

## Protective Activity of *Glycyrrhizaglabra* against Histopathological Changes in White Albino Rats

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### Abstracts

The study was aimed to evaluate the protective activity of methanol-water extract of *Glycyrrhizaglabra* root (GL) against histopathological changes induced by cyclophosphamide in white albino rats. Multiple doses for drug and extract were used to investigate the accumulation effect of drug and extract on liver and kidney.

Results show that drug causes different harmful changes in rat organs in all doses concentrations used in study and extract have protective activity to prevent changes in tissue in 1000, 750 and 250 mg/kg, but dose 500 was failure to protect liver and lowest effect on kidney.

Conclusion of present study is *Glycyrrhizaglabra* useful for protective body organs against side effect of drugs and harmful effect of oxidative stress.

**Keywords:** *Glycyrrhizaglabra*, cyclophosphamide, liver, kidney.

### Introduction

*Glycyrrhizaglabra* (GL) is one of important medical plant use from long time in different country in variant applications (Fenwikeet *et al.*, 1990), *Glycyrrhiza* was classified under leguminaceae and it have 14 species (Grieve, 1995), the roots is considered as important parts of plant because it have phytochemical compounds which important in treatments like Glycyrrhetic acid and Glycyrrhizin (Isbrucker and Burdock, 2006).

Review of literature clarified the GL roles in different researches, some of these showed that GL have antimutagenesis activity against some alkylating agent like Ethylmethanesulfonate (EMS) in mice test (Mistsheret *et al.*, 1986), so Alekperova (2002) improved that the GL has antimutagenesis activity by use with another plant it was decreased chromosome aberration in mice bone marrow that induced by physical and chemical factor, the GL have antioxidant activity by protect LDL from free radical effect (Fuhrman *et al.*, 1997) and protect the liver tissue from oxidative stress induced by voltarine drug (Hamza, 2007). Because of the GL contain phenolic compounds it is have anticancer activity by decrease anti apoptotic suppression protein Bcl-2 (Rafi *et al.*, 2003). In another hand it appeared anticancer activity, Kanazawa *et al.*, (2003) improved anticancer activity of GL by using isoliquiritin to enhancement protein of cell that responsible on stop lifecycle in G2/M and S phase. Also it uses to treated cold, antitussive and arthritis (Hoffman, 1996; Paoliniet *et al.*, 1998).

Cyclophosphamide is anticancer drug, alkylating agent that interfere with transcription and translation of nucleic acid as a result this effect on cell proliferation, it has been used as mutagenicity factor in wide range of experiments (Al-Terehi *et al.*, 2012)

### Materials and methods

- 1- Plant extract : GL root powder homogenize with solvent mixture (methanol: distilled water) (20:80 v/v) in blender for 30 min, the mixture was infiltration and dry in oven 50 °C for 24 hours, the product store in dark container (Sato *et al.*, 1990)
- 2- Drug: cyclophosphamide (Baxter, German).
- 3- Doses use 20, 15, 10, 5 mg/kg of cyclophosphamide, plant extract doses were 1000, 750, 500, 250 mg/kg
- 4- Animal: use white albino rat 300±50 mg weight and 12 weeks.
- 5- Experimental design : animals was divided in 4 groups
  - 1) Group treated by 20 mg/kg CP with 1000 mg/kg GL for 7 days.
  - 2) Group treated by 15 mg/kg CP with 750 mg/kg GL for 10 days.
  - 3) Group treated by 10 mg/kg CP with 500 mg/kg GL for 15 days.
  - 4) Group treated by 5 mg/kg CP with 250 mg/kg GL for 35 days.
  - 5) Group treated by D.W. As negative control.
  - 6) Group treated by CP (20, 15, 10, 5) mg/kg only as positive control.

Animals were sacrificed, after exposure time was finished, liver, and kidney were collected to prepare sectioning. Sectioning was prepared according to Humason (1997).

## Results

Histological studying show histopathological changes in rats' organs that treated by cyclophosphamide only while rats treated by drug and plants extract show low effects.

Animals treated 15 and 20 mg/kg of cyclophosphamide causes necrosis in some glomeruli and missed other glomeruli that clarified as space in figure (1,A). Also drug causes edema in kidney tissue that showed in figure (1,B).

In figure (1,D) bleeding and shrinkage in glomeruli. In another hand drug causes missed nucleus in cells tubules of kidney and renal tubules filled with homogenous a cellular eosinophilia materials, this is show in figure (1,E). In liver dose 20 mg/kg of drug causes necrosis in liver tissue with hemolysis in central vein, while 10mg/kg of drug causes vascular injection in kidney and liver.

When rats treated by plant extract with drugs as showed in experimental design all dose concentrations have able to protect tissue except the dose 500mg/kg it can't protect liver tissue from harmful changes figure (1,F ) AND (2,B) show normal tissue in rats treated by drug and plant extract in 1000, 750, 250 mg/kg and 20, 15, 5 mg/kg respectively.

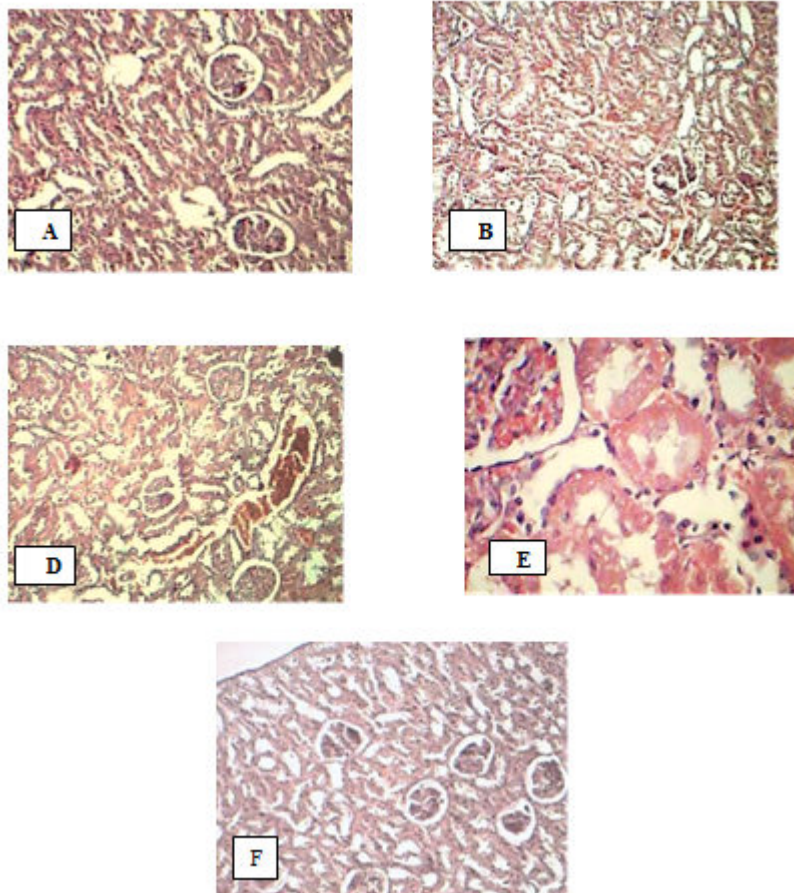


Figure (1) cross section of kidney tissue of rats treated by cyclophosphamide (A, B, D, and E) and for rats treated by cyclophosphamide and plant extract (F).

A, necrosis in some glomeruli and missed other glomeruli.

B, drug causes edema in kidney tissue and fragment in glomeruli.

D, drug causes bleeding and fragment in glomeruli.

E, missed in tubular cell nucleus. F, normal tissue.

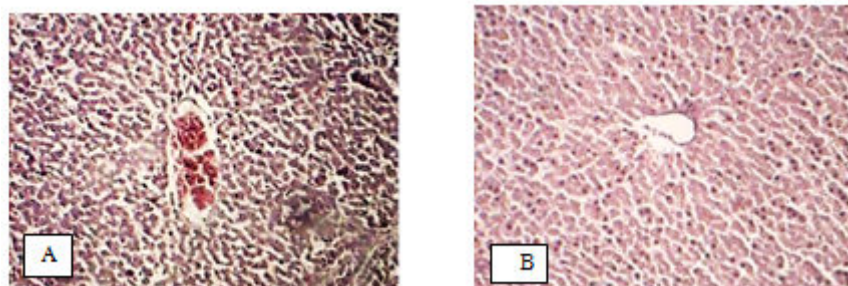


Figure (2) cross section of liver tissue of rats treated by cyclophosphamide (A) and rats that treated by cyclophosphamide and plant extract (B).

A, congestion and necrosis in central vein of liver.

B, normal tissue.

### Discussion

The reasons of choose liquors in present study was its large application in world and low side effects which were improved in researches. As showed in literaturereview , there are different uses of liquesce in medical, food and industrial .

Researcherstudying side effect of some drugs like histological changes, cytotoxic and genotoxic effects thus uses in present study cyclophosphamide which causes histologicalchanges in liver and kidney in different concentration didn't uses in previous studies, results showed that kidney more effect than liver as showed in figure 1and 2, study suggested that liver have detoxification function thus its affected by toxic compound was low compare with other organs, this results deal with Cohen *et al.*, (1992) they improved that drug causes congestion in bladder and hyperplasia in rats treated by cyclophosphamide, also it causes hyperplasia and delayed in embryonic fetal growing (Lucia and Azoubel, 2005).

This changes result from effect of acroline compound which is main composition of cyclophosphamide metabolized products, it consider as cytotoxic in vivo and in vitro experiments (Sakata *et al.*, 1989). Ray and Potu found that cyclophosphamidecausesstopped in ovulation process in femaleofrats that treated by 100 mg/kg . Conclusion from other studies, these changes may be causedby oxidative stress which causes elevated in free radicals that invasion cell compartments and causes changes in its composition and functions; studying improved that cyclophosphamide causes generation freeradicals and oxidative stress (salvia *et al.*, 1999).

When ratstreatedby drug and plantextract, plant extract improved good activity in protect liver and kidney from harmful effects of cyclophosphamide, this may because antioxidant activity of GL, Hamza (2007) improve that GL lowest formed necrosis in liver induction by oxidativestress. The antioxidant activity of GL was improved using beta-caroteinn spry method by Al-turiaheet *al.*,(2012).The protective activity of this extract may be its consist formdifferent phytochemical compounds roles in protective activity of liver formed cytotoxiccompound such as aflatoxinsand CCl<sub>4</sub>.(Jeonget *al.*, 2002).

Antioxidant enzymehave main roles in detoxification of some compounds such as GSH that have roles in interaction with toxic compound and its metabolic forms (Ranaet *al.*, 2002) . hamza (2007) suggested that GL induce GSH enzyme.Kent *et al.*, (2002) found that GL inhibition many enzymesresponsible on metabolism of some compound to cytotoxic forms like cytochrome 3A4 and P450s.

### References

- Fenwike, G. R. ; Lotuomski, J. and Nieman, C. (1990). LiquoriceGlycyrrhizaglabra L. Composition uses and analysis. FoodChemistry., **38**, 119-143.
- Isbrucker, R. and Burdock, G.(2006) . Risk and safety assessment onthe consumption of licorice root (Glycyrrhiza sp. ) its extract and powder as a food ingredient, with emphasis on the pharmacology and toxicology of glycyrrhizin. Regulatory toxi. and pharma.,**46**,167-192.
- Alekperov, U. K. (2002) . Plant antimutagens and their mixture ininhibition of genotoxic effect of xenobiotics and aging processes.Institute of Genetics. , **2**, 8-11.
- Fuhrman B. ; Buch, S. ; Vaya, J. ; Belinky, PA. ; Coleman, R. andHayek, A. (1997) . Licorice extract and its major polyphenolGlabirdin protect low- density lipoprotein against lipidperoxidation in vivo and ex vivo studies in human and inatherosclerotic apolipoprotien deficient mice. Am. J. Clin. Nutr.**66**, 267-275.
- Hamza, A. A. (2007). Curcuma longa , Glycyrrhizaglabra andMoringaoleifera Ameliorate Diclofenac-induced Hepatotoxicityin rat.Ame. J. of pharm. and toxo. **2** , 80-88.
- Mistsher, L. A. ; Drake, S. ; Gollapudi, S.R. ; Harris, J.A. andShankel, D.M. (1986) . Isolation and identification of higher plantagent active in antimutagenic assay system Glycyrrhizaglabra.Basic life Sci. ,

39 ,153-165 .

- Kanazawa , M. ; Satomi, Y. ; Mizutani, Y. ; Ukimura, O. ; Kawauchi, A. ; Sakai, T. ; Baba, M. ; Okuyama, T. ; Nishino, H. ; Miki, T.(2003). Isoliquiritigenin inhibits the growth of prostate cancer .Kyoto, Japan , Eur. Urol.,**43**, 580-586.
- Paolini, M.; Pozzetti, L.; Sapore, A. and Cantelli-Forti, G. (1998).Effect of licorice and glycyrrhizin on murine liver Cyp-dependent monooxygenases. Life Sci.,**62**, 571-582.
- Sato, T. ; Onse, Y. ; Nagase, H. and Kito, H. (1990). Mechanism of antimutagenicity of aquatic plant extracts against (benzo (a)pyrene) in the Salmonella assay .J. Mut. Res . ,**241**,283-290 .
- Humason, G. (1997). Humason animal tissue techniques. 5th ed.London.
- Cohen, S. M. ; Emily, M. G. and Margaret, S. J. (1992) . Acrolein Initiates rat urinary bladder carcinogenesis. Cancer Res.,**52**,3577-3581.
- Lucia, M. B. and Azoubel, R. (2005) .Cyclophosphamide effect on the epithelial covering of rat fetuses tongue a morphometric study .Int. J. Morphol.,**23**, 105-109 .
- Sakata, T.; Smith, R. A. ; Garland, E. M. and Cohen, S. M.(1989) .Rat urinary bladder epithelial lesions induced by acrolein. J. Exp.Pathol. Toxicol. Oncol.,**9**, 159-170.
- Salvia, R. ; Fiore, M. ; Aglitti, T.; Fasta, F. ; Ricordy, R. ; and Cozzi,R.(1999) . Inhibitory action of melatonin on H<sub>2</sub>O<sub>2</sub> and cyclophosphamide induced DNA damage. Mutagenesis, **14**, 107-112.
- Jeong, H. ; You, H. J. ; Park, S. J. and Chun, A. K. (2002)Hepatoprotective effects of 18β - Glycyrrhetic acid on carbon tetrachloride-induced liver injury : inhibition of cytochrome P450 2 E1 Expression. Pharmac. Res. **46**, 221-227.
- Rana, S. V. ; Allen, T. and Singh, R. (2002) .Inevitable glutathione then and now . Indian J. Exp. Biol. **40**, 706-716.
- Kent, M. U. ; Michael, A. ; Mira, R. and Paul, F. H. (2002). The Licorice root derived isoflavanglabridin inhibits the activities of human cytochrome P450 , 3A4 , 2B6 and 2C2 . DMD . **30**,709-715.
- Al-Terehi, M. . Al Saadi , A. H. Al Ameri, Q. (2012). *In vivo* study of antimutagenic and antioxidant activity of *Glycyrrhiza glabra* root extract . research in pharmacy ,**2**,27-34.