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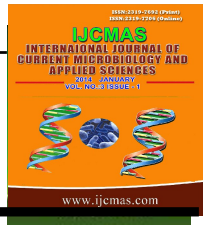


**Review Article**

# Antimicrobial activity of Yashtimadhu (*Glycyrrhiza glabra* L.) - A Review

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**A B S T R A C T**

The emergence of pandrug resistant bacteria has become a major problem.There is a continuous effort by the pharmaceutical industries to develop new antimicrobial agents for the treatment of the infections. Due to the increase of resistance to antibiotics, there is a pressing need to develop new and innovative antimicrobial agents. One approach is to screen local medicinal plants which represent a rich source of novel antimicrobial agents. Yashtimadhu (Glycyrrhiza glabra)is one such plant which has shown remarkable activity against large number of organisms, such as bacteria, fungi, viruses, parasites etc. This review has tried to give an account of multifold activity of various bioactive molecules of Yashtimadhu (Glycyrrhiza glabra)against various microorganisms.

## Introduction

The control of hospital-acquired infection caused by multi-drug resistant bacilli has proved to be a problem over the last 20 years. Such infections are often extremely difficult for the clinician to treat because of the widespread resistance of these bacteria to the major groups of antibiotics. So there is a continuous effort by the pharmaceutical industries to develop new antimicrobial agents for the treatment of the infections. The use of herbal medicines by traditional healers for the treatment of diseases remains the main stay of health care system. It is gaining increasing popularity especially among the rural population in the developing countries since it is an effective and cheap source of medical care.

The World Health Organization (WHO) estimated that about an 80% population of developing countries relies on traditional medicines, mostly plant drugs, for their primary health care needs. Particularly in

rural India, uses of raw plant products as well as some concoction of Ayurvedic medicines are sought after to a great proportion, because of cheap availability, and in urban areas too those are popular.(Debasmita Dubey, *et al*, 2012).

India is blessed with a great heritage of traditional knowledge on medicines. Ayurved, being the most ancient and still successfully practiced science amongst all these systems, needs a special attention while searching for solutions to the unresolved health problems. There exists a serious need to validate the uses of different therapeutic modalities which are in practice and can serve as a potent, safer and cost effective solution to many global disorders. (Manasi Deshpande et, al, 2011)

Yashtimadhu (*Glycyrrhiza glabra*)is one such plant which symbolizes all that is wondrous in nature because, the whole plant has been used as traditional medicine for household remedy against various human ailments from antiquity. It has been a mainstay of Ayurvedic and other traditional medicines. In ancient Ayurvedic System, more than 1250 preparations are described containing Yashtimadhu as one of its constituents. (Korhalkar A, *et al*, 2013**)**Many amongst these preparations have been successfully used in various infectious conditions.

## Method

Various scientific research and review articles published in English from 2000 to 2013 were identified through pubmed and Google scholar websites using MeSH terms, *Glycyrrhiza glabra* as anti fungal, antimicrobial agents. More than 200 research articles including few review papers were searched. These articles were grouped according to the various antimicrobial activities of *Glycyrrhiza glabra* and compiled in different sections in this review.

## Antifungal Activity

### *Candida albicans*

Over the past two decades fungal infections have evolved into important cause of morbidity and mortality in modern medicine. The prevalence of resistance to antifungal agents has significantly increased. So it makes necessary to discover new classes of antifungal compounds to treat fungal infections. There are reports which have indicated that ethanolic extract of *Glycyrrhiza glabra* has got a very good anti mycotic activity against *Candida albicans*. We found four in vitro studies on *Candida albicans.*

Active componant of *Glycyrrhiza glabra*, 18-beta glycyrrhetinic acid (18-beta GA)was studied in this paper.It showed that the in vitro growth of the *C. albicans* strains was markedly reduced, in a pH-dependent manner, by relatively low doses (6.2 microg/mL) of 18-beta GA.(Pellati D, *et al*, 2009)

This study tested Glabridin and licochalcone A of Glycyrrhiza glabra. Both licochalcone A and glabridin prevented yeast-hyphal transition in *C. albicans.* These results suggested a therapeutic potential of licochalcone A and glabridin for *C. albicans* oral infections.(Messier C, *et al*, 2011).

Glabridin componant of *Glycyrrhiza glabra* was studied in Amphotericin B resistant *C. albicans*, in this study. The ethanol root extract of *Glycyrrhiza glabra* showed a wider spectrum of activity

against various *C. albicans* strains. (Atiya Fatima, *et al*, 2009)

Meghashri and Shubha Gopal used the extracts and fractions of *Glycyrrhiza glabra* to evaluate the susceptibility against *Candida albicans* and *Trichophyton rubrum.* Both the fungi showed susceptibility to *Glycyrrhiza glabra* with MICs ranging from 0.8 to 200 mg/mL.(Meghashri, Shubha Gopal ,2009)

**Antibacterial Activity**

In the following articles we have tried to explore the scientific basis of use of *Glycyrrhiza glabra* in microbial infections.

In this study by Gupta VK *et al*, Glabridin, the active component of Glycyrrhiza glabra, exhibited antimicrobial activity against both Gram-positive and Gram-negative bacteria as well as mycobacteria.The antimycobacterial activity of *Glycyrrhiza glabra* was found at 500 microg/mL concentration. The results indicated that licorice can be used as potential antitubercular agent. (Gupta VK, *et al*. 2008)

The methanol extract of *Glycyrrhiza glabra* was used by Jae-Kwan Hwang, *et al*, to study the antibacterial activity of five plants against the cariogenic bacterium Streptococcus mutans. Five tropical plants, *Baeckea frutescens, Glycyrrhiza glabra, Kaempferia pandurata, Physalis angulata* and *Quercus infectoria,* exhibited potent antibacterial activity against the cariogenic bacterium *Streptococcus mutans.* In particular, *Glycyrrhiza glabra, K. pandurata* and *P. angulata* conferred fast killing bactericidal effect against S. mutans in 2 min at 50μg/ml of extract concentration**.** (Jae-Kwan Hwang, *et al*, 2004).

This study evaluated the antibacterial activity against Propionibacterium acne using ethanol extract of Glycyrrhiza glabra. It showed a remarkable antibacterial activity against Propionibacterium acne, with only negligible induction of resistance. The study found a marked development of resistance in the bacteria treated with erythromycin. (Nam C, *et al*, 2003)

Four papers were found which studied antibacterial effect against *Helicobacter pylori.*

The study by Fukai T.*et al* found that glabridin and glabrene componants of *Glycyrrhiza glabra* had anti-H. pylori activity against a clarithromycin (CLAR) and amoxicillin (AMOX)-resistant strain.(Fukai T, *et al*, 2002).

This study described the in vitro cytotoxicity testing against Helicobacter pylori by agar diffusion assay and study of antiadhesive properties of aqueous extract, raw polysaccharides and purified polysaccharide fractions of *Glycyrrhiza glabra* by means of an in situ adhesion assay with FITC-labeled bacteria on tissue slides of human stomach resectates. They found that the aqueous extract (1mg/mL) of *Glycyrrhiza glabra* significantly inhibited the adhesion of *Helicobacter pylori* to human stomach tissue. Aqueous extracts and polysaccharides from the roots of *Glycyrrhiza glabra* were strong antiadhesive systems. They also found strong anti adhesive effects against *Porphyromonas gingivalis.* (Nicole Wittschier, *et al*, 2009)

This study investigated the in vitro anti Helicobacter pylori activity of liquorice extract, glycyrrhizic acid, glycyrrhetinic

acid and a novel lipophilic derivative of glycyrrhetinic acid monoglucuronide (GAMG), acetylated GAMG (aGAMG), against 29 different H. pylori strains. Glycyrrhetinic acid was the most potent compound (MIC50 /90, 50/100 mg/L), inhibiting 79.3% of the strains at MIC ≤50 mg/L. Clarithromycin-resistant strains were susceptible at 12.5 and 25 mg/L, and metronidazole-resistant strains at 25–50 and at 200 mg/L. Liquorice extract, and glycyrrhizic acid were not effective, even at higher concentrations of 400 and 1600 mg/L. (Rea Krausse, et al 2004).

The findings of this study on GutGard (GutGard is a deglycyrrhizinated root extract of *Glycyrrhiza. glabra,),* revealed significant decrease in the *H. pylori*, gastric load and was found to be safe and well tolerated. Treatment with GutGard was found to be 73.2% or 3.73 times more effective than placebo. It was concluded by the authors that, GutGard supplementation could be considered as an effective alternative remedy for the management of *H. pylori.* (Sreenivasulu Puram, *et al*, 2013)

Aqueous and ethanolic extract of *Glycyrrhiza glabra* roots were assessed for the antimicrobial activity screening. Four bacterial spp. (two Gram positive and two Gram negative) - *Bacillus subtilis* MTCC (121), *Staphylococcus aureus* MTCC (96), *Pseudomonas aeruginosa* MTCC (429), *Escherichia coli* MTCC (443) and one fungal spp. *Candida albicans* MTCC (183) were used in this study. A stronger and broader spectrum of antimicrobial activity was observed in aqueous and ethanolic extracts of Glycyrrhiza glabra, as compared to the vehicle, dimethyl formamide (DMF).The diethyl ether fraction of ethanolic extract of *Glycyrrhiza glabra* showed significant antifungal and antibacterial activity in this study. (S. M. Patil, *et al*, 2009)

The finding of this paper showed the effect of glycyrrhizic acid on the growth and acid-production of *Streptococcus mutans* in vitro. The MIC for glycyrrhizic acid was 1.57 mg/mL. It inhibited the multiplication and acid-production of *Streptococcus mutans* (ATCC25175) significantly and the effects became stronger with increasing concentration. (Liu G, *et al*, 2010).

In this study, the antimicrobial properties of aqueous extracts of 40 medicinal plants were studied. *Staphylococcus aureus* MTCC 1144, *Bacillus licheniformis* MTCC 7425, *Bacillus brevis* MTCC 7404, *Bacillus subtilis* MTCC 7164, *Staphylococcus epidermidis* MTCC 3615, *Pseudomonas aeruginosa* MTCC 1034, *Escherichia coli* MTCC 1089, and laboratory isolates such as *Vibrio cholerae* , *Shigella flexneri* and *Candida krusei* were used in this study. 14 medicinal plant**s** had outstanding antimicrobial activity**.** Prominent species with antimicrobial activity included amongst others-Glycyrrhiza glabra. (H.N. Thatoi, *et al*, 2008).

Patil R. C. *et al* used aqueous, alcohol and hydroalcohol extracts of *Glycyrrhiza glabra* to evaluate the antimicrobial effect on multiple drug resistant (MDR) strains of *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Serratia marcescens, Proteus mirabilis* and *Salmonella typhi* from clinical isolates in Mumbai, Maharashtra, India. The result demonstrated that *Glycyrrhiza glabra* extracts had more antibacterial activity than the *Tinospora cordifolia* extracts.

Aqueous *Glycyrrhiza glabra* extract showed maximum antimicrobial activity against all the screened MDR strains followed by alcohol and hydroalcohol. (Patil, R. C.*et al*.2007)

In this animal study on mice, the effect of glycyrrhizin on Pseudomonas aeruginosa burn wound infection was studied in severely burned mice. The effect of glycyrrhizin on MBD (murine β-defensin) production by EK (epidermal keratinocytes), was investigated. The impaired resistance to *Pseudomonas aeruginosa* wound infection was restored in the test group when treated with glycyrrhizin and it was found inhibitory to the production of CCL2 (Chemokine ligand2) and IL-10. It improved the MBD production by EK surrounding the burn area. (Tsuyoshi Yoshida, *et al*, 2010).

Antimycobacterial activity was indicated in two studies. In this 12 weeks study, liquorice (Glycyrrhiza glabra) was used as an adjuvant in conjunction with anti-TB drugs used as DOTS. It was observed in the study that the supervised use of liquorice improved patient compliance to anti-TB drugs by providing early relief of symptoms. Sputum conversion was found in 80% patients. Fever and cough was relieved in all patients in liquorice group. (Inderpal S. *et al*, 2006).

Glabridin as the active constituent of ethanolic extract from the roots of *Glycyrrhiza glabra* was used against Mycobacterium tuberculosis in this study. The antimycobacterial activity was observed at 500 g/mL against Mycobacterium tuberculosis H37Ra and H37Rv strains through BACTEC assay. These findings of this study has established glabridin as a potent lead molecule for antimycobacterial activity. (Vivek . Gupta, *et al*, 2008).

In past decade, the use of Glycyrrhiza species for treatment of various oral infections is on rise. The following works have successfully demonstrated the use of licorice in periodontic, endodontic and dental caries infections.

This study compared the effect of adjunctive low dose doxycycline and licorice on gingival crevicular fluid (GCF) matrix metalloproteinase-8 (MMP-8) levels in patients with chronic periodontitis. This study showed that licorice extract can prevent the production of MMPs by host cells and can be as useful as antibiotics like doxycycline to cure periodontal and other inflammatory diseases. (Shirin Zahra Farhad, *et al*, 2013).

The results of this in vitro study showed that alcohol extracts of Neem, Liquorice, Clove, Cinnamon, Babool have strong antimicrobial activity against oral micro organisms like *Streptococcus mutans.* 50% concentration of extracts showed better microbial inhibition than 10% concentration except in clove extract. Extracts of Liquorice, Clove, Cinnamon, Babool had strong antimicrobial activity against *Enterococcus faecalis.* Liquorice at a concentration of 50% and at volume 75µl had an inhibitory effect on *Streptococcus mutans* and *Enterococccus faecalis.* (Dhanya Kumar N.M. Preena Sidhu, 2011).

In this in vitro study, antibacterial activity of ethanolic root extract of *Glycyrrhiza glabra* was screened against *Streptococcus mutans, Streptococcus sanguis, Streptococcus salivarius, Streptococcus mitis,* and *Lactobacillus acidophilus*. The ethanolic extract was found to be more effective against *Streptococcus mutans*

and was less effective against *Streptococcus salivarius* and *Streptococcus mitis, Lactobacillus acidophilus, Streptococcus sanguis* .The MIC and MBC values of ethanolic extract were found to be low compared to the aqueous extract. (Geetha R.V, Anitha Roy, 2012)

The antimicrobial effect of deglycyrrhizinated licorice root extracts against *Streptococcus mutans* UA159 in both the planktonic and biofilm phases was investigated in this study. The minimum inhibitory concentration and minimum bactericidal concentration was determined and time-kill kinetic, growth, adhesion, and biofilm assays were performed. The results showed that, deglycyrrhizinated licorice root extracts had strong antimicrobial activity against *S. mutans* in the planktonic phase and it significantly inhibited biofilm formation by *S. mutans* UA159 at concentrations over 4 μg/ml for glucose or 16 μg/ml for sucrose, respectively, regardless of the presence of saliva-coating. (Ahn SJ, *et al*, 2012). This study evaluated the in vitro as well as in vivo cariostatic efficacy of aqueous and ethanolic extracts of liquorice and assessed their acceptability among child patients. The findings of this study indicated that liquorice was safe, well accepted among child patients, showed fall in mutans streptococci colony counts and a rise in pH after a rinse with both aqueous and ethanolic extracts. The efficacy of liquorice extracts was evaluated in vitro also. The antimicrobial activity of the extracts was assessed and it was found that the ethanolic extract of liquorice had better antimicrobial activity than the aqueous extracts.**(**Eesha Jain, *et al*, 2013).

*Streptococcus mutans, Streptococcus sanguis, Actinomyces viscosus,* and *Enterococcus faecalis* were used as oral pathogens in this in vitro study. In vitro antibacterial activity of *Glycyrrhiza glabra* was assessed quantitatively and qualitatively by determining the inhibition zone diameter and MIC. *Glycyrrhiza glabra* extract showed good antibacterial activity against all oral pathogens. (Fereshteh Sedighinia, *et al*, 2012).

The aim of this review was to state the scope of *Glycyrrhiza glabra* as an antimicrobial agent. Time and again *Glycyrrhiza glabra* has proven to be very effective antimycotic, antimicrobial agent. In recent years, because of emergence of MDR stains, the focus of drug manufacturers is on herbal compounds. Ayurveda has been using these compounds for centuries .The evidence based proof is now being available from the work that is going on all over the world. It is evident from the data of the research in last decade, that majority of the studies are in vitro. Substantial evidence is available on animal studies. (Korhalkar A, *et al*, 2013)On the other hand studies on human subjects are fewer in number. This review hopefully can though light on the expanse of antibacterial activity of *Glycyrrhiza glabra*. As demonstrated by the examples included in this review, there is considerable evidence that *Glycyrrhiza glabra* extracts, have the potential to be developed into agents that can be used as preventive or curative antibacterial agents.

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