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## Evaluation of role of liquorice (*Glycyrrhizaglabra*) as an adjuvant in patients of pulmonary tuberculosis

Inderpal Singh Grover<sup>1</sup>, Inderpal Kaur<sup>1</sup>, Jaswant Rai<sup>1</sup>, Nirmal Kajal<sup>2</sup>

<sup>1</sup>Department of Pharmacology, <sup>2</sup>Department of Chest and TB, Government Medical College Amritsar, Amritsar, India

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### ABSTRACT

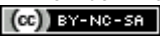
**OBJECTIVE:** To evaluate the role of Liquorice in Pulmonary Tuberculosis and its effect on adverse effects of First line Antitubercular drugs in tubercular patients. **METHODS:** Present study was a prospective, double blind, randomized, placebo control comprised of 60 patients on first line Antitubercular Therapy in DOTS strategy. **RESULTS:** In this study administration of liquorice 500 mg and matched placebo capsule twice daily for 12 weeks plus DOTS therapy was associated with better sputum conversion rate. In liquorice group, cough was relieved in 96.15% patients, fever in all and expectoration in 96.15%. In placebo group, cough was relieved in 87.4%, fever in 80.9% and expectoration in 92.5%. A significant mean increase in HRQL scores by 6.76(24.40%) in liquorice group than in placebo group. At the end of 12 weeks significant mean increase in SGPT and SGOT by 8.3IU/L (26.2%) and 2.2 IU/L (6.4%) in placebo group and non-significant mean increase by 1IU/L (2.9%) and 1.3 IU/L (3.9%) in Liquorice group. **CONCLUSION:** The present study recommends Liquorice as an adjuvant to DOTS therapy is beneficial in pulmonary tuberculosis patients in relieving symptoms and attenuating the adverse effects of anti-TB drugs, thus improving patient's treatment acceptance and early rehabilitation of TB patients.

**Keywords:** DOTS, Liquorice, Anti TB Drugs, MDR-TB, RNTC

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**Address for Correspondence:** Inderpal Kaur, Associate Professor Department of Pharmacology, Government Medical College Amritsar, India; Email: [inderpalpharma@gmail.com](mailto:inderpalpharma@gmail.com)

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## INTRODUCTION

Tuberculosis is one of the oldest diseases known to mankind. It is a well-known fact that tuberculosis (TB) is one of the largest causes of death worldwide. According to World Health Organization (WHO) one third of the world's population i.e. about 1.7 billion people are infected with mycobacterium tuberculosis of which 1.3 billion live in developing countries. In India more than 40% of the population is infected with tuberculosis. Every year 1.8 million people develop tuberculosis of which nearly 0.8 million are infectious (Sputum positive). [1]

After the discovery of effective chemotherapy against T.B, it was expected that the disease would be eventually controlled. But then came the scourge of late twentieth century Human Immunodeficiency Virus (HIV). The lethal combination of HIV infection and tuberculosis along with poor distribution of resources, multidrug resistance to tubercle bacilli and poverty added fuel to fire of tuberculosis epidemic. [2] The problem of multi drug resistance (MDR) has further complicated the situation. Globally, MDR-TB is present in 3.8% of new TB patients and 20% of patients who have a history of previous treatment.[3] MDRTB treatment is more difficult, toxic, and expensive and time consuming.

After the failure of National Tuberculosis Programme, DOTS (Directly Observed Treatment Short Course Chemotherapy) was adopted worldwide. Dr Wallace Fox gave the greatest gift to the world i.e. short course Chemotherapy (SCC). He is considered to be father of clinical trials for chemotherapy of tuberculosis. SCC is based on two phases first early killing or initial intensive phase, second sterilizing or continuation phase

As single drug therapy is insignificant and insufficient for the treatment of T.B, multi drug therapy is required so as to avoid drug resistance, to kill rapidly growing organisms to achieve greater level of efficiency, to provide the safest most effective therapy in shortest period of time and to ensure patients adherence to therapy. WHO explored the safety of herb products which are widely used but little understood keeping in view the long treatment schedule of first line anti-T.B drugs and its related side effects, various studies have been conducted on herbal medicines to evaluate their uses. WHO has also recommended importance of those herbs which may be effective in conditions, where modern therapy's safety may be lacking. [4]

WHO has recommended the use of Liquorice as demulcent for sore throat, expectorant for treatment

of cough, bronchial catarrh, prophylaxis and treatment of gastric/duodenal ulcers, dyspepsia, anti-inflammatory for treatment of allergic reactions, rheumatism and arthritis, to prevent Liver toxicity and to treat tuberculosis and adrenocorticoid insufficiency. As all first line anti-tuberculosis drugs are metabolized in Liver, so hepatotoxicity is a common problem in tubercular patients leading to derangement of hepatic enzymes i.e. ALT and AST. [5]

Liquorice with its documented evidence of antioxidant and hepatoprotective activity may be useful in tubercular patients.

## Aim and Objectives

1. To evaluate the role of Liquorice (Glycyrrhizaglabra) as an adjuvant to newly diagnosed sputum smear positive patients of pulmonary tuberculosis on Directly Observed Treatment Short Course Therapy (DOTS) under Revised National Tuberculosis Control Programme (RNTCP).
2. To observe and record the adverse events of anti-TB drugs and to see the beneficial effect of Liquorice on adverse effects of anti-TB drugs.
3. To determine the impact of Liquorice as an adjuvant to DOTS on the Health Related Quality Of Life (HRQL) scores.

## MATERIAL AND METHODS

This was prospective double blind, randomized, placebo-controlled intention to treat study. 60 newly diagnosed sputum smear positive of category I patients on DOTS under RNTCP attending OPD of chest and T.B Hospital attached with Government Medical College, Amritsar were enrolled. The duration of study was 24 weeks and the therapy was given for 12 weeks.

Exclusion criteria:-

1. Patients on Diuretics (Thiazides, Loop diuretics and Sprinolactone).
2. Cardiac, chronic renal insufficiency and patients with cirrhosis of liver.
3. Patients with antihypertensive, corticosteroids or hormones.
4. Patients who are overweight.
5. Pregnancy and lactation.

Patients were enrolled from category I of DOTS as defined under Revised National Tuberculosis Control Programme (RNTC). In category I, only newly diagnosed sputum smear positive patients were taken into the present study.

Drug Regimen used were

Category I in DOTS – 2(RHZE) 3 → 4 (RH) 3

Drugs were administered by the DOT provider only during the first visit and the medicines for the rest of the week were given to the patient and was asked to bring the empty packs of blisters when the patient came for the next visit. Patients were administered either Liquorice or placebo capsules along with DOTS for a period of 12 weeks. Capsule liquorice 500 mg and matched placebo capsule with inert lactose indistinguishable to each other was administered at an interval of 2 hours of the ATT to prevent any drug interaction.

Blinding was done at the beginning of the study. After blinding and randomization, the patients were assigned to any one group consisting of either conventional anti-tubercular therapy and capsule placebo or conventional ATT with capsule Liquorice 500 mg twice daily for 12 weeks.

Tubercular patients between 15 and 65 years of age, being put on anti tubercular drugs under RNTCP for category I were subjected to a specially designed questionnaire developed to ascertain the quality of life of tuberculosis patients. The questionnaire contained questions relating to symptoms (Symptom Score-Score I) as well as physiological, psychological and social interaction of patients (Socio-psychological and exercise adaptation Score-Score-II).

#### Parameters of Study

1. Sputum examination of patients at the start of treatment and thereafter at the end of intensive phase i.e. 8 weeks in both group A and group B.
2. SGPT and SGOT were done in both group A and group B at an interval of 4,12 and 24 weeks after taking initial baseline at 0 week.
3. Serum uric acid was estimated in both group A and group B at an interval of 4,12 and 24 weeks after taking initial baseline at 0 week.
4. Serum Sodium and Serum Potassium: Serum sodium and potassium were done at baseline in both groups and then at 12 weeks of treatment.

The results of the study were then tabulated in the form of mean  $\pm$  standard deviation (SD) and analyzed using student -'t' test. The level of significance was determined as its p value with  $p < 0.05$  taken as statistically significant.

## RESULTS

Sixty subjects had participated in this prospective double blind, randomized, placebo-controlled intention to treat study. The patients were randomized to either group A or group B consisting of ATT and cap liquorice 500 mg BD or the matched placebo. The patients were selected from OPD of Chest and T.B Hospital attached to Government Medical College, Amritsar. Two

Groups were randomly divided as A and B with 30 patients in each group.

Group A- ATT (for Cat-I) + Cap Liquorice 500 mg BD

Group B- ATT (for Cat-I) + Cap placebo 500 mg BD

Cap liquorice or placebo was given 2 hours after the ATT, to avoid any drug interaction. Base line parameters are described in Table I.

The effect of liquorice as an add on therapy with ATT on SGPT, SGOT, serum uric acid and symptoms of patients like cough, fever, body aches, weight loss, breathlessness and adverse events of ATT were evaluated and compared as described in Table II -V.

At 0 day all the 30 patients in liquorice and placebo group were sputum positive. At the end of 8-weeks, in Group A (Liquorice) 6 patients (20%) were sputum positive i.e. 80% patients sputum conversion was seen. In Group B, 9 patients (30%) were sputum positive i.e. sputum conversion was seen in 70% of patients as described in Table III

In group B there was significant sustained increase in SGPT and SGOT levels were observed at the end of 12 weeks. The mean increase in SGPT and SGOT levels were significant within the group but this increase was non-significant when compared between both groups from 12 to 24 weeks.

In group A there was insignificant mean increase in serum uric levels from 0 to 12 weeks and 12 to 24 weeks. In group B the mean increase in serum uric acid levels was significant from 0 to 12 weeks and 12 to 24 weeks. The mean increase in serum uric acid levels in both the groups was significant from 0 to 12 weeks and 12 to 24 weeks of study as described in Table V.

## DISCUSSION

Tuberculosis is one of the leading causes of morbidity and mortality in developing countries. In India more than 2 million people are affected with the disease. The conventional therapy to treat tuberculosis is of long duration and varies from 6 months to 18 months. Anti tubercular therapy has its own adverse effects rendering the patient to non-compliance thus leading to increase incidence of drug resistance. DOTS has the potential to reduce the economic and social burden of tuberculosis, however few studies have explicitly examined the question for urgent need for success of DOTS with proper adherence and reducing the side effects related with ATT. Medicinal plants from Ayurveda and from foreign origin have been successfully employed to treat tuberculosis. [6]

Liquorice has been one of the major constituent of various Ayurvedic antitubercular preparations and there is strong correlation between tuberculosis and Ayurveda.[7] Various reports have shown that the incidence of use of herbal drugs with or without Western drugs is on the rise. [8]

The present study was conducted to see the beneficial effect of Liquorice as an adjuvant to DOTS therapy. WHO also recommended that Liquorice may be used to treat tuberculosis. Traditionally Liquorice has been used as a cough suppressant and anti tussive agent. [9]

### LIQUORICE AS AN ADJUVANT TO DOTS

The cough was relieved in 96.15% patients at the end of 8 weeks in Group A and in Group B 87.4% patients. All the 27 patients in group A were afebrile at the end of 8 weeks and in group B, 80.9% patients were afebrile. In group A and B expectoration was relieved in 96.15% and 92.5% patients respectively at the end of 8 weeks. Simultaneously body aches were relieved in all the patients in group A and 86.6% patients in group B. Relief from breathlessness was observed in all the 5 patients in group A and in 75% patients in group B at the end of 8 weeks. None of the patients reported with appetite loss in group A but 42.9% patients in group B reported with loss of appetite as shown in Fig I

### SGPT AND SGOT

In the present study in group B there was significant sustained increase in SGPT and SGOT levels at the end of 12 weeks. The mean increase in SGPT and SGOT levels were significant with in the group but this increase was non-significant when compared between both groups from 12 to 24 weeks. Liquorice as an adjuvant to DOTS has shown favourable effect on liver transaminase levels. Hepatoprotective activity of liquorice is attributed to its ability to inhibit both free radical generation and lipid peroxidation. [10]

### SERUM URIC ACID

There was a significant mean increase in serum uric acid levels in both the groups from 0 to 12 weeks and 12 to 24 weeks of study but liquorice as an adjuvant to DOTS showed favorable effects on serum uric acid levels.

### SERUM SODIUM AND POTASSIUM

There was no significant mean increase in serum sodium levels from 0 to 12 weeks with in group A and group B and between both the two groups. There was no significant mean decrease in serum potassium levels from 0 to 12 weeks with in group A and group B and between both the two groups.

500mg Liquorice twice daily does not cause sodium retention and potassium loss.

### Health Related Quality of Life SCORES

In group A, mean increase in HRQL scores at 8 weeks by 6.76(24.40%) and in group B by 5.33(19.31%) was observed. The HRQL scores were significantly higher in group A. Liquorice as an adjuvant to DOTS showed better HRQL scores at the end of intensive phase.

### SAFETY PROFILE

No gastrointestinal symptoms were observed in liquorice group out of 6 at base line where as in placebo group 1(20%) patient reported symptoms from 5 patients at the end of 8 weeks. No joint pains were observed in both the groups at baseline. It was in 2(6.67%) patients in Liquorice group, 10(33.3%) in placebo group at the end of 8 weeks. No patient had calf tenderness at baseline in both the groups. In group A 3(10%) patients and in group B 9(30%) patients reported with calf tenderness at the end of 8 weeks.

Liquorice can act as potential anti-tubercular agents that can be used in combination with the standard anti-tubercular drugs. [11] This would reduce the dose of conventional anti-tubercular agents, thus reducing the dose related side-effects.

### CONCLUSION

The present study has demonstrated favorable effects of Liquorice as an add on therapy to DOTS in tubercular patients. Liquorice has shown better relief of symptoms and significantly favorable effects on liver transaminase levels and serum uric acid levels. [12,13] It has also shown improved Health Related Quality of Scores in pulmonary tuberculosis patients.

In this study administration of liquorice 500 mg and matched placebo capsule twice daily for 12 weeks plus DOTS therapy was associated with:

1. Better sputum conversion rate; 80% in liquorice group and 70% in placebo group.
2. In liquorice group, cough was relieved in 25 (96.15%) patients, fever in all the 27 patients and expectoration in 25(96.15%) patients. In placebo group, cough was relieved in 22(87.4%) patients fever in 17(80.9%) patients and expectoration in 25(92.5%) patients.
3. A significant mean increase in HRQL scores by 6.76(24.40%) in liquorice group was observed than in placebo group which was 5.33(19.31%).

AT THE END OF 12 WEEKS:-

1. Significant mean increase in SGPT b 8.3IU/L (26.2%) in placebo group and non-significant

mean increase by 1IU/L (2.9%) in Liquorice group.

- Significant mean increase in SGOT by 2.2 IU/L (6.4%) in placebo group and non significant mean increase by 1.3 IU/L(3.9%) in Liquorice group.

From the observations made in the present study it can be concluded as:

Liquorice an indigenous herb as an adjuvant to DOTS has shown better relief of symptoms viz cough, fever, expectoration and other symptoms of tuberculosis. This has shown additive type of synergism.

- Liquorice has shown favourable effect on decreasing adverse events of anti-TB drugs.
- Less sustained rise in liver transaminase levels.
- Better control of serum uric acid and levels.

- Improved Health Related Quality Of Life Scores.
- The supervised use of liquorice can be recommended as an add on therapy to DOTS.

No adverse effects were observed with 500 mg twice daily dose of liquorice.

The present study recommends that Liquorice as an adjuvant to DOTS therapy is beneficial in pulmonary tuberculosis patients in early relieving a symptoms and attenuating the adverse effects of anti-TB drugs, thus improving patient's acceptance to DOTS therapy and early rehabilitation of TB patients. However a longer and larger multicentric trial with this indigenous agent is further needed to evaluate its long term efficacy and safety profile.

There is no conflict of interest regarding publication of this paper.

**TABLE I**

<b>BASELINE CHARACTERISTICS OF PATIENTS IN STUDY GROUP</b>		
Characteristics	Group A	Group B
Number of Patients	30	30
Age (yrs) ±SD	34.93±15.9	30.2±13.73
Sex (M:F)	19:11	17:13
SGOT (IU/L±SD)	32.9±6.24	30.73±3.74
SGPT (IU/L±SD)	33.36±6.5	31.6±4.47
Na+ (meg/L±SD)	140.76±4.11	140.03±2.83
K+ (meg/L±SD)	4.15±0.40	4.23±0.45
S.Uric acid (mg/dl±SD)	4.98±0.88	4.83±0.43
Alcoholic	8 (26.6%)	10 (33.33%)
Addicts	3(10%)	1(3.33%)

Table 1 includes data of all the enrolled 60 patients with random division into two groups. This data includes the baseline characteristics like demographic profile and haematological parameters.

**TABLE II**

<b>CLINICAL PRESENTATION OF PATIENTS IN GROUP A AND GROUP B AT 0 AND 8 WEEKS</b>				
Characteristics	Group A(Liquorice)		Group B (Placebo)	
	0 week	8 week	0 week	8 week
Cough	26(86.6%)	1(3.84%)	27(90%)	5(18.5%)
Fever	22(73.3%)	0	21(70%)	4(19.04%)
Expectoration	26(86.6%)	1(3.84%)	27(90%)	2(7.40%)
Body Aches	18(60%)	0	15(50%)	2(13.33%)
Breathlessness	5(16.6%)	0	4(13.33%)	1(25%)
Nausea/Vomiting /indigestion	6(20%)	0	5(16.6%)	1(20%)
Appetite less	8(26.66%)	0	7(23.33%)	3(42.85%)

**TABLE III**

<b>SPUTUM STATUS AT 0 WEEK AND 8 WEEKS IN GROUP A (LIQUORICE) AND GROUP B (PLACEBO)</b>			
Groups	Number of Patients		
	Sputum Positive		Sputum Conversion
	0 week	8 week	8 week
A	30	6	24
B	30	9	21

**TABLE IV**

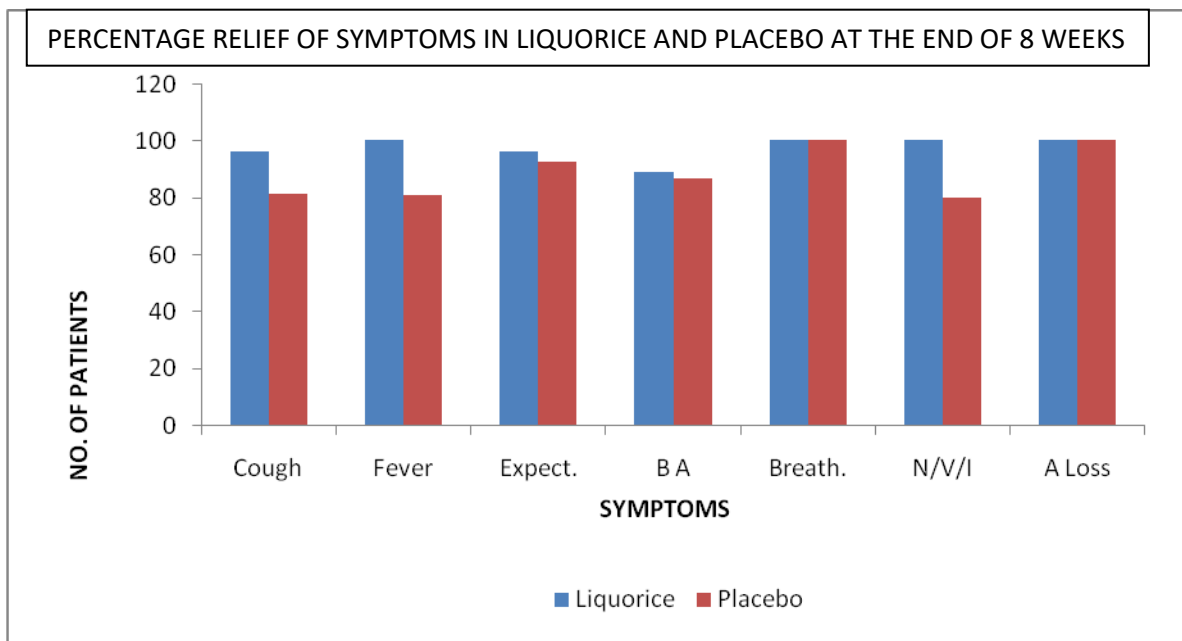
Characteristics	Group	Time period of study in weeks			
		0	4	12	24
SGOT	A	32.9±6.24	33.9±6.81	34.2±7.14	36.4±9.6
	B	30.73±4.47	35.6±8.43	38.5±11.2	39.6±11.25
SGPT	A	33.36±6.5	34.3±7.6	34.36±7.6	37.2±9.9
	B	31.6±4.47	36.13±8.9	39.96±11.	40.73±11.
Serum uric acid	A	4.97±0.88	4.8±0.48	4.8±0.48	4.93±0.65
	B	4.83±4.47	5.15±0.49	5.6±1.12	5.67±1.06

**TABLE V**

**MEAN CHANGE AND PERCENTAGE CHANGE OF SGPT, SGPT & SERUM URIC ACID (IU/L) BETWEEN 0-12, 12-24 AND 0-24 IN GROUP A AND GROUP B**

Characteristic	Group	Mean Change			Percentage Change		
		0,12	12,24	0,24	0,12	12,24	0,24
SGPT	A	1	2.84	3.9	2.9	8.2	11.6
	B	8.3	0.8	9.1	26.2	2.0	28.7
SGOT	A	1.3	2.2	3.5	3.9	6.4	10.6
	B	7.8	1.1	8.9	25.4	2.8	28.9
S. Uric Acid	A	-0.1	0.1	0	-2.0	2.0	0
	B	0.8	-0.07	0.8	16.6	-1.25	16.6

**FIGURE: I**



## REFERENCES

1. Jani Y, Bhambhani GD, Thakor N. Knowledge and awareness of tuberculosis in caregivers of paediatric tuberculosis patients of north Gujarat region, India: a cross sectional study. *International Journal of Research in Medical Sciences*. 2015;3572–5.
2. Narasimhan P, Wood J, Macintyre CR, Mathai D. Risk factors for tuberculosis. *Pulm Med*. 2013;2013:828939.
3. Seung KJ, Keshavjee S, Rich ML. Multidrug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis. *Cold Spring Harb Perspect Med*. 2015 Apr 27;5(9)
4. Benzie IFF, Wachtel-Galor S, editors. *Herbal Medicine: Biomolecular and Clinical Aspects* [Internet]. 2nd ed. Boca Raton (FL): CRC Press/Taylor & Francis; 2011
5. Jeong I, Park J-S, Cho Y-J, Yoon HI, Song J, Lee C-T, et al. Drug-induced Hepatotoxicity of Anti-tuberculosis Drugs and Their Serum Levels. *J Korean Med Sci*. 2015 Feb; 30(2) :167–72.
6. Rai R. Herbal remedies in cure of tuberculosis prevalent among ethnic communities in Central India. *Tropical plant research: an international journal*, 2016;10.
7. Huang KH, Wan CC. [Use of liquid extract of liquorice for pulmonary tuberculosis]. *Shandong Yi Kan Shantung Med Publ*. 1959 Jun;21:17–8.
8. Ceballos R LA. Use of Herbal Medicines and Implications for Conventional Drug Therapy *Medical Sciences. Alternative & Integrative Medicine* [Internet]. 2013
9. Gupta R. Yastimadhu (*Glycyrrhiza glabra*) – An important plant of Ayurvedic system of medicine. *Journal of Medicinal Plants Studies* 2016; 4(4): 30-31
10. Jeong HG, You HJ, Park SJ, Moon AR, Chung YC, Kang SK, et al. Hepatoprotective effects of 18beta-glycyrrhetic acid on carbon tetrachloride-induced liver injury: inhibition of cytochrome P450 2E1 expression. *Pharmacol Res*. 2002 Sep;46(3):221–7.
11. Gautam R, Saklani A, Jachak SM. Indian medicinal plants as a source of antimycobacterial agents. *J Ethnopharmacol*. 2007 Mar 21;110(2):200–34.
12. Hajiaghahmohammadi AA, Ziaee A, Samimi R. The efficacy of licorice root extract in decreasing transaminase activities in non-alcoholic fatty liver disease: a randomized controlled clinical trial. *Phytother Res PTR*. 2012 Sep;26(9):1381–4.
13. Liquorice (*Glycyrrhiza Glabra* Linn) as a Valuable Medicinal Plant *International journal of Advanced Biological and Biomedical Research* 2013; 1(10): 1281-1288