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Protective Activity of *Glycyrrihzaglabra* against Histopathological Changes in White Albino Rats

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Abstracts
The study was aimsto evaluation the protective activity of methanol-water extract of *Glycyrrihzaglabra*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 onliver 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 *Glycyrrihzaglabra*useful for protective body organs against side effect of drugs and harmful effect of oxidative stress.
Keywords: *Glycyrrihzaglabra* ,cyclophosphamide, liver, kidney.

Introduction

Glycyrrihzaglabra (GL) is one of important medical plant use from long time in different country in variant applications (Fenwike*et al*., 1990), ***Glycyrrihza***was classified under ligumenacea and it have 14 species (Grieve, 1995), the roots is considered as important parts of plant because it havephytochemicalcompoundswhich important in treatments like Glycyrrihetinic acid and Glycyrrhizin (Isbruker and Burdock, 2006).
Review of literature clarified the GL roles in different researches, some of these showed that GL have antimutagenesis activity against some alkalating agent like Ethylmethansulfonat (EMS) in aims test (Mistsher*et al*., 1986), soAlekperove (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 *Bc-L2* (Rafi *et al*., 2003).
In another hand it appeared anticancer activity, Kanazaawa*et al* ., (2003) improved anticancer activity of GL by using isoliquritignin 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; Paolini*et al*., 1998).
Cyclophosphamide is anticancer drug, alkalating 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: distal water) (20:80 v\v) in blander 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: cyclophosphomidetamp let (Baxter, German).
3- Doses use 20 , 15, 10 , 5 mg\kg of cyclophosphomide, plant extract doses were 1000, 750, 500, 250 mg\kg
4- Animal: use white albino rat 300±50 mg weight and 12 weak.
5- Experimental design : animals was divided in 4 group
   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 750mg\kg GL for 10 days.
   3) Group treated by 10 mg\kg mg 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 victimized, 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.

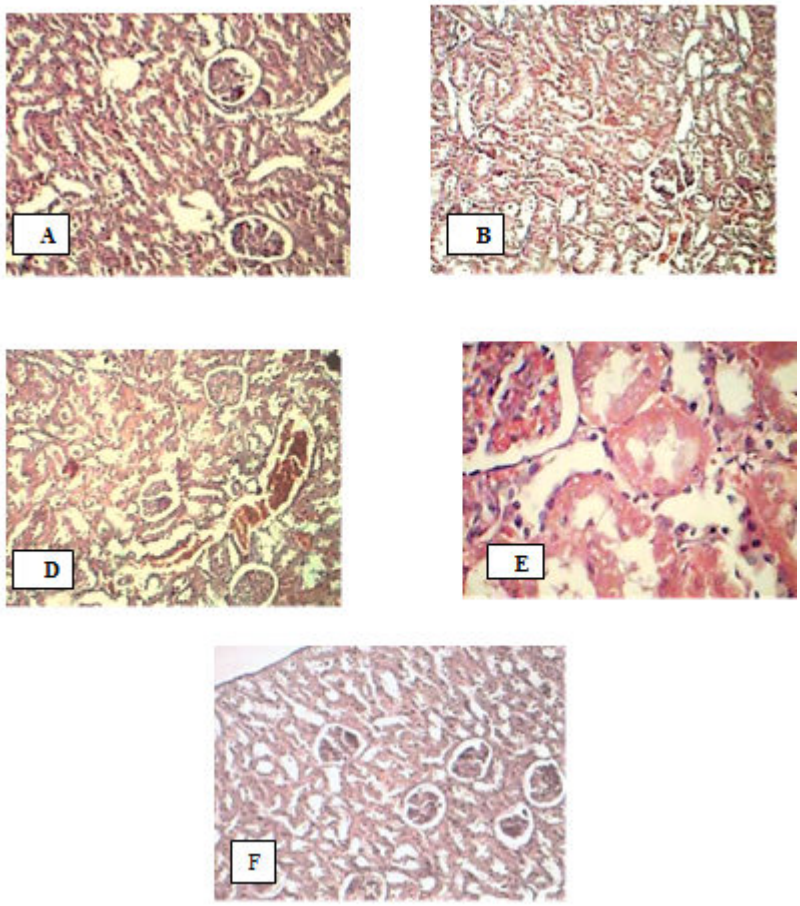

Figure (1) cross section of kidney tissueof rats treated by cyclophosphamide (A, B, D, and E) and for rats treated by cyclophosphamide and plant extract (F).

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.

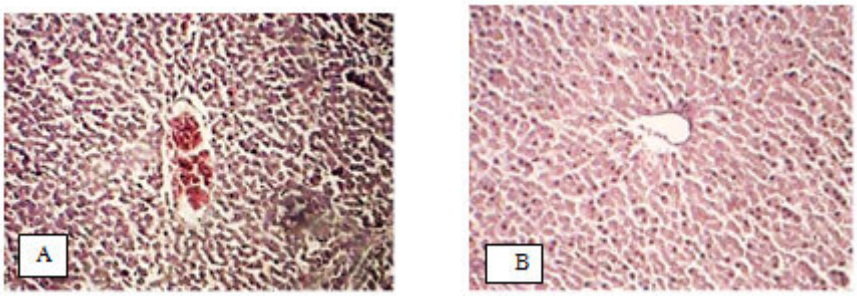

Figure (2) cross section of liver tissue of rats treated by cyclophosphamide (A) and rats that treated by cyclophosphamide and plant extract (B).
A, congestion and necrosis in central vein of liver.
B, normal tissue.

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 .

Researchersstudying 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-carotein spry method by Al-turiahe*et 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_4.(Jeong*et 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 (Rana*et 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.

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