lachnantha* (Aellen & Rech. f.) is belonging to the family Amaranthaceae and is distributed in different countries such as South Iraq, Kuwait, and Saudi Arabia. (González *et al*., 2018) support the potential of ethanolic extract of *Gaillardia megapotamica* as an anticancer agent. *Ruta chalepensis* extract has a noticeable effect against HEP-G2 and Vero cells with an IC50 of 1.79 µg/mL and 522.08 µg/mL, respectively (Elizondo-Luévano *et al*., 2022). Till now, and based on our search, no more literature is available about the phytochemistry of *A. lachnantha* and there is insufficient data about its pharmacological properties and biological activity.

Haloxylon salicornicum (Moq.) Bunge ex Bioss. belongs to the family Chenopodiaceae. According to recent studies, the aerial parts of this plant are rich in chemical components; therefore, it is considered a good source of nutrients for human and animal feeding. The phytochemical analysis of the aerial parts of *H. salicornicum* showed the presence of flavonoids, tannins, saponins, volatile oils, and alkaloids. *H. salicornicum* was found to have antidiabetic, and antimicrobial activity (Awaad *et al*., 2001).

Horwoodia dicksoniae Turrill belongs to the family Brassicaceae. The ethanol extract of *H. dicksoniae* showed antitumor activity against Hep-G2 and MCF-7 cancer cell lines *in vitro*. In this study, the metabolic profile, antioxidant activity, and the anticancer activity *in vitro* against Hep-G2 and MCF-7 cell lines were determined on the methanol extract of four plant species namely, *G. capillaris*, *A. lachnantha*, *H. salicornicum*, and *H. dicksoniae.*

MATERIAL AND METHOD

Plants were collected from the deserts, around Sakakah city, the Aljouf region, KSA. The plant materials were carefully removed from the soil.

Preparation of plant extracts. The plant's aerial parts (stem, leaves, and fruits) were separated, and dried in the shade, and then processed into a fine powder using an electric grinder. The powder is kept in the container until it is used in subsequent tests. 200 g of powders were extracted using MeOH 80 % by maceration until exhaustion. The alcoholic extract was filtered and concentrated using a rotary evaporator at a temperature no higher than 45 °C under decreased pressure. The crude extract was used to profile the polyphenols content by HPLC and antioxidant activity by spectrophotometer.

Determination of total phenolic. Using the Folin-Ciocalteau reagent and gallic acid as a standard, the total content of phenolics in the extracts was measured according to Singleton *et al.* (1999).

Determination of total saponins. Saponin content was assessed using vanillin solution and reported in (mg) as saponin equivalents per gram of extract.

Determination of anthocyanins. The anthocyanins content was evaluated according to the modified method of (Padmavati *et al*., 1997). The anthocyanin concentration (µmole/g) = ([A530 - 0.33 x A657]/31.6) X (volume [mL]/ weight [g]).

Determination total antioxidant capacity (TAC). Free radical scavenging activity was also determined by using the method of (Blois, 1958).

Plant extracts and doxorubicin preparation. Each methanol extract was made at different doses of 6.25, 12.5, 25, 50 and 100 µg/ml dissolved in DMSO (1 %). As a positive control, doxorubicin (Dox.) was likewise produced at the same quantities and dissolved in DMSO (1 %).

Cancer cell lines and *in vitro* studies. Human breast adenocarcinoma (MCF-7), hepatocellular carcinoma (HepG-2 were obtained from the American type of culture

collection. The cells were grown at 37 °C with 5 % CO_2 in RPMI-1640 media supplemented with 10 % fetal bovine serum (FBS), 2mL glutamine, 100 units/ml penicillin, and 100 units/ml streptomycin.

Determination of inhibition concentration 50 % (IC_{50}) for extracts. The MCF-7 and HepG-2 cell lines were used to examine the plant extracts' cytotoxicity using the sulforhodamine B (SRB) assay according to (Vichai & Kirtikara, 2006). Following a 72-hour exposure to the tested extracts, cells were fixed with 10 % trichloroacetic acid (TCA) for 1 hour at 4 °C. After washing, cells were exposed to 0.4 % SRB solution for 10 min in dark place. Tris-HCl was used to dissolve the SRB-stained cells after dried overnight, and color intensity was assessed at 570 nm.

Detection of phenolics and flavonoids by HPLC. The phenolic compounds analysis was done utilizing a Perkin-Elmer HPLC system (USA) equipped with a binary LC-250 gradient pump and LC-290 UV/Vis detector. Samples were separated on C18 Hypersil ODS column (100 x 4.6 mm). Absorption at 280 and 330 nm was used to monitor phenolic chemicals. By comparing the relative retention times of each sample's individual phenolic compounds to those of the reference mixture chromatogram, the compounds' individual identities were determined.

Statistical analysis. One-way analysis of variance (ANOVA) through the MINITAB program (Ver. 12.21) and sigma plot program were used to test the significance difference of the generated data.

RESULTS

Metabolomic profiling. Phytochemical analysis data of the studied plants are illustrated in Figure 1A, B, C and D. Total phenolic concentrations as shown in Table IA, were high in *H. dicksoniae* and *H. salicornicum* 0.33 and 0.31 mg/g extract, respectively. *A. lachnantha* showed moderate total phenolic concentration (0.2 mg /g extract) in comparison with all tested plants. The lowest phenolic concentration was recorded in *G. capillaries*. All tested plants had high content of saponins especially *H. dicksoniae* (107.3 mg/g extract), however, *A. lachnantha* recorded the lowest concentration (25.9 mg/g extract). The data showed also that a big amount of anthocyanin content (1.27 µmole/g extract) was obtained in *A. lachnantha*, followed by *H. dicksoniae* (0.48 µmole/g extract) as shown in Figure 1C.

Total antioxidant capacity (TAC). *G. capillaris*, *H. dicksoniae* and *H. salicornicum* recorded high values of TAC (151, 149.25 and 131.65 µg ascorbic acid equivalent/ g extract), respectively (Fig. 1D). Data variations of TAC content in all studied samples were significant ($p \leq 0.05$).

Cytotoxicity of different extracts on HepG-2 and MCF-7 cell lines. Compared with the positive control, Dox. (IC50: 3.07 µg/ml), the IC_{50} of *G. capillaris*, *A. lachnantha*, *H. salicornicum* and *H. dicksoniae* on HepG-2 cell lines were 32.12, 77.72, 23.72 and 74.13 µg/ml, respectively (Table I and Fig. 2A). As compared with the Dox. (IC_{50}: 2.41 µg/ml), the IC_{50} of *G. capillaris*, *A. lachnantha*, *H. salicornicum*, and *H. dicksoniae* on MCF-7 were 3.5, 68.76, 36.66, and 97.08 µg/ml respectively (Table I and Fig. 2B).

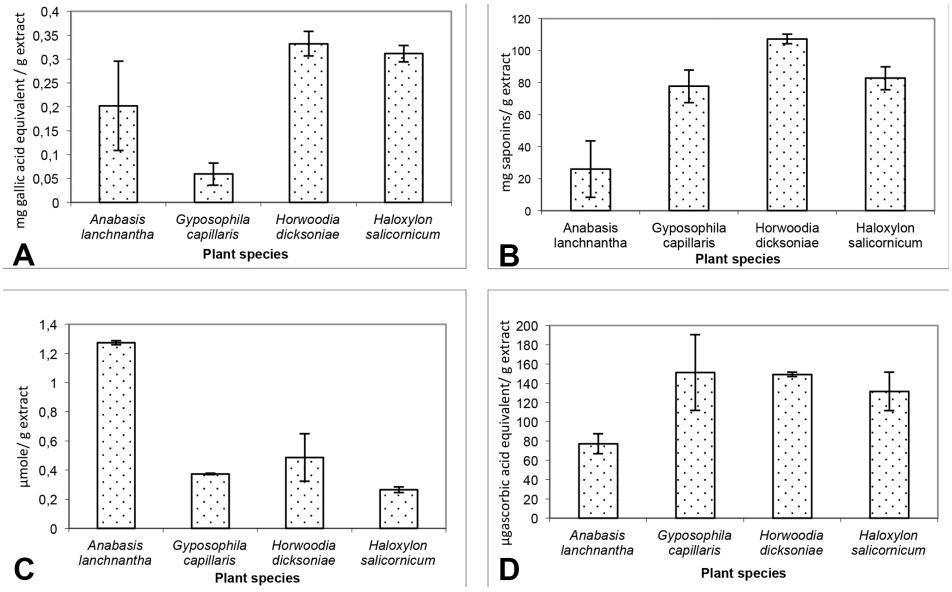

Fig. 1. Phytochemical analysis of total phenolic (A), saponins (B), anthocyanin (C) and TAC (D) in aerial parts of the plants under the study.

Table I. The inhibition concentration 50 % (IC_{50}) of plant extracts versus the positive control, doxorubicin on Hep-G2 and MCF-7 cell lines *in vitro* after 72 h post-treatments.

Plant species	Extracted from	IC_{50} (HepG-2) (µg/ml)	IC_{50}(MCF-7) (µg/ml)
Gyposophila capillaris	Aerial parts	32.12 (active)	3.5 (active)
Anabasis lanchnantha	Aerial parts	77.72 (inactive)	68.76 (inactive)
Haloxylon salicornicum	Aerial parts	23.72 (active)	36.66 (moderately active)
Horwoodia dicksoniae	Aerial parts	74.13 (inactive)	97.08 (inactive)
Dox.		3.07	2.41

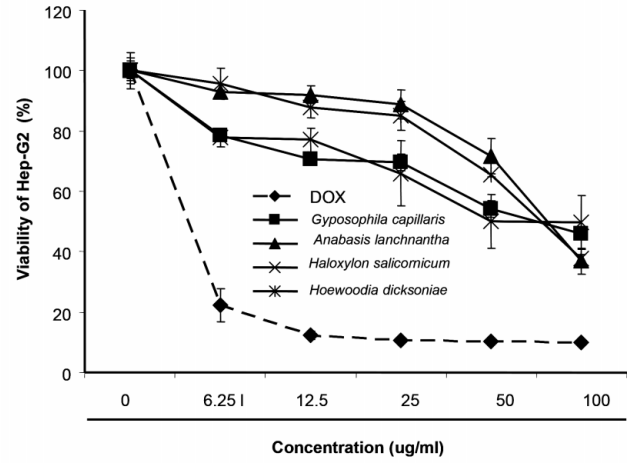

Fig. 2. A. Show the viability percentage (%) of different plant extracts against the HepG-2 cell line. Using 96-well plates, the HepG-2 cell line was cultured in complete RPMI and treated with different concentrations of the methanolic plant extracts. The tumor cell line then incubated for 72 h. the chemotherapeutic drug, doxorubicin (Dox.) was used as a positive control. The treated cells were used to determine the viability of the tumor cells after 72 h by SRB assay. The experiment was repeated twice. B. Show the viability percentage (%) of different plant extracts against the MCF-7 cell line. Using 96-well plates, the MCF-7 cell line was cultured in complete RPMI and treated with different concentrations of the methanol plant extracts. The tumor cell line then incubated for 72 h. the chemotherapeutic drug, doxorubicin (Dox.) was used as a positive control. The treated cells were used to determine the viability of the tumor cells after 72 h by SRB assay. The experiment was repeated twice.

HPLC analysis for polyphenols of *G. capillaris*. The *G. capillaries* methanol extract showed the highest cytotoxic effect against MCF-7 cell lines. HPLC was used to determine the major phenolic and flavonoid compounds in this extract. The major phenolic compounds were chlorogenic, e-vanillic, catechol, and salicylic acid. Where pyrogallol, benzoic, P-OH-benzoic, cinnamic and ellagic acids are represented with moderate concentrations (Table IIA and Fig. 3). Moreover, two flavonoids, namely hesperidin and rutin were dominant and identified in high amounts in the extract. While the narginin and rosmarinic acid represented with moderate concentrations (Table IIB).

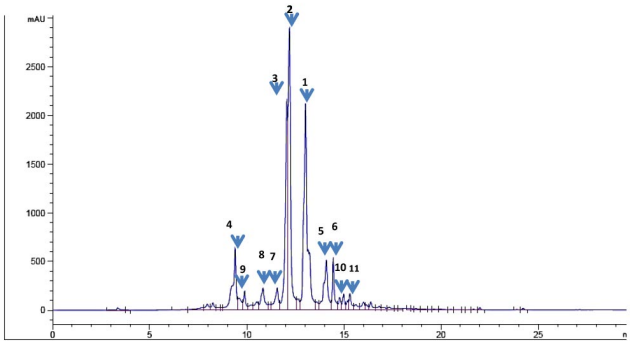

Fig. 3. HPLC data peaks of MeOH extracts showing the phenolic compounds (µg/ml) from Gyposophila capillaris aerial parts.

Table II. A. Assignment of the HPLC data peaks of phenolic of MeOH extracts from the aerial parts of *G. capillaris*.

No.	Phenolic	Conc. µ g/ml
1.	Chlorogenic	60.84
2.	e-vanillic	50.36
3.	Catechol	42.63
4.	Saylcilic	39.51
5.	Pyrogallol	23.96
6.	Benzoic	20.81
7.	P-OH-benzoic	20.33
8.	Cinnamic	16.08
9.	Ellagic	15.4
10.	3-OH- Tyrosol	6.66
11.	Epicatechein	5.65

Table II. B. Assignment of the HPLC data peaks of flavonoids of MeOH extracts from aerial parts.

No.	Flavonoids	Conc. µ g/ml
1	Hesperidin	1444.92
2	Rutin	282.72
3	Narginin	26.97
4	Rosmarinic	13.2
5	Quercetin	4.35
6	Kampherol	4.1
7	Hispertin	4.09
8	Aspegenin	2.68
9	Narengenin	0.92
18	7-OH flavone	0.86
11	Quercetrin	----

DISCUSSION

Plant-derived compounds have been used as anticancer agents in a clinical setting such as paclitaxel and vincristine (Seca & Pinto, 2018). Sixty percent of anticancer drugs presently in use come in some way from natural sources (Cragg *et al*., 2009). In this study, we have explored four methanol aerial parts extracts from selected medicinal plants, i.e., *Gypsophila capillaris*, *Anabasis lachnantha*, *Haloxylon salicornicum* and *Horwoodia dicksoniae* for their cytotoxic activity on the human HepG-2 and MCF-7 cell lines. Before testing their ability to kill the tumor cells *in vitro*, we determined the phenolics, saponins, anthocyanins, and TAC concentrations.

Based on the metabolomics analysis, the results showed that *H. salicornicum* and *H. dicksoniae* have high contents of phenolics, saponins and TAC and low content of anthocyanin. Furthermore, a high content of anthocyanin was found in *A. lachnantha*., *H. dicksoniae* and *H. salicornicum*. Data variations of phenolics, saponins, anthocyanin and TCA content of the studied plants were significant ($p \leq 0.05$).

The data showed that there is a direct positive correlation ($p \leq 0.05$) between antioxidant activities and increasing in the plants content of bioactive components such as phenolics and saponins. These results concurred with several research that claimed a linear relationship existed between the total amount of phenolics and the antioxidant capacity (Sammar *et al*., 2019), whereas another study reported no correlation (Yu *et al*., 2002).

Referring to the HPLC analysis for *G. capillaris*, the high antioxidant activity of this plant is referred to as the high content of hesperidin, rutin and narginin. This data is in agreement with the finding of Yoo *et al*. (2004). According to Tai *et al*. (2012), chlorogenic acid and vanillic acid as polyphenol compounds has distinctive antioxidant activity, and this explain the high antioxidant activity for *G. capillaris* that it had a high content of chlorogenic, e-vanillic acids and Catechol.

In our cytotoxic screening by SRB, In order to find and create possible anticancer natural chemicals, we utilized the American National Cancer Institute's criteria to classify a crude extract as promising for further study based on the IC50 values lower than 30 g/mL (de Mesquita *et al*., 2009). The IC50 of the four extracts varied in their cytotoxicity on HepG-2 and MCF-7 cell lines. *H. salicornicum* was considered an active extract against HepG-2, *G. capillaris* extract was moderately active, while *A. lachnantha* and *H. dicksoniae* were inactive against HepG-2 cell lines.

Using the MCF-7 cell line, the SRB assay showed the IC50 of *G. capillaries* was 3.5 µg/ml which consider a very strong active extract, *H. salicornicum* IC50 was 36.66 µg/ml which consider a moderately active extract while *A. lachnantha*, and *H. dicksoniae* were 68.76, and 97.08 µg/ml, respectively, which indicated that those two extracts were inactive against MCF-7 cells. Our results were in disagreement with a previous study which showed that *H. dicksoniae* extract have high cytotoxic activity against HepG-2 and MCF-7 cell lines (Fawzy *et al*., 2011).

Since the phytochemical evaluation indicated the *G. capillaries* have a potent TAC. One of the main classes of chemicals that serve as antioxidants or free radical terminators are plant phenolics. The redox characteristics of the phenolic compounds were thought to be responsible for their antioxidant actions (Cai *et al*., 2004). To assess the most powerful portion of the active plants, more research is also being done.

ACKNOWLEDGMENTS. The authors extend their appreciation to the deanship of Scientific Research at Jouf University for funding this work through research grant no (DSR2020-04-459).

MAHALEL, U. A.; ABDEL-FARID, I. B.; ROWEZAK, M. M.; EL-NAGGAR, S. A.; EL-SAID, K. S.; MASSOUD, D. & HAMED, A. I Cribado fitoquímico y actividad anticancerígena *in vitro* de algunas plantas medicinales cultivadas en el Reino de Arabia Saudita. *Int. J. Morphol., 42(2)*:362-367, 2024.

RESUMEN: Este estudio evaluó la detección fitoquímica, la capacidad antioxidante y las actividades anticancerígenas *in vitro* de cuatro plantas, *Gypsophila capillaris*, *Anabasis lachnantha*, *Haloxylon salicornicum* y *Horwoodia dicksoniae*, que pertenecen a cuatro familias diferentes: Caryophyllaceae, Amaranthaceae, Chenopodiaceae y Brassicaceae, respectivamente. Los ensayos de fenólicos totales, antocianinas, saponinas, capacidad antioxidante total (TAC) y DPPH se determinaron mediante espectrofotómetro. La actividad anticancerígena *in vitro* se evaluó utilizando dos líneas celulares de cáncer humano; carcinoma hepatocelular (HepG-2) y adenocarcinoma de mama (MCF-7) para estimar la concentración de inhibición del 50 % (IC50). Los resultados indicaron que *H. dicksoniae* tiene las concentraciones más altas de fenólicos y saponinas, mientras que *H. salicornicum* tiene el DPPH más alto. La mayor concentración de TAC se encontró en *G. capillaries*. Entre los extractos probados, *G. capillaries* y *H. salicornicum* tienen actividad potencial contra líneas celulares MCF-7 y HepG-2 *in vitro*. El contenido de polifenoles en *G. capillaries* se perfiló mediante cromatografía líquida de alta resolución (HPLC). La concentración más alta entre los compuestos fenólicos fue clorogénica (60,8 µg/ml), mientras que la concentración más alta entre los compuestos flavonoides fue la hesperidina (1444,92 µg/ml). En resumen, los extractos de *Gypsophila capillaris* y *H. salicornicum* tienen una potente actividad anticancerígena contra las líneas celulares HepG-2 y MCF-7.

PALABRAS CLAVE: Screening metabolómico, Antioxidante; Anticáncer; HepG-2, MCF-7.

REFERENCES

Awaad, A. S.; Sokkar, N. M. & Soliman, G. M. Flavonoids and coumarins from hammada elegans [Bunge] Botsch and its biological activity. *Bull. Fac. Pharm. Cairo Univ., 39(1)*:121-7, 2001.

Blois, M. S. Antioxidant determinations by the use of a stable free radical. *Nature, 181(4617)*:1199-200, 1958.

Bodeker, G. & Kronenberg, F. A public health agenda for traditional, complementary, and alternative medicine. *Am. J. Public Health, 92(10)*:1582-91, 2002.

Cai, Y.; Luo, Q.; Sun, M. & Corke, H. Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer. *Life Sci., 74(17)*:2157-84, 2004.

Cragg, G. M.; Grothaus, P. G. & Newman, D. J. Impact of natural products on developing new anti-cancer agents. *Chem. Rev., 109(7)*:3012-43, 2009.

de Mesquita, M. L.; de Paula, J. E.; Pessoa, C.; de Moraes, M. O.; Costa-Lotufo, L. V.; Grougnet, R.; Michel, S.; Tillequin, F. & Espindola, L. S. Cytotoxic activity of Brazilian Cerrado plants used in traditional medicine against cancer cell lines. *J. Ethnopharmacol., 123(3)*:439-45, 2009.

Elizondo-Luévano, J. H.; Gomez-Flores, R.; Verde-Star, M. J.; Tamez-Guerra, P.; Romo-Sáenz, C. I.; Chávez-Montes, A.; Rodríguez-Garza, N. E. & Quintanilla-Licea, R. *In vitro* cytotoxic activity of methanol extracts of selected medicinal plants traditionally used in Mexico against human hepatocellular carcinoma. *Plants (Basel), 11(21)*:2862, 2022.

Fawzy, G. A.; Al Taweel, A. M.; Abdelbaky, N. A. & Marzouk, M. S. Biologically active flavonoid glycosides from *Horwoodia dicksoniae* Turrill. *Planta Med., 77*:PL25, 2011.

González, M. L.; Joray, M. B.; Laiolo, J.; Crespo, M. I.; Palacios, S. M.; Ruiz, G. M. & Carpinella, M. C. Cytotoxic activity of extracts from plants of central Argentina on sensitive and multidrug-resistant leukemia cells: isolation of an active principle from *Gaillardia megapotamica*. *Evid. Based Complement. Alternat. Med., 2018*:9185935, 2018.

Hammond, J. A.; Fielding, D. & Bishop, S. C. Prospects for plant anthelmintics in tropical veterinary medicine. *Vet. Res. Commun., 21(3)*:213-28, 1997.

Krasteva, I.; Inglis, N.; Sacchini, F.; Nicholas, R.; Ayling, R.; Churchward, C.; March, J.; Lainson, A.; Mclean, K.; Hughes, V.; *et al*. Proteomic characterisation of two strains of *Mycoplasma mycoides* subsp. mycoides of differing pathogenicity. *J. Proteom. Bioinform., S13*, 001, 2014.

Laszczyk, M. N. Pentacyclic triterpenes of the lupane, oleanane and ursane group as tools in cancer therapy. *Planta Med., 75(15)*:1549-60, 2009.

Mandaville, J. P. Flora of Eastern Saudi Arabia. Hoboken, Routledge, 2013.

Mukherjee, A. K.; Basu, S.; Sarkar, N. & Ghosh, A. C. Advances in cancer therapy with plant based natural products. *Curr. Med. Chem., 8(12)*:1467-86, 2001.

Padmavati, M.; Sakthivel, N.; Thara, K. & Reddy, A. R. Differential sensitivity of rice pathogens to growth inhibition by flavonoids. *Phytochemistry, 46(3)*:499-502, 1997.

Sammar, M.; Abu-Farich, B.; Rayan, I.; Falah, M. & Rayan, A. Correlation between cytotoxicity in cancer cells and free radical-scavenging activity: *In vitro* evaluation of 57 medicinal and edible plant extracts. *Oncol. Lett., 18(6)*:6563-71, 2019.

Seca, A. M. & Pinto, D. C. Plant secondary metabolites as anticancer agents: successes in clinical trials and therapeutic application. *Int. J. Mol. Sci., 19(1)*:263, 2018.

Sher, H. & Aldosari, A. Overview on the ecological and geographical appraisal of important medicinal and aromatic plants: An endangered component in the flora of Saudi Arabia. *Sci. Res. Essays, 7(16)*:1639-46, 2012.

Srivastava, N.; Majumder, A. & Rastogi, S. Adverse drug reactions of anti-cancer drugs and its management: a review. *Int. J. Adv. Res. Med. Chem., 1(1)*:19-27, 2019.

Tai, A.; Sawano, T. & Ito, H. Antioxidative properties of vanillic acid esters in multiple antioxidant assays. *Biosci. Biotechnol. Biochem., 76(2)*:314-8, 2012.

Vemuri, S. K.; Banala, R. R.; Subbaiah, G.; Srivastava, S. K.; Reddy, A. G. & Malarvili, T. Anti-cancer potential of a mix of natural extracts of turmeric, ginger and garlic: A cell-based study. *Egypt. J. Basic Appl. Sci., 4(4)*:332-44, 2017.

Yoo, K. M.; Lee, K. W.; Park, J. B.; Lee, H. J. & Hwang, I. K. Variation in major antioxidants and total antioxidant activity of Yuzu (Citrus junos Sieb ex Tanaka) during maturation and between cultivars. *J. Agric. Food Chem., 52(19)*:5907-13, 2004.

Yu, L.; Haley, S.; Perret, J.; Harris, M.; Wilson, J. & Qian, M. Free radical scavenging properties of wheat extracts. *J. Agric. Food Chem., 50(6)*:1619-24, 2002.

Corresponding author:
Diaa Massoud
Biology Department
College of Science
Jouf University
SAUDI ARABIA

E-mail: dfm00@fayoum.edu.eg