Jagua Publication

www.jpub.org

Journal of Applied Health Sciences and Medicine 3(6) (2023): 17 –27

Research Article

# Evaluation of the Antimicrobial Activity of Licorice (*Glycyrrhiza* glabra) Plant Against Representative Oral pathogens

**Ashraf O. Abdellatif[1*], Huzifa A. Ahmed[1], Omran M. Osman[1], Mohamed A. Ideris[1], Kamal A. A. Mohammed[2], Mohammed O. Alqamar[3]**

[1]Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Karary University, Khartoum, Sudan

[2]Department of Pharmacology, Faculty of Medicine & Health Sciences, University of Dongola, Dongola, Sudan.

[3]Department of Pharmacognosy, Faculty of Pharmacy, Karary University, Khartoum, Sudan.

**Abstract:**

*Introduction:* Oral health is important for general health because, without proper oral hygiene, bacteria can reach levels that might lead to oral infections. Pathogens' resistance to traditional antibiotic products available on the market represents a point of common interest to the scientific community throughout the world and has led to a pressing need to develop new and innovative antimicrobial agents, and among the potential sources of new agents, plants have represented a good alternative. This research is looking at the biological activities of the licorice (*Glycyrrhiza glabra*) plant as an antimicrobial agent for oral infections.

*Method:* The antimicrobial activities of various extract fractions prepared from methanol, chloroform, and cyclohexane were evaluated against selected oral pathogens, including *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Candia albicans*, using the agar-well diffusion method.

*Results:* The results indicated that methanolic extract had antimicrobial activity against the selected isolates, with a zone of inhibition equal to 23mm for *S. aureus*, 14mm for *E. coli*, 15mm for *P. aeruginosa*, and 22mm for *C. albicans*. Regarding sensitivity, the results showed that *S. aureus* and *C. albicans* were the most sensitive isolates toward the tested licorice extracts. The results also showed that licorice extract in chloroform and cyclohexane had no activity against the tested isolates of Gram-negative bacteria.

*Conclusion:* In conclusion, our study provides further evidence of the antimicrobial activity of *G. glabra*, especially against the selected isolates, and encourages the use of this plant in a suitable dosage form to treat the oral cavity infection that could possibly be caused by the tested microbes.

**Keywords:** licorice, antimicrobial activity, oral pathogen.

How to cite:
Abdellatif et al. 2023. "Evaluation of the Antimicrobial Activity of Licorice (*Glycyrrhiza glabra*) Plant Against Representative Oral pathogens". *Journal of Applied Health Sciences and Medicine* 3(6): 17 – 27.
https://doi.org/10.58614/jahsm363

Received: May 18, 2023
Accepted: June 12, 2023
Published: June 20, 2023

Corresponding author:
Ashraf O. Abdellatif
ashrafpharm11@karary.edu.sd

## 1. Introduction

It is essential to find new antimicrobial chemicals that are safe, efficient, and economical because to the bacteria's developed resistance to antibiotics (Abdellatif & Mohammed, 2023).

The number of effective therapies for illnesses is declining due to an international problem called antimicrobial resistance. The abuse of antibiotics in both agriculture and medicine is the main cause of antibiotic-resistant bacteria, which can result in potentially fatal health problems (Chokshi et al., 2019). The world urgently requires new drugs with unique chemistry and modes of action to fight the public health danger posed by antimicrobial resistance (Majumder et al., 2020). Oral health depends on a diversity of bacteria that exist in the oral cavity. The oral microbiome is made up of bacteria, fungi, viruses, and other microorganisms that interact with each other and the host to maintain a healthy balance. This balance is crucial for maintaining oral health because it prevents the colonisation of pathogenic microorganisms and fosters the growth of a strong immune system. However, an imbalance in the oral microbiota may lead to the development of oral illnesses such dental caries (tooth decay), oral cancer, and periodontal disease (Sampaio-Maia et al., 2016). Without good dental hygiene, bacteria can build up to levels that could cause oral infections like tooth decay and gum disease, and untreated oral diseases may raise the risk of bad health problems. Therefore, oral health is crucial for overall and whole-body health. In order to preserve healthy teeth and gums and prevent tooth decay and gum disease, it is essential to practise good oral hygiene (Fiorillo, 2019; Sharma et al., 2018). It also lowers the risk of developing heart disease, stroke, diabetes, and other diseases, as well as the need for dental work such as fillings, crowns, bridges, implants, and dentures.

Research on plant-based antimicrobial natural active components is becoming increasingly important (Rios & Recio, 2005). For ages, traditional medicine in many nations has employed plants as a good alternative and potential source of new antimicrobial medicines to treat a variety of illnesses, including microbial infections (Sibanda & Okoh, 2007; Taylor, 2013). They contain a variety of bioactive chemicals that can be employed as natural antibacterial agents to fight off bacteria, fungus, and viruses, among other organisms (Rios & Recio, 2005).

Because they are typically safe and have fewer side effects than synthetic pharmaceuticals, folk medicine frequently uses medicinal plants as a source of new antimicrobial agents. This has several benefits over synthetic drugs. In addition, they are more accessible and less expensive than synthetic medications (Anand et al., 2019; Shakya, 2016).

Licorice *(Glycyrrhiza glabra)*, a member of the *Fabaceae* family of plants, has been used medicinally for thousands of years in a variety of cultures (Dastagir & Rizvi, 2016). Licorice has a number of medicinal uses, including treating eczema (Xu et al., 2020), sore throats (Kuriyama & Maeda, 2019), coughs, colds, bronchitis, and lung diseases (Smruti, 2021; Wahab et al., 2022), and ulcers (Shahare et al., 2021). It can also be taken sublingually to treat ulcers. Additionally, it has been noted to help with

https://doi.org/10.58614/jahsm363

heart health, reduce inflammation, and the treatment of infections (Pastorino et al., 2018; Wahab et al., 2022). The objective of the current investigation is to assess the antibacterial efficacy of the licorice plant *(Glycyrrhiza glabra)* against a number of oral infections.

## 2. Methodology

### 2.1. Plant materials

The licorice root *(Glycyrrhiza glabra)* was procured from Khartoum's local markets in Sudan. The Medicinal and Aromatic Plants and Traditional Medicine Research Institute in Khartoum, Sudan, has recognised and verified it. In the herbarium of the Pharmacognosy Department, Faculty of Pharmacy, and Karary University, Sudan, a voucher specimen has been deposited.

### 2.2. Bacterial and fungal cultures

Three bacteria and one fungal clinical isolate were chosen as representative oral cavity-infecting microorganisms for the screening of the antimicrobial activity. All of the isolates came from the Khartoum Medical Services Administration Hospital's Central Lab's Microbiology Department. *Staphylococcus aureus* (CLMSA0002214), *Escherichia coli* (CLMSA0002226), *Pseudomonas aeruginosa* (CLMSA0002228), and *Candida albicans* (CLMSA0002243) were the chosen microbiological isolates.

### 2.3. Preparation of crude extract using solvents with different polarities

The Karary University's Pharmacognosy Department prepared the crude extracts. After being dried at 40 degrees Celsius in an oven, the licorice roots were crushed using a pestle and mortar into a crusty powder. 100 grammes of crusty powder were placed in a separator funnel and macerated for 24 hours in separate flasks of cyclohexane, methanol, and chloroform. The crude extracts were vacuum evaporated to dryness after the solvents were drained. Up until there was no more root powder left, the processes of maceration and evaporation were repeated. The combined extracts were concentrated at 65°C in a rotary evaporator using a cotton filter (Biobase, China). To get rid of any solvent that might have remained in the crude extract, the final residues were dried. The generated crude extracts are hermetically sealed, kept in the refrigerator, and kept in the dark to avoid contamination or chemical deterioration.

### 2.4. Preparation of tested extracts

To make the stock solutions, the various extract fractions (methanol, chloroform, and cyclohexane) taken from the licorice roots were weighed and diluted in dimethyl sulphoxide (DMSO) 0.1%. Until they were employed in the tests, the prepared solutions were kept in the refrigerator. The antibacterial and antifungal effects of each extract were investigated at a dosage of 20 mg/ml.

### 2.5. Screening for the antibacterial and antifungal activities using agar well diffusion method

25 L of the tested extract (20 mg/ml) were put into a well (6 mm). From a culture of 12–18 hours on nutritional agar for bacteria and 48–72 hours on Sabouraud dextrose agar for fungi, about five pure colonies of each microbial culture were chosen; the selected colonies were then floated in sterile normal saline solution. Using a Shimadzu dual-beam UV-visible spectrophotometer (Kyoto, Japan), a solution of 0.5 McFarland turbidity was measured at 600 nm and the suspension was adjusted to match it. 100 microliters of each microbe were put to the surface of nutrient agar plates at a concentration of 1-5 x $10^6$ cells/ml, as directed by Ramadan and his co-authors. The plates were then kept at 37°C for 18 to 24 hours to allow for bacterial growth. The mean SD of the studies conducted in triplicate served as the measurement of the inhibitory zone in millimetres. Gramme positive, Gramme negative, and fungi-specific positive control antibiotics included ampicillin (10 g), gentamicin (10 g) discs, and amphotericin B (5 g). Sensitive species were considered to produce halos that were 13 mm or bigger (Ramadan et al., 2020).

## 3. Results

### 3.1. The antimicrobial activities of licorice roots extract in different fractions

*The antimicrobial activities of the methanol fraction extract of licorice roots*

Different fraction extracts' antimicrobial activity was assessed using the agar-well diffusion method, and results were reported by determining the zone of inhibition in millimetres. Cyclohexane fraction, chloroform fraction, and methanol fraction were the tested extracts from *Glycyrrhiza glabra* roots.

On each of the oral isolates examined, the *G. glabra* methanolic fraction's antibacterial efficacy varied. With a zone of inhibition of 23 mm for *S. aureus*, 14 mm for *E. coli*, 15 mm for *P. aeruginosa*, and 22 mm for *C. albicans*, it was most efficient against these microorganisms.

In contrast to Gram-negative bacteria, this result shows that the methanolic extract has good activity against Gram-positive bacteria and *C. albicans*. Interestingly, the *G. glabra* methanolic fraction showed the largest inhibition zone against *S. aureus*, measuring 23 mm, which is superior to standard ampicillin. Additionally, *C. albicans* (22 mm) showed antifungal activity against the methanol fraction of *G. glabra* roots that was comparable to normal amphotericin B (21.9). As demonstrated in Table 1, methanolic extract has showed promise as a therapeutic application against oral clinical isolates of *S. aureus* and *C. albicans* when compared to conventional positive controls.

**Table 1.** The antimicrobial activities of *Glycyrrhiza glabra* methanol fraction extract by the agar- well diffusion method. The results are represented as a zone of inhibition in millimeters ± SD.

| Test | Methanol fraction | | | |
|---|---|---|---|---|
| **Tested microbe** | ***S. aureus*** | ***E. coli*** | ***P. aeruginosa*** | ***C. albicans*** |
| **Tested extract zone of inhibition** | 23±0.22 | 14±0.19 | 15±0.14 | 22±0.18 |
| **Positive control zone of inhibition** | 22.9± 0.14 | 26.3± 0.15 | 17.3± 0.12 | 21.9± 0.12 |

### 3.2. The antimicrobial activities of the chloroform fraction extract of licorice roots

According to tests on *C. albicans* and *S. aureus*, the chloroform extract of licorice had an inhibitory zone of 21 mm against *S. aureus* and 13 mm against *C. albicans*. As indicated in Table 2, the chosen Gram-negative isolates, including *E. coli* and *P. aeruginosa*, did not exhibit any sensitivity to the chloroform fraction.

**Table 2.** The antimicrobial activities of *Glycyrrhiza glabra* cyclohexane fraction extract by the agar-well diffusion method. The results are represented as a zone of inhibition in millimeters ± SD

| Test | Chloroform fraction | | | |
|---|---|---|---|---|
| **Tested microbe** | ***S. aureus*** | ***E. coli*** | ***P. aeruginosa*** | ***C. albicans*** |
| **Tested extract zone of inhibition** | 21±1.5 | NA | NA | 13±1.0 |
| **Positive control zone of inhibition** | 22.9± 0.14 | 26.3± 0.15 | 17.3± 0.12 | 21.9± 0.12 |

### 3.3. The antimicrobial activities of the cyclohexane fraction extract of licorice roots

The licorice cyclohexane extract had an 18-mm zone of inhibition for *S. aureus* and a 20-mm zone for *C. albicans* when it came to antibacterial activity. Isolates of *P. aeruginosa* and *E. coli* did not exhibit any susceptibility to the cyclohexane fraction (Table 3). According to the findings, the cyclohexane fraction exhibits non-detectable antibacterial activity against the chosen Gram-negative bacteria but good antimicrobial activities against *S. aureus*, a Gram-positive bacterium. It also has good antifungal activities against *C. albicans*.

**Table 3.** The antimicrobial activities of *Glycyrrhiza glabra* cyclohexane fraction extract by the agar-well diffusion method. The results are represented as a zone of inhibition in millimeters ± SD.

| Test | Cyclohexane fraction | | | |
|---|---|---|---|---|
| **Tested microbe** | ***S. aureus*** | ***E. coli*** | ***P. aeruginosa*** | ***C. albicans*** |
| **Tested extract zone of inhibition** | 18±1.0 | NA | NA | 20±1.7 |
| **Positive control zone of inhibition** | 22.9± 0.14 | 26.3± 0.15 | 17.3± 0.12 | 21.9± 0.12 |

### 3.4. Microbial sensitivity toward different fractions of licorice extracts

As shown in figures 1 and 2a, the results demonstrated that all licorice extract fractions (methanol, chloroform, and cyclohexane) had good activity against *S. aureus*, with the methanolic fraction exhibiting superior activity with a zone of inhibition of 23 mm. According to the findings, only the licorice extract's methanolic fraction was effective against *E. coli*, with a 14 mm zone of inhibition (Figs. 1 and 2b).

Figures 1 and 2c of the data demonstrate that only the methanolic portion of the licorice extract was effective against *P. aeruginosa*, with a zone of inhibition of 15 mm. It's interesting to note that all of the licorice fractions examined had positive antimicrobial effects on *C. albicans*, as evidenced by the zones of inhibition that were discovered and depicted in Figures 1 and 2d.

Overall, the most effective component of the studied extracts was the methanolic extract of licorice roots since it significantly inhibited all tested isolates, including the Gram-negative organisms (*E. coli and P. aeruginosa*). Interestingly, the acquired zones of inhibition, which were very similar in their values to the standard positive control, indicated that the methanolic extract of licorice roots shown promising antibacterial action against both *S. aureus* and *C. albicans*.

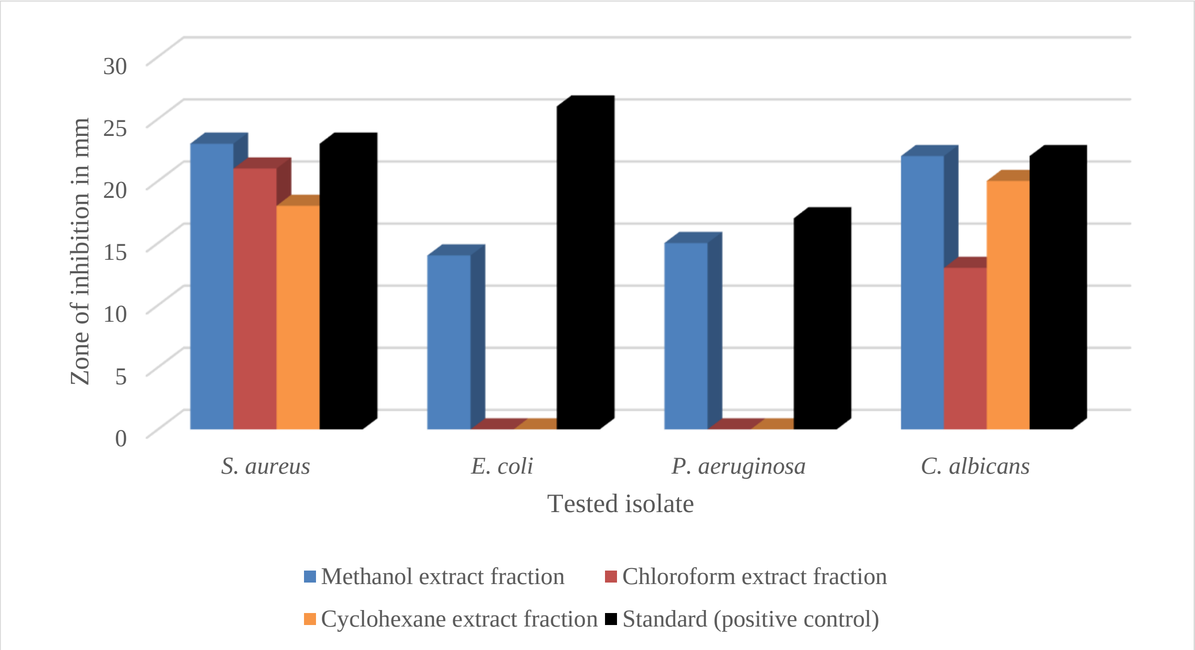


**Figure 1.** sensitivity of selected microbes toward the tested extract of licorice roots. Data are represented as zones of inhibition in mm

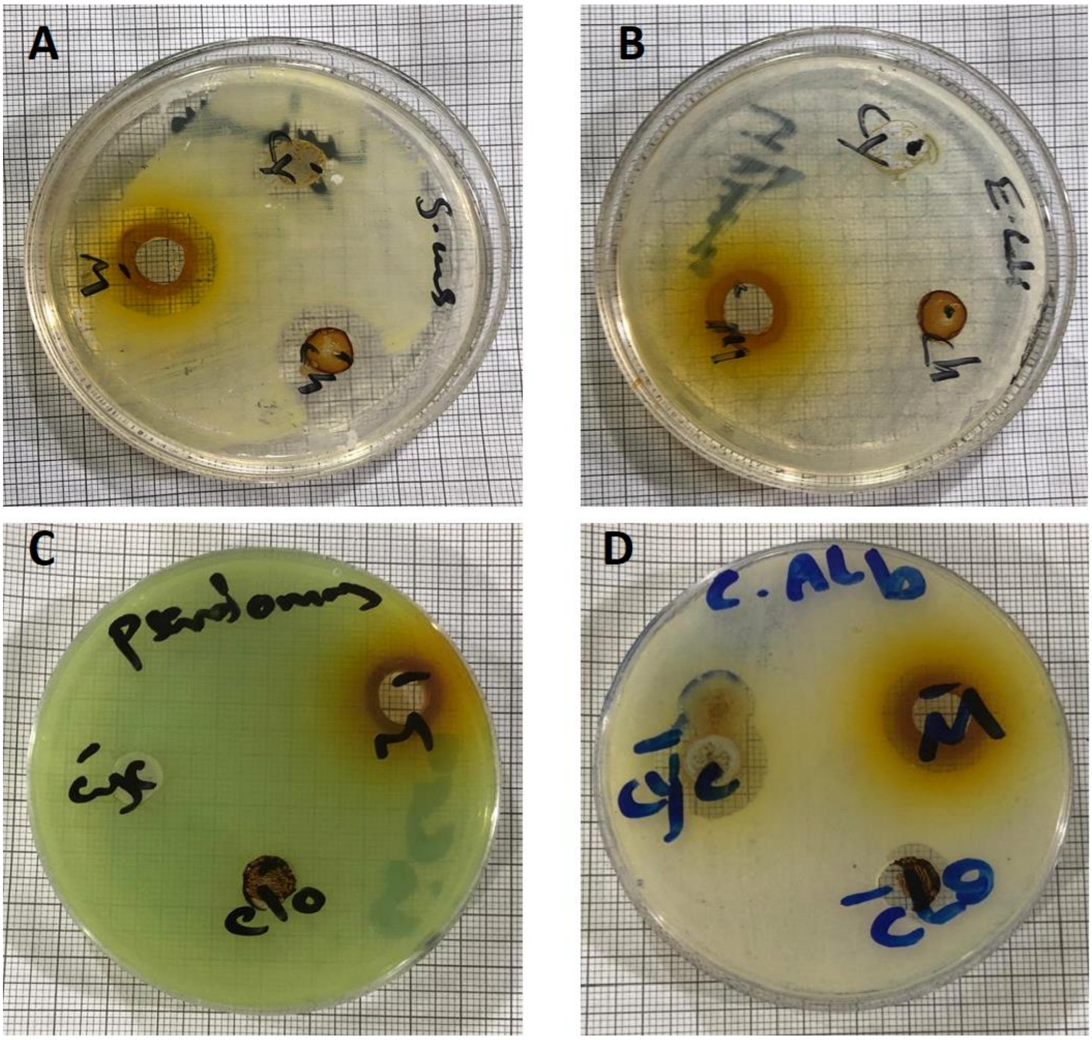


**Figure 2.** A picture of the inhibition zones produced by the different licorice extract fractions when tested against *S. aureus* (A), *E. coli* (B), *P. aeruginosa* (C), and *C. albicans*

## 4. Discussion

Alternative medicines to treat microbial infections are urgently needed as a result of the escalating antibiotic resistance (Abdellatif et al., 2022). For hundreds of years, plant-based herbal medicines have been a crucial component of traditional medicine. They have attracted considerable interest in recent decades and have been used as antibacterial agents and as a source for new compounds with powerful therapeutic effects (Cragg & Newman, 2013; Gurnani et al., 2014; Sam, 2019).

Licorice *(Glycyrrhiza glabra)* has been used traditionally in many cultures as a medicine to treat a wide range of conditions, including rheumatic pain, asthma, bronchitis, peptic ulcers, arthritis, and allergy issues (Damle, 2014).

The current study intended to assess the in vitro antibacterial activity of *G. glabra* root extract against particular oral infections. As evaluated by measuring inhibition zones, the data obtained demonstrated positive antibacterial efficacy against the investigated pathogens, particularly against *S. aureus* and *C. albicans*. This study has therefore confirmed and expanded the data on the in vitro activity of licorice extract against the chosen clinical isolates, particularly *S. aureus*, a significant clinical oral resistant pathogen, and is comparable to earlier findings that revealed the various inhibitory effects of this plant (Fukai et al., 2002).

The results of this study showed that *G. glabra*, especially the methanolic extract fraction, can act on Gram-positive, Gram-negative, and yeast fungi as it inhibited the growth of *S. aureus*, *E. coli*, *P. aeruginosa*, and *C. albicans*, which is thought to be the most common pathogen, particularly in immunocompromised patients (Bodey et al., 2002).

The capacity of the methanol fraction to function as an optimal solvent for the extraction of both hydrophilic and lipophilic compounds from plant parts, including licorice roots, accounts for its better activity when compared to the chloroform and cyclohexane fractions. From licorice roots, it can extract a variety of phytochemicals, including phenolics, flavonoids, alkaloids, and terpenoids.

Due to the polarity of these solvents and their capacity to extract all phytochemical components with antibacterial activities, the results showed that chloroform and cyclohexane extracts exhibited no activity against the chosen Gram-negative isolates.

Additionally, the fundamental differences between the cell wall architectures of Gram-negative bacteria may contribute to the absence of activity of these fractions. The differences in the cell walls of Gram-positive and Gram-negative bacteria affect how they respond to antimicrobial drugs. Antibiotics, bile salts, and other hazardous substances are kept out of gram-negative bacteria's cells by their outer membrane and lipopolysaccharide (Epand & Epand, 2011; Saga & Yamaguchi, 2009).

The licorice extract's antibacterial activity has a multifaceted mechanism because it contains a variety of active ingredients. Numerous phytochemicals with antimicrobial properties, such as alkaloids, flavonoids, anthocyanins, tannins, quinones, phenolics, terpenoids, and saponins, may be the cause of the activity (Barbieri et al., 2017; Rahman et al., 2021).

(Othman et al., 2019; zçelik et al., 2011) Alkaloids and flavonoids have been demonstrated to have antibacterial effects against both bacteria and fungus, including C. albicans. The inhibition of DNA and protein synthesis, interference with the creation of cell walls, and disruption of plasma membranes are the mechanisms through which alkaloids exert their antimicrobial effects (Yan et al., 2021). On the other hand, flavonoids prevent the production of nucleic acids, the function of cytoplasmic membranes, energy metabolism, cell attachment, the creation of biofilms, and the formation of porins on the cell membrane, altering the permeability of the membrane and lessening pathogenicity (Xie et al., 2015). The majority of licorice's antibacterial properties are attributed to its isoflavonoid components, particularly hispa glabridin and B,4'-O-methyl glabridin, glabridin, gabriel, and 3-hydroxyglabrol (Murphy & Dow, 2021).

Anthocyanins have been shown to have an antibacterial effect on a number of microorganisms, including bacteria, due to their ability to interact with both membrane and intracellular components of bacteria (Cisowska et al., 2011). Typically, anthocyanins have a greater impact on Gram-positive bacteria than they do on Gram-negative bacteria. Quinone, another component of the extract, exhibits its antibacterial capabilities by blocking the synthesis of bacterial DNA (Smeriglio et al., 2016).

The licorice root extract's tannins, phenolic compounds, saponins, and terpenoids have been shown to have closely related antimicrobial activities through the inhibition of extracellular microbial enzymes, deprivation of the substrates necessary for microbial growth, direct action on microbial metabolism through inhibition of oxidative phosphorylation, metal ion deprivation, or formation of complexes with the cell membrane of bacteria, resulting in morphological changes.

Licorice extract is a promising candidate to be used as an antimicrobial agent for infections of the oral cavity caused by the tested microbes due to the presence of the aforementioned phytochemical components, which have a wide range of activities and variable mechanisms of action. It may be even more beneficial if it is added to pharmaceutical formulations like gum, toothpaste, mouthwash, and dental products to treat dental caries, endodontic infections, and other conditions that affect the teeth.

## 5. Conclusion

The findings of this study support the use of herbal remedies to combat microbial resistance by encouraging further study into the field of antimicrobial agents derived from plant sources in order to obtain a wide range of pharmacological activities with fewer side effects than those caused by using modern drugs. The findings also show that *G. glabra* has antibacterial activity, but more study is required to determine the active ingredients in vivo using various disease models and to create pharmaceutical applications. The precise molecular mechanisms and targets for cell growth inhibition must also be clarified through further research in order to enable for the logical creation of more potent medicines to treat oral infections.

## References


[1] Abdellatif, A. O., Ali, I. N., Mohamed, M. A., Ibrahim, M. A., & Mohamed, W. A. (2022). Evaluation of the Antibiotic Resistance Pattern at the Medical Services Administration Hospital in Khartoum, Sudan, 2021. Journal for Research in Applied Sciences and Biotechnology, 1(4), 50-56.

[2] Abdellatif, A. O., & Mohammed, K. A. (2023). A REVIEW OF THE EFFECTS OF EXCESSIVE ANTIBIOTIC PRESCRIPTION ON PUBLIC HEALTH.

[3] Amraei, S., & Ahmadi, S. (2022). Recent studies on antimicrobial and anticancer activities of saponins: A mini- review. Nano Micro Biosystems, 1(1), 22-26.

[4] Anand, U., Jacobo-Herrera, N., Altemimi, A., & Lakhssassi, N. (2019). A comprehensive review on medicinal plants as antimicrobial therapeutics: potential avenues of biocompatible drug discovery. Metabolites, 9(11), 258.

[5] Barbieri, R., Coppo, E., Marchese, A., Daglia, M., Sobarzo-Sánchez, E., Nabavi, S. F., & Nabavi, S. M. (2017). Phytochemicals for human disease: An update on plant-derived compounds antibacterial activity. Microbiological research, 196, 44-68.

[6] Bodey, G. P., Mardani, M., Hanna, H. A., Boktour, M., Abbas, J., Girgawy, E., . . . Raad, I. I. (2002). The epidemiology of Candida glabrata and Candida albicans fungemia in immunocompromised patients with cancer. The American journal of medicine, 112(5), 380-385.

[7] Chokshi, A., Sifri, Z., Cennimo, D., & Horng, H. (2019). Global contributors to antibiotic resistance. Journal of global infectious diseases, 11(1), 36.
[8] Cisowska, A., Wojnicz, D., & Hendrich, A. B. (2011). Anthocyanins as antimicrobial agents of natural plant origin. Natural product communications, 6(1), 1934578X1100600136.
[9] Cragg, G. M., & Newman, D. J. (2013). Natural products: a continuing source of novel drug leads. Biochimica et Biophysica Acta (BBA)-General Subjects, 1830(6), 3670-3695.
[10] Damle, M. (2014). Glycyrrhiza glabra (Liquorice)-a potent medicinal herb. International journal of herbal medicine, 2(2), 132-136.
[11] Dastagir, G., & Rizvi, M. A. (2016). Glycyrrhiza glabra L.(Liquorice). Pakistan journal of pharmaceutical sciences, 29(5).
[12] Epand, R. M., & Epand, R. F. (2011). Bacterial membrane lipids in the action of antimicrobial agents. Journal of Peptide Science, 17(5), 298-305.
[13] Fiorillo, L. (2019). Oral health: the first step to well-being. In (Vol. 55, pp. 676): MDPI.
[14] Fukai, T., Marumo, A., Kaitou, K., Kanda, T., Terada, S., & Nomura, T. (2002). Antimicrobial activity of licorice flavonoids against methicillin-resistant Staphylococcus aureus. Fitoterapia, 73(6), 536-539.
[15] Griffin, S. G. (2000). Aspects of antimicrobial activity of terpenoids and the relationship to their molecular structure.
[16] Gurnani, N., Mehta, D., Gupta, M., & Mehta, B. (2014). Natural products: source of potential drugs. Afr J Basic Appl Sci, 6(6), 171-186.
[17] Kuriyama, A., & Maeda, H. (2019). Topical application of licorice for prevention of postoperative sore throat in adults: A systematic review and meta-analysis. Journal of Clinical Anesthesia, 54, 25-32.
[18] Maddox, C. E., Laur, L. M., & Tian, L. (2010). Antibacterial activity of phenolic compounds against the phytopathogen Xylella fastidiosa. Current microbiology, 60, 53-58.
[19] Majumder, M. A. A., Rahman, S., Cohall, D., Bharatha, A., Singh, K., Haque, M., & Gittens-St Hilaire, M. (2020). Antimicrobial stewardship: Fighting antimicrobial resistance and protecting global public health. Infection and drug resistance, 13, 4713.
[20] Murphy, M. J., & Dow, A. A. (2021). Natural cosmeceutical ingredients for the management of hyperpigmentation in Hispanic and Latino women. The Journal of Clinical and Aesthetic Dermatology, 14(8), 52.
[21] Othman, L., Sleiman, A., & Abdel-Massih, R. M. (2019). Antimicrobial activity of polyphenols and alkaloids in middle eastern plants. Frontiers in microbiology, 10, 911.
[22] Özçelik, B., Kartal, M., & Orhan, I. (2011). Cytotoxicity, antiviral and antimicrobial activities of alkaloids, flavonoids, and phenolic acids. Pharmaceutical biology, 49(4), 396-402.
[23] Pastorino, G., Cornara, L., Soares, S., Rodrigues, F., & Oliveira, M. B. P. (2018). Liquorice (Glycyrrhiza glabra): A phytochemical and pharmacological review. Phytotherapy research, 32(12), 2323-2339.
[24] Rahman, M. M., Rahaman, M. S., Islam, M. R., Hossain, M. E., Mannan Mithi, F., Ahmed, M., . . . Sobarzo- Sánchez, E. (2021). Multifunctional therapeutic potential of phytocomplexes and natural extracts for antimicrobial properties. Antibiotics, 10(9), 1076.
[25] Ramadan, M. A., Shawkey, A. E., Rabeh, M. A., & Abdellatif, A. O. (2020). Promising antimicrobial activities of oil and silver nanoparticles obtained from Melaleuca alternifolia leaves against selected skin-infecting pathogens. Journal of Herbal Medicine, 20, 100289.
[26] Rios, J.-L., & Recio, M. C. (2005). Medicinal plants and antimicrobial activity. Journal of ethnopharmacology, 100(1-2), 80-84.
[27] Saga, T., & Yamaguchi, K. (2009). History of antimicrobial agents and resistant bacteria. Jmaj, 52(2), 103-108.

[28] Sam, S. (2019). Importance and effectiveness of herbal medicines. Journal of pharmacognosy and phytochemistry, 8(2), 354-357.

[29] Sampaio-Maia, B., Caldas, I., Pereira, M., Pérez-Mongiovi, D., & Araujo, R. (2016). The oral microbiome in health and its implication in oral and systemic diseases. Advances in applied microbiology, 97, 171-210.

[30] Scalbert, A. (1991). Antimicrobial properties of tannins. Phytochemistry, 30(12), 3875-3883.

[31] Shahare, N., Chouhan, S., & Darwhekar, G. (2021). Herbs used in treatment of mouth ulcer-a review. International Journal of Pharmacognosy and Chemistry, 68-74.

[32] Shakya, A. K. (2016). Medicinal plants: Future source of new drugs. International journal of herbal medicine, 4(4), 59-64.

[33] Sharma, N., Bhatia, S., Sodhi, A. S., & Batra, N. (2018). Oral microbiome and health. AIMS microbiology, 4(1), 42.

[34] Sibanda, T., & Okoh, A. (2007). The challenges of overcoming antibiotic resistance: Plant extracts as potential sources of antimicrobial and resistance modifying agents. African Journal of Biotechnology, 6(25).

[35] Smeriglio, A., Barreca, D., Bellocco, E., & Trombetta, D. (2016). Chemistry, pharmacology and health benefits of anthocyanins. Phytotherapy research, 30(8), 1265-1286.

[36] Smruti, P. (2021). A review on natural remedies used for the treatment of respiratory disorders. Int. J. Pharm, 8, 104-111.

[37] Taylor, P. W. (2013). Alternative natural sources for a new generation of antibacterial agents. International journal of antimicrobial agents, 42(3), 195-201.

[38] Wahab, S., Ahmad, I., Irfan, S., Siddiqua, A., Usmani, S., & Ahmad, M. P. (2022). Pharmacological Efficacy and Safety of Glycyrrhiza glabra in the treatment of respiratory tract infections. Mini Reviews in Medicinal Chemistry, 22(11), 1476-1494.

[39] Xie, Y., Yang, W., Tang, F., Chen, X., & Ren, L. (2015). Antibacterial activities of flavonoids: structure-activity relationship and mechanism. Current medicinal chemistry, 22(1), 132-149.

[40] Xu, W., Li, Y., Ju, M., Lai, W., Lu, X., Shi, H., . . . Li, L. (2020). A multicenter, randomized, double-blind, placebo-controlled study of compound glycyrrhizin capsules combined with a topical corticosteroid in adults with chronic eczema. Evidence-Based Complementary and Alternative Medicine, 2020.

[41] Yan, Y., Li, X., Zhang, C., Lv, L., Gao, B., & Li, M. (2021). Research progress on antibacterial activities and mechanisms of natural alkaloids: A review. Antibiotics, 10(3), 318.