Chemistry International 9(2) (2023) 61-67

International Scientific Organization
http://iscientific.org/
Chemistry International
www.bosaljournals.com/chemint/

Antimicrobial and antioxidant properties of water and methanolic extract of *G. glabra* native to Pakistan

Muhammad Khalid Saeed, Naseem Zahra*, Asma Saeed, Khurram Shahzad, Shaista Nawaz, Syed Hussain Imam Abidi and Quratulain Syed

Food and Biotechnology Research Centre, PCSIR Laboratories Complex, Lahore, Pakistan
*Corresponding author's E. mail: drnaseemzahra@gmail.com

A R T I C L E   I N F O

Article type:
Research article
Article history:
Received December 2022
Accepted February 2023
April 2023 Issue
Keywords:
Glycyrrhiza glabra
Antibacterial
Antioxidant
IC_{50}

A B S T R A C T

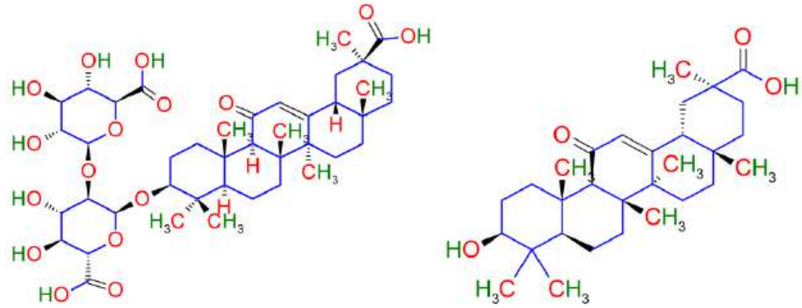
The licorice root extracts have a variety of therapeutic benefits, including treatment of throat infections, tuberculosis, respiratory disorders, liver diseases, cardiovascular, anticancer, hepatoprotective, antibacterial, anti-inflammatory, antioxidant and immunodeficiency. The current study entails the antibacterial and antioxidant activities of licorice in water and methanolic extracts. The antimicrobial activity was assessed against *Staphylococcus aureus, Escherichia coli, Staphylococcus sciuri, Pseudomonas, Bacillus subtilis and Salmonella typhi Aerugenosa*. This was done by disc diffusion methods and the results revealed that methanolic extract was potentially more effective that exhibited good inhibitory action on *E. coli* (inhibitory zone 19±0.05 mm) and *S. sciuri* (inhibitory zone 17±0.04 mm) than water extract against the tested bacterial strains at 0.5 mg/ml concentration. The results of antioxidant activity showed that methanolic extract exhibited potent antioxidant activity (% Inhibition 65.2±2.3) with an IC_{50} of 192.51±3.30µg/mL in the 2,2-diphenyl-1-picrylhydrazyl assay, while water extract exhibiting (% Inhibition 53.6±2.1) with a value of IC_{50} 235.51±4.10 µg/mL at concentration 0.5 mg/ml. This study concludes that the tested licorice extracts have remedial prospective and may be suggested for use as an antibacterial agent and natural antioxidant in the food industry.

Capsule Summary: The antibacterial and antioxidant activities of licorice in water and methanolic extracts were evaluated. The extract showed promising activity against *Staphylococcus aureus, Escherichia coli, Staphylococcus sciuri, Pseudomonas, Bacillus subtilis and Salmonella typhi Aerugenosa* along with potential antioxidant activity.

Cite This Article As: M.K. Saeed, N. Zahra, A. Saeed, K. Shahzad, S. Nawaz, H.I. Abidi and Q. Syed. Antimicrobial and antioxidant properties of water and methanolic extract of *G. glabra* native to Pakistan. Chemistry International 9(2) (2023) 61-67.
https://doi.org/10.5281/zenodo.8117614

INTRODUCTION

Consumers are increasingly interested in natural plant products, owing to a widespread belief that natural components are safe. Since the dawn of human civilization, several plants have been commonly employed as best source of medicinal purposes. The need for herbal medications is steadily growing over time. These herbs have various functional qualities and they are high in natural bioactive constituents. When these components are present in meals, they reduce the risk of illness and humans use these plants extracts as healthful dietary supplements (Dogan et al., 2018).



Glycyrrhizin (a) Glycyrrhetinic acid (b)

Fig. 1: The structure major compound of *Glycyrrhiza glabra*

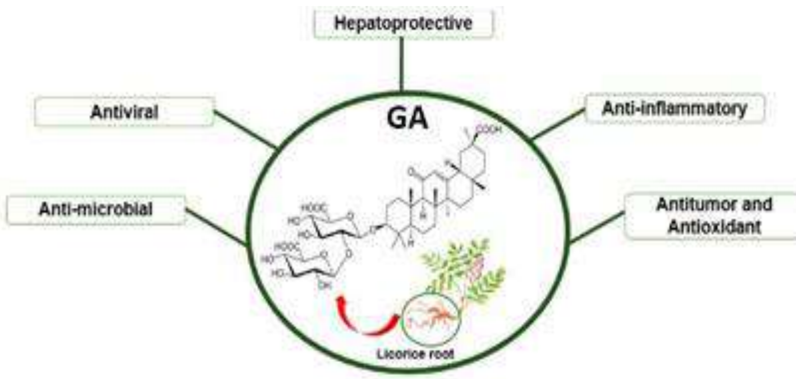


Fig. 2: Principal pharmacological activities of GA (Nascimento et al., 2022)

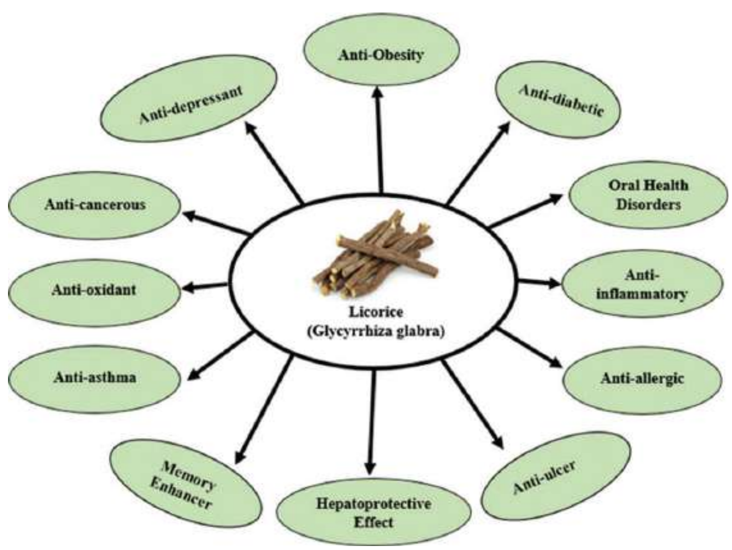


Fig. 3. Medicinal potentials of licorice (Noreen et al., 2021)

Licorice is a tiny perennial plant with many subterranean stems, violet to purple blooms, composite leaves and a pod encompasses 3-5 brown seeds. Licorice roots are cylindrical in form, measuring 0.5±2.5 cm in diameter and 15±20 cm in length. It grows in dry grassy plains and sunny mountainsides and is widely used as a sweetening and flavouring agent in the food industries and it has also been proposed for a variety of clinical applications such as respiratory, skin, joint, digestive system health, and others (Can et al., 2021).

It is a potent natural sweetener, 50-170 times sweeter than that of sucrose. A Greek physicist Pedanius Dioscorides termed licorice as "sweet root" because of its sweet taste (Kao et al., 2013). It is widely used in beverage, tea, confectionery, pharmaceutical and cosmetics all over the world (Hassan et al., 2020). The chemical constituents of the roots have several bioactive compounds like 5-24% glycyrrhizin, 3-16% sugars, 20-30% starch, 4-6% cinder, anethole 2-3%, saponins, flavonoids, isoflavonoids, chalcones, triterpenes, sterols, amino acids, gum and essential oils etc. (Tanideh et al., 2014; Bahmani et al., 2015; Nazari et al., 2017).

Glycyrrhizin, also known as glycyrrhizic acid (molecular weight 822.92 g/mol; chemical formula $C_{42}H_{62}O_{16}$ (Figure 1a), is a biologically active licorice that is transformed to glycyrrhetinic acid (Fig. 1b) in the human stomach. It is water-soluble pentacyclic triterpenoid glycoside which is responsible for the sweetness of licorice. Its aglycone is accountable for a variety of medicinal characteristics for clinical use such as hepatoprotective, anti-inflammatory, antiviral, relieving ulcers, anticancer effects, hot flashes of menopause, antioxidant (Figure 2), neuroprotective and decreasing low density lipoprotein (Icer and Sanlier, 2017; Antonella et al., 2020; Kwon et al., 2020). Phytochemical compounds found in licorice include phenols, isoflavonoids, saponins, isoglycyrrhizin, flavanones,18-glycyrrhetinic acid, glabridin, licochalcone A, liquiritigenin and licochalcone E (Wang et al., 2015; Gamal et al., 2020). It's some pharmaceutical effects are given in Figure 3.

The reactive oxygen species are constantly produced by the body when consuming oxygen normally for respiration and cell-mediated invulnerable functions. The production of free radicals or reactive oxygen during metabolism, exposure and other activities that exceed a biological system's antioxidant capacity results in oxidative stress, that is associated to heart disease, neurodegenerative diseases, cancer, and the ageing process. Antioxidants may protect the human body from free radicals and are frequently added to meals to avoid oxidative chain reactions. They work by preventing the start and propagation steps of the reaction, causing it to terminate and delaying the oxidation process (Yadav et al., 2016; Karim et al., 2022). The most often utilized antioxidants at the moment are BHA, propylgallate, BHT and tert-butyl hydroquinone. Legislation restricts the use of these synthetic antioxidants due to concerns about their hazardous and carcinogenic consequences (Saeed[1] et al., 2018; Wang et al., 2021). Consequently, there is a rising awareness in natural and safe use of antioxidants in different food purposes as well as a emergent trend in customer inclination for natural antioxidants, all of which has increased the motivation to investigate natural antioxidant sources (Awa et al., 2020). The current study was carried out to analyze the antibacterial and possible antioxidant capabilities of licorice root in different extracts.

MATERIAL AND METHODS

Material and extraction

Licorice roots (1 kg) was acquired from local market in Lahore, Pakistan. Extraction of the material was done as reported formerly (Gulçin, 2006). It was initially dried in a hot air oven for 6 hours. 50 g licorices were crushed into a fine powder in a mill and combined with 500 mL hot water by magnetic stirrer for 30 minutes. The extract was then filtered through muslin cloth and Whatman no. 1 filter paper. The filtrates were dried in a hot air oven at 60-65°C. Similarly, 50 g powder was mixed with 500 mL methanol for extraction. The remains were extracted again under the same circumstances until the extraction solvents were transparent. The extracts were filtered using Whatman No. 1 filter paper and the residue was collected and methanol was evaporated using a rotary evaporator at 40°C. These were refrigerated in plastic bags at -20°C for further study.

Evaluation of anti-microbial activity by Disc-diffusion assay

A disc-diffusion assay was carried out for the study of antibacterial activity (CLSI, 2006). Briefly, the methanol and water extracts were placed on sterile filter paper discs (9 mm diameter, chromatographic Whatman No. 3 paper) to load 0.5 mg of the provided extracts per disc. The filter paper discs were then put on agar plates that had been evenly infected with the test microorganisms and kept for 18 hours incubation at 35±2.5°C. As a negative control, a methanol-soaked paper disc was employed and for positive control, commercial 6mm diameter discs containing 0.03 mg of nitrofurantoin in use. The existence of distinct zones showed that the extracts had inhibitory action, which was quantified in mm.

Determination of DPPH assay free radical scavenging activity

The antioxidant capacity of the licorice extracts was assessed by its ability to scavenge the stable 2, 2-diphenyl-1-picrylhydrazyl (DPPH) free radical. This test was performed using the method explained by Brand-Williams (1995) with slight amendments (Saeed[1] et al., 2022). In brief, a 0.0004% DPPH solution in methanol was prepared, and 2.9 mL of this solution was added to 0.1 mL of sample solution at various doses (0.1-0.5 mg/mL). 30 minutes later, the absorbance was measured at 517 nm with spectrophotometer Model: Shimadzu-1700. The DPPH radical scavenging activity was expressed as a inhibition (%) using the following Eq. 1.

$$\text{Inhibition (\%)} = [(A_B - A_S) / A_B] \times 100 \qquad (1)$$

Where, A_B denotes the absorbance of the control reaction and A_S denotes the absorbance of the test compound. From the graph of inhibition percentage plotted versus extract concentration IC_{50} was computed.

Table 1: Antimicrobial screening of water and methanolic extract of Licorice

Microbes	Zone of Inhibition (mm)	
	Water	Methanol
Gram-positive		
Escherichia coli	16±0.04	19±0.05
Pseudomonas aerugenosa	12±0.02	14±0.03
Salmonella typhi	10±0.01	12±0.02
Gram-positive		
Staphylococcus aureus	12±0.02	16±0.04
Bacillus subtilis	11±0.01	15±0.04
Staphylococcus aureus	15±0.03	17±0.05

Statistical Evaluation

The experiments were carried out in triplicate. SPSS was used to examine the data, which was reported as mean standard deviation (Windows 2007, SPSS Inc.). Djeussi et al. (2020) classified the Radical Scavenging Activity as high if the IC_{50} was less than 50 ppm, moderate if it was between 50 and 100 ppm, and low if it was greater than 100ppm. The antibacterial activity was classified as mild (12 mm), moderate (12-20 mm) or strong (> 20 mm) based on the size of the inhibitory zone at every concentration.

RESULTS AND DISCUSSION

Antimicrobial activity

Using the disc diffusion technique, the antimicrobial activity of licorice aqueous and methanol extracts against Gram *+ve* and Gram *–ve* bacteria (*Bacillus subtilis, Staphylococcus sciuri, Staphylococcus aureus, Escherichia coli, Salmonella typhi and Pseudomonas aerugenosa*) was assessed. According to the data given, both aqueous and methanol extracts revealed considerable antibacterial efficacy against all of the microorganisms tested (Table 1). Among bacteria, the methanol extract was most active against *E. coli* (inhibition zone 19±0.05 mm) and least active against *S. typhi* (inhibition zone 12±0.02 mm) at 0.5 mg/mL. These findings are consistent with previous research (Nitalikar et al., 2010; Chopra et al., 2013; Hamad et al., 2020). Moreover, multiple studies have demonstrated that licorice's main ingredient, glycyrrhizic acid, has powerful inhibitory effects on Gram +ve and Gram -ve bacteria (Long et al., 2013; Rodino et al., 2015; Nigussie et al., 2021).

The antibacterial activity of this herb extracts may be attributed to the presence of active constituents such as saponins, alkaloids, flavonoids, glycosides, phenols, and tannin (Mamedov & Egamberdieva, 2019; Wang et al., 2020; Bao et al., 2021). Some secondary metabolites' antibacterial action could be described as follows: diterpenes, phenolic compounds flavonoids by altering microbe cell membranes, inhibiting energy metabolism and nucleic acid synthesis (Gupta et al., 2017; Tamokou et al., 2017; Wahab et al., 2021). Licorice root extracts have been shown to be potentially useful and can be utilized as natural alternative preventives to reduce food poisoning infections and preserve food while avoiding the health risks associated with chemically antibacterial agent applications.

DPPH scavenging activity

DPPH free radical activity was determined and the extract was found to have good antioxidant activity. The antioxidant activity of plants has been identified as one of the indicators for measuring dietary functioning. The antioxidant efficiency of licorice was tested using the DPPH radical scavenging ability technique extract at 0.1-0.5 mg/ml concentration. According to the findings, licorice's methanol extract shows higher free radical scavenging activity with % Inhibition 65.20% than its water extract (53.60%) (Figure 4). The existence of flavonoids in the plants is most probably accountable for the observed free radical scavenging actions. Plant phenolics are a prominent category of chemicals that operate as principal antioxidants (Selyutina et al., 2019; Ageeva et al., 2022).

The computed IC_{50} for *G. glabra* methanol extract was 359.45µg/mL which is greater than the value given by Sanja et al. (2018). It was claimed that IC_{50} of *G. glabra* from Serbia was 11.50mg/g. The DPPH scavenging activity of licorice extract is directly proportional to concentration in a dose-dependent way to a point, after which it revealed an unfavorable pattern and no antioxidant activity of extracts (Somaris et al, 2020). This tendency was also checked by Yu-Jin et al., (2020), who revealed that too much licorice ingestion (more than 2 mg/kg/day of pure glycyrrhizinic acid: a liquorice component) might cause muscular weakness and hypokalemia. However, recent pharmacological investigations have revealed that licorice extracts exhibit substantial antioxidant activity (Quintana et al., 2019; Reigada et al., 2020), which is due to antioxidants like flavonoids (Zhang et al., 2019) and triterpenes (Zang et al., 2020). Licorice's anti-aging (Zhao et al., 2018), anticancer (Chen et al., 2017) and anti-inflammatory properties have been linked to its antioxidant activity (Zhou et al., 2022).

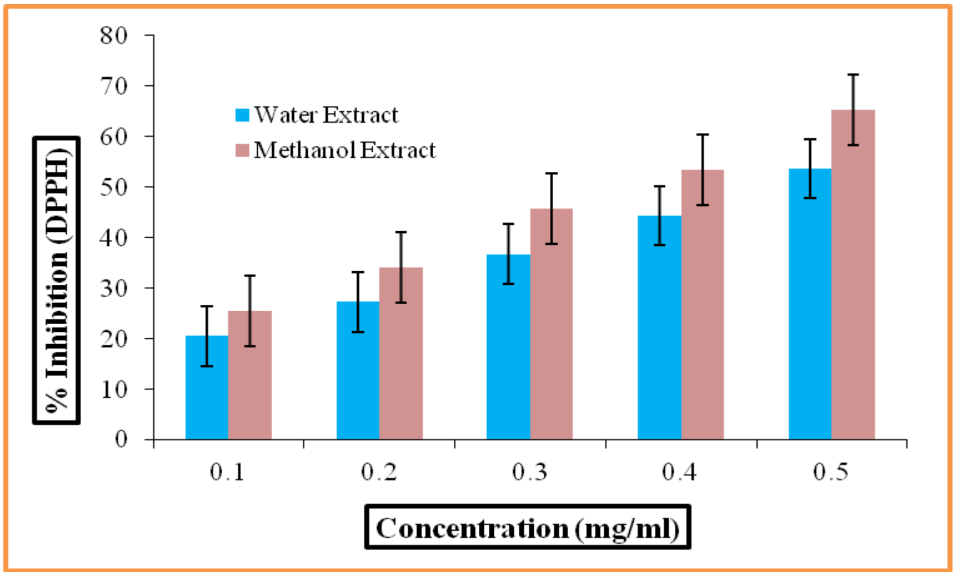


Fig. 4: Percentage Inhibition (DPPH) of Water and Methanol extract of Licorice

CONCLUSION

Glycyrrhiza glabra is widely renowned for its expectorant and demulcent properties. Based on the findings, it was concluded that the methanolic extract of *G. glabra* contains antimicrobial components that should be investigated further for antibacterial efficacy against diverse bacterial strains. The extract is also an excellent source of antioxidant. To protect customers from toxic health effects, it is critical to have effective quality control techniques for the herbal and pharmaceutical products and there should be standardised screening of extracts.

REFERENCES

Ageeva, A.A., Kruppa, A.I., Magin, I.M., Babenko, S.V., Leshina, T.V., Polyakov, N.E., 2022. New Aspects of the Antioxidant Activity of Glycyrrhizin Revealed by the CIDNP Technique. Antioxidants 11, 1591.

Antonella, D.Z., Chiara, C.M., Zsolt, S., Melinda, K., Zsolt, G., Alessandro, D., Valerio, G. and Zsolt, M., 2020. "Effect of an in-vivo and/or in-meat application of a liquorice (Glycyrrhiza glabra L.) extract on fattening rabbits live performance, carcass traits and meat quality", Animal Feed Science and Technology 260, 114333.

Awa K.A., Badji K.D., Sagna, M.B., Guisse A., Bassene E. 2020. Phytochemical Screening and Antioxidant Activity of the Fruits of Boscia senegalensis (Pers.) Lam. (Capparaceae). Pharmacognosy Journal 12, 1042-1049.

Bahmani, M., Sarrafchi, A., Shirzad, H., Shahinfard, N., Rafieian-Kopaei, M., Shahsavari, S., Baharvand-Ahmadi, B., Taherikalani, M. and Ghafourian, S., 2015. "Pharmaceutical, phytochemical, and economical potentials of Glycyrrhiza glabra L: a review", Journal of Chemical and Pharmaceutical Sciences 8, 683–692.

Bao, F., Bai, H.Y., Wu, Z.R., Yang, Z.G., 2021. Phenolic compounds from cultivated Glycyrrhiza uralensis and their PD-1/PD-L1 inhibitory activities. Natural Product Research 35, 562–569.

Brand-Williams, W., Cuvelier, M. E., and Berset, C. L. W. T., 1995. Use of a free radical method to evaluate antioxidant ac-tivity. LWT-Food science and Technology 28, 25-30.

Can, P., Huan, W., Yulong, Z., Fulong, Y., Yue, S., Yaqin, Z., Ziyu, Z., Chijing, Z., Yunjing, Z., Jiayi, K. and Daiyin, P., 2021."The difference of origin and extraction method significantly affects the intrinsic quality of licorice: A new method for quality evaluation of homologous materials of medicine and food", Food Chemistry 340, 127907.

Chen, X., Liu, Z., Meng, R., Shi, C., Guo, N., 2017. Antioxidative and anticancer properties of Licochalcone A from licorice. Journal of Ethnopharmacology, 198, 331–337.

Chopra P.K.P. G, saraf B D., inam F and deo S S. Antimicrobial and antioxidant activities of methanol extract roots of glycyrrhiza glabra and HPLC analysis. International Journal of Pharmaceutical Sciences 5, 157-160.

CLSI M2–A9; 2006. Clinical and Laboratory Standard Institute: Performance Standards for Antimicrobial Disk Susceptibility Test: Approved Standard, 9th ed. CLSI: Wayne, PA, USA.

Djeussi, D.E., Noumedem, J.A.K., Mihasan, M., Kuiate, J. and Kuete, V. 2020. Antioxidant activities of methanol extracts of thirteen Cameroonian antibacterial dietary plants. Journal of. Chemistry 1, 8886762.

Dogan, S.C., Baylan, M., Erdoğan, Z., Küçükgül, A., Bulancak, A., 2018. The effects of Licorice (Glycyrrhriza glabra) root on performance, some serum parameters and antioxidant capacity of laying hens. Brazilian Journal of Poultry Science 20, 699-706.

Gamal M. H., Elaziz A. I., Hassan S. A., Shalaby M. A., Mohdaly A. A., 2020. Chemical Composition, Antioxidant, Antimicrobial and Anticancer Activities of Licorice (Glycyrrhiza glabra L.) Root and Its Application in Functional Yoghurt. Journal of Food and Nutrition Research 8, 707-715.

Gulçin, ˙I., 2006. Antioxidant activity of caffeic acid (3,4-dihydroxycinnamic acid). Toxicology, 217, 213–220.

Gupta P.D., Birdi T.J., 2017. Development of botanicals to combat antibiotic resistance. Journal of Ayurveda Integrative Medicine 8, 266–75.

Hamad G M., Elaziz A.A., Hassan S A., Shalaby M A, Mohdaly A.A., 2020. Chemical Composition, Antioxidant, Antimicrobial and Anticancer Activities of Licorice (Glycyrrhiza glabra L.) Root and Its Application in Functional Yoghurt Journal of Food and Nutrition Research 8, 707-715.

Hassan, E., Akbar, K., Javad, H., Samad, N.E. and Lars-Gernot, O., 2020. "Genetic structure and variation in Iranian licorice (Glycyrrhiza glabra L.) populations based on morphological, phytochemical and simple sequence repeats markers", Industrial Crops and Products 145, 112140.

Icer MA, Sanlier N., 2017 A review: Pharmacological effects of licorice (Glycyrrhiza glabra) on human health, 6, 12-26.

Kao T.C, Wu C.H, Yen G.C., 2014. Bioactivity and potential health benefits of licorice. Journal of Agricultural Food Chemistry 62, 542-53.

Karim I, Khalid M. and Mughal A. A., 2022. Comparative study of antioxidative properties of Jhelum valley fruits. Pure and Applied Biology 11, 861-870.

Kwon Y.J., Son D.H., Chung T.H., Lee Y.J., 2020. A review of the pharmacological efficacy and safety of licorice root from corroborative clinical trial findings. Journal of Medicinal Food 23, 12- 20.

Long, D.R., Mead, J., Hendricks, J.M., Hardy, M.E., Voyich, J.M., 2013. β -Glycyrrhetinic Acid Inhibits Methicillin-Resistant Staphylococcus aureus Survival and Attenuates Virulence Gene Expression. Antimicrobial Agents and Chemotherapy 57, 241–247.

Mamedov, N.A., Egamberdieva D., 2019. Phytochemical Constituents and Pharmacological Effects of Licorice: A Review. Plant and Human Health 3, 1–21.

Mostafa, M.O., 2017. "Apoptotic and anti-Proliferative effects of licorice extract (Licochalcone A) and paclitaxel chemotherapy on human oral squamous cell carcinoma cell line (In vitro study)", Faculty of Dentistry, Cairo University.

Nascimento, M. H. M, Araujo, D.R., 2022. Exploring the Pharmacological Potential of Glycyrrhizic Acid: From Therapeutic Applications to Trends in Nanomedicine. Future Pharm, 2, 1–15.

Nazari S, Rameshrad M, Hosseinzadeh H., 2017. Toxicological effects of Glycyrrhiza glabra (Licorice): A review. Phytotherapy Research 31, 1635-50.

Nigussie D., Davey G., Legesse B.A., Fekadu A., Makonnen E., 2021. Antibacterial activity of methanol extracts of the leaves of three medicinal plants against selected bacteria isolated from wounds of lymphoedema patients. BMC Complementary Medicine and Therapies 21, 1-10.

Nitalikar M. M., Munde K. C., Dhore B. V. and Shikalgar S. N., 2010. Studies of Antibacterial Activities of Glycyrrhiza glabra Root Extract, International Journal of PharmTech Research 2, 899-901.

Noreen S., Mubarik F., Farooq F., Khan M., Khan A.U., Pane Y.S., 2021. Medicinal Uses of Licorice (Glycyrrhiza glabra L.): A Comprehensive Review. Open Access Macedonian Journal of Medical Sciences 27(9), 668-675.

Quintana, S.E., Cueva, C., Villanueva-Bermejo, D., Moreno-Arribas, M.V., Fornari, T., García-Risco, M.R., 2019. Antioxidant and antimicrobial assessment of licorice supercritical extracts. Industrial Crops and Products 139, 111496.

Reigada, I., Moliner, C., Valero, M.S., Weinkove, D., Langa, E., Gómez Rincón, C. 2020. Antioxidant and Antiaging Effects of Licorice on the Caenorhabditis elegans Model Journal of Medicinal Food 23, 72–78.

Rodino, S., Butu, A., Butu, M., Cornea, P.C., 2015. Comparative Studies on Antibacterial Activity of Licorice, Elderberry and Dandelion. Digest of. Journal of Nanomaterials and Biostructures 10, 947–955.

Saeed M. K, Zahra N., Abidi S. H. I. and Syed Q., 2022. Phytochemical Screening and DPPH Free Radical Scavenging Activity of Aloe vera (Aloe barbadensis Miller) Powder. International Journal of Food Science and Agriculture 6, 301-308.

Saeed M. K., Zahra N., Taj R., Ahmad I., Ashraf M., Kalim I., Masood S. and Nisa A., 2018. Assessment of nutritional facts and antioxidant efficacy of clove (Syzygium aromaticum L.) collected from Lahore, Pakistan in water and methanol extracts. International Research Journal of Biological Sciences 7, 13-16.

Sanja, V., Filip, Š., Izabella, S., Istvan, Z., Imre, O. and Suzana, J., 2018. "Chemical composition, antioxidant and anticancer activity of licorice from Fruska Gora locality", Industrial Crops and Products 112, 217-224.

Selyutina, O.Y., Polyakov, N.E., 2019. Glycyrrhizic acid as a multifunctional drug carrier—From physicochemicalproperties to biomedical applications: A modern insight on the ancient drug. International Journal of Pharmaceuticals 559, 271–279.

Somaris, E., Quintana, D.H., David, V., Mónica, R. and García-Risco, T., 2020. "Fractionation and precipitation of licorice (Glycyrrhiza glabra L.) phytochemicals by supercritical antisolvent (SAS) technique", LWT - Food Science and Technology 126, 109315.

Tamokou J.D.D., Mbaveng A.T., Kuete V., 2017. Antimicrobial activities of African medicinal spices and vegetables, Medicinal Spices and Vegetables from Africa 5, 207–37

Tanideh N., Rokhsari P., Mehrabani D., Mohammadi S. S., Sabet S.F., Ashraf M.J., Koohi H. O, Shamsian S, Ahmadi N., 2014. The Healing Effect of Licorice on Pseudomonas aeruginosa Infected Burn Wounds in Experimental Rat Model. World Journal of Plastic Surgery 3, 99-106.

Wahab S., Annadurai S., Abullais S. S., Das G., Ahmad W., Ahmad M. F., Kandasamy G. , Vasudevan R., Ali, S. and Amir M., 2021. Glycyrrhiza glabra (Licorice): A Comprehensive Review on Its Phytochemistry, Biological Activities, Clinical Evidence and Toxicology. Plants 10, 2751; 1-18.

Wang, H., Ge, X., Qu, H., Wang, N., Zhou, J., Xu, W., Xie, J., Zhou, Y., Shi, L., Qin, Z., 2020. Glycyrrhizic Acid Inhibits Proliferation of Gastric Cancer Cells by Inducing Cell Cycle Arrest and Apoptosis. Cancer Management Research 12, 2853–2861.

Wang, L., Yang, R., Yuan, B., Liu, Y. and Liu, C., 2015. "The antiviral and antimicrobial activities of licorice, a widely-used Chinese herb", Acta Pharmaceutica Sinica B 5, 310-315.

Wang,W., Xiong, X., He, Z., Zhu, Q., Liao, C., Jiang, G. 2021. Analysism occurrence, toxicity and environmental health risks of synthetic phenolic antioxidants: A review. Environmental Research 201, 111531.

Yadav A., Kumari R., Yadav A., Mishra J.P., Srivatva S., Prabha S., 2016. Antioxidants and its functions in human body. Research in Environmental Life Sciences 9, 1328–1331.

Yu-Jin, K., Da-Hye, S.,Tae-Ha, C. and Yong-Jae, L., 2020. "A Review of the pharmacological efficacy and safety of licorice root from corroborative clinical trial findings", Journal of Medicinal Food 23, 12-20.

Yu-Jin, K., Da-Hye, S.,Tae-Ha, C. and Yong-Jae, L., 2020. "A Review of the pharmacological efficacy and safety of licorice root from corroborative clinical trial findings", Journal of Medicinal Food 23, 12-20.

Zang, Y. (2020). Pharmacological activities of coumarin compounds in licorice: a review. Natural Product Communications 15(9), 1934578.

Zhang, F.X., Song, J.X., Liu, X.D., Shan, H. 2019. Antioxidation and immune activity of licorice flavonoids. Chinese Journal of Veterinary Sciences 39, 1180–1183.

Zhao, F.F., 2018. The Effect of Glycyrrhiza Uralensis Fisch on D-Gal Induced Aging Rats and the Analysis of the Target Metabolomics Based on Taurine Pathway. Master's Thesis, Shanxi University, Taiyuan, China.

Zhou, Q., Zhang, S., Geng, X., Jiang, H., Dai, Y. Wang, P., Hua, M., Gao, Q., Lang, S., Hou, L. 2022. Antioxidant Effects of Roasted Licorice in a Zebrafish Model and Its Mechanisms. Molecules 27, 7743.