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Hepatoprotective Activity of Aqueous Extract of Some Astraceae Plants against Carbon Tetrachloride-Induced Hepatotoxicity in Rats

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Abstract

This study was performed to evaluate the in vivo toxicity and hepatoprotective activity of aqueous extract of of *Echinacea purpurea* and *Stevia rebaudiana* aerial parts belonging to Family *Asteraceae*.The acute toxicity examination for aqueous extract of *Echinacea purpurea* and *Stevia rebaudiana* aerial parts clearly indicated that, the extract under investigation is non-toxic and safe in rats up to 6000 and 5500 mg/kg b.wt respectively .The aqueous extracts of *Echinacea purpurea* and *Stevia rebaudiana* aerial parts at a dose of 600 and 550 mg/kg body weight exhibited moderate protective effect by lowering the serum levels of alanine aminotransferase (ALT) aspartate aminotransferase (AST),total protein and albumin Compared with different doses of carbon tetrachloride treated group.

Key wards: Hepatoprotective, *Echinacea purpurea*, *Stevia rebaudiana*, *Asteraceae*, Carbon tetra chloride, sylimarine

introduction

Liver is a vital organ of paramount importance involved in the maintenance of metabolic functions and detoxification of the exogenous and endogenous challenges like xenobiotics, drugs, viral infections and chronic alcoholism (**Dienstag and Isselbache, 2011**).

Although viruses are the main cause of liver diseases, excessive drug therapy, environmental pollution and alcoholic intoxication are not uncommon. Liver disease is a worldwide problem; Conventional drugs used in the treatment of liver diseases are sometimes inadequate and can have serious adverse effects.

Herbal medicines are in great demand in the developed as well as developing countries for primary healthcare because of their wide biological and medicinal activities, higher safety margins and lesser costs (**Chattopadhyayand Bhattacharyya, 2007**).

Asteraceae species have been used in the Brazilian folk medicine for several therapeutic purposes **(Ferrari *et al.*, 2012)** and some of *Asteraceae* plants are used in protection of liver (**Morais and Castanha, 2011**).

The herb *Echinacea purpurea* and (purple coneflower, *Asteraceae*), where commercially available preparations are widely used in the prevention or treatment of upper respiratory tract infections because of their immune modulator and stimulant properties (**Bielory2004; Carr and Nahata, 2006**).

Stevia rebaudiana (Bertoni) family *Asteraceae* is an herbaceous perennial plant indigenous to Paraguay and Brazil where its leaves are used by the local Guarani Indians as natural sweetener for hundreds of years. About 150 stevia species are known, among them *Stevia rebaudiana*is the only one with significant sweet tasting properties. This plant is of worldwide importance today because its leaves are used as non-nutritive high potency sweetener primarily in Japan

extracts ware filtrated by filter papers, were stored in refrigerator for further use.

Animals: Male albino rates weighting 120_150 gm were obtained from animal-house of Faculty of Pharmacy – Al-Azhar Univ. Cairo, were used at different intervals during the experimental period. Animals were maintained under standard conditions of temperature (22±1°C), relative humidity (55±10%), and 12-h light: 12-h dark cycle, and fed a standard pellet diet with water. They were housed in standard polypropylene cages with wire mesh top. The use of animals was in accordance with the rules of the Institutional animal ethical committee.

Experimantal design

Liver toxicity was induced in rats following subcutaneous injection of CCl_4 (1:1 v/v in corn oil) in the lower abdomen at the dose of 3 ml/kg (**Théophilea *et al*, 2006**). Thirty adult male Wistar albino rats (120_150g b.wt.) were randomly divided into (XI) groups of six animals for each one of plants. Rats of group I, normal control and group II, high dose control (3 ml/kg) from CCl_4. Animals of group III, low dose control (1) ml/kg of CCl_4 intoxicated control were received water only, Animals of group IV the Silymarin group received silymarin at a dose of 25 mg/kg with high dose CCl_4. Groups V silymarine at a dose of 25 mg/kg with low dose CCl_4. VI, VII and VIII groups different dose (high, modret, low doses) from plant extracts for *Echinacea purpurea (*600, 400 and 275 ml/kg) for *Stevia rebaudiana* (550, 375 and 275 ml/kg) with high dose (3 mg/kg) from CCl_4. IX, X, XI groups different dose from plant extracts for *Echinacea purpurea (*600, 450 and 300 ml/kg) for *Stevia rebaudiana* (550, 375 and 275 ml/kg) with low dose (1 ml/kg) from CCl_4. All medications were given orally by gastric intubation for 8 days.

,Korea, China and South America. The consumption of stevia extract in Japan and Korea is about 200 and 115 tons/year, respectively **(Kinghorn and Soejarto, 2002)**. The water extract of *Stevia rebaudiana* has beneficial effects on human health, including hypoglycemic **(Jeppesen *et al*., 2002),** hypotensive (**Melis 1992**) and renal effects (**Melis, 1995).** We can say that aqueous extract of *Stevia rebaudiana* has potential hepatoprotective activity **(DAS, 2012).**

So we need to test the efficacy of *Echinacea purpurea* and *Stevia rebaudiana* on the liver.in thes study of the efficacy of aqueous plant extract of *Echinacea purpurea* and *Stevia rebaudiana* were tested against CCl_4 induced liver damage in rats .

Material and methods

Plant material

Echinacea purpurea: *Echinacea* plants were parchased from commercial sellers and the taxonomic identification of plant materials was confirmed by Dr. Atea Essa Mohammed, lecturer of plant taxonomy, faculty of science, Helwan University. They were cleaned, air-dried at lab temperature, then dried in oven at 40°C till constant weight, and finally ground to fine powder.

Stevia rebaudiana: Stevia plants were collected from fild in agricalure research center in cairo, Egypt (ARC) sellers and the taxonomic identification of plant materials was confirmed by Dr. Atea Essa Mohammed, lecturer of plant taxonomy, faulty of science, Helwan University. They were cleaned, air-dried at lab temperature, then dried in oven at 40 °C till constant weight, and finally ground to fine powder.

Preparation of extraction: 100 g of dry aerial plant powder was suspended in water at ratio of 1:6600 and then the

After 48 h of CCl_4 treatment, rats were anesthetized by anesthetic ether and blood samples were drawn. Sera were separated to be used for the biochemical estimations serum (AST, ALT, Total protein, Albumin).

On the last day of the treatment, rats of group I was given a single subcutaneous dose of corn oil (3 ml/kg), while animals of the groups II, IV VI, VII , VIII were received a single subcutaneous high dose (3 ml/kg) of CCl_4 after extract. while III, V, IX, X , XI .were received a single subcutaneous low dose(1 kg/kg)

Results

Table 1 Result for *Echinacea purpurea*

H=high conc from extract M= moderate conc from extract L= low conc from extract

Liver profile		high dose of CCl_4(3 ml/kg)				low dose of CCl_4(1 ml/kg)			
NO.	doses	Alt	Ast	Total protein	Albumin	Alt	Ast	Total protein	Albumin
		(U/L)		(g/dl)		(U/L)		(g/dl)	
1	**normal control** Range Mean ±SE	**17-23 21.50±1.76**	**29-34 32.8±1.25**	**6.9-7.6 7.20±0.26**	**3.9-4.3 4.10±0.17**	**17-23 21.50±1.76**	**29-34 32.8±1.25**	**6.9-7.6 7.20±0.26**	**3.9-4.3 4.10±0.17**
2	**CCl_4 control** Range Mean ±SE	**251-286 270.2±3.74**	**241 -249 245 ± 3.28**	**4.1-4.7 4.4±0.25**	**2.6-3.1 2.85 ±0.57**	**188 - 193 190.5 ±1.67**	**168-179 173.5 ±4.24**	**5.2-5.67 5.43 ± 0.32**	**3.16 - 3.89 3.52 ±0.19**
3	**lymarin+CCl_4** Range Mean ±SE	**148.3-152 150.20±1.67**	**143-149 145±4.24**	**4.96 -5.19 6.80±0.32**	**2.76- 3.89 3.32 ± 0.19**	**118.3-122 120.15±1.67**	**118-129 125±4.24**	**5.69-5.88 6.80±0.32**	**3.54 -3.96 3.75 ± 0.19**
4	**H+CCl_4** Range Mean ±SE	**218.3-222 220.20±1.67**	**218-229 225±4.24**	**4.2-4.43 4.31±0.32**	**2.7-3.2 2.95 ±0.19**	**168.3-172 170 ±1.67**	**148-151 149.5±1.24**	**5.32-5.43 5.37 ± 0.32**	**3.14 -3.68 3.41 ±0.19**
5	**M+CCl_4** Range Mean ±SE	**248.3 - 252 250.20±1.67**	**229-129 125±4.24**	**3.9 - 4.1 6.80±0.32**	**2.7- 3 2.85 ± 0.19**	**201 – 203.9 202.4 ±1.01**	**196-199 197.5 ±1.24**	**4.9 - 5.1 5 ± 0.32**	**2.96 – 3.09 3.02 ± 0.19**
6	**L+CCl_4** Range Mean ±SE	**256-259 257.7 ±1.67**	**260 -263 261.5 ±4.24**	**3.79-3.96 3.87±0.32**	**2.6-2.99 2.79 ±0.19**	**226-229 227.5 ±1.67**	**219 -223 221 ± 2.24**	**4.79-4.96 4.87±0.32**	**2.66-2.99 2.82 ±0.19**

doses show that, (170±1.67, 202.4±1.01, 227.5±1.67 IU/L), (149.5±1.24, 197.5±1.24, 221±2.24 IU/L), (5.37±0.32, 5±0.32, 4.87±0.32 g/dl) (3.41±0.19, 3.02±0.19, 2.82±0.19 IU/L) respectively, compared with CCl_4 control (190.5±1.67 IU/L), (173.5±4.24 IU/L) , (5.43±0.32 g/dl) and (3.52±0.19 g/dl) but sylimarin group (120.15±1.67 IU/L), (125±4.24

Table 1 showed that

Aqueous extract of *Echinacea purpurea* at different dose levels (600 , 450 and 300 mg/kg/day) with low dose of CCl_4(1 mg/kg) were evaluated, Oral administration resulted show that, alanine aminotransferase, aspartate transaminase, Total protein and Total albumin of each 3

3.87±0.32 g/dl) and (2.95±0.19, 2.85±0.19, 2.79 ±0.19 g/dl) comparing with CCl_4 control group ther results (270.2±3.74 IU/L) ,(245±3.28 IU/L) ,(4.4±0.25 g/dl) and (2.85±0.57 g/dl) but sylimarin group result show that (150.20±1.67 IU/L), (145±4.24 IU/L) (6.80±0.32 g/dl) and (3.32±0.19 g/dl).

Table 2 Result for *Stevia rebaudiana*

Liver profile		High dose of Ccl_4				Low dose of Ccl_4			
		ALT	AST	Total protein	Albumin	ALT	Ast	Total protein	Albumin
No	group	(U/L)		(g/dl)		(U/L)		(g/dl)	
1	**normal control**								
	Range	**17-23**	**29-34**	**6.9-7.6**	**3.9-4.3**	**17-23**	**29-34**	**6.9-7.6**	**3.9-4.3**
	Mean ±SE	**21.50±1.76**	**32.8±1.25**	**7.20±0.26**	**4.10±0.17**	**21.50±1.76**	**32.8±1.25**	**7.20±0.26**	**4.10±0.17**
2	**CCl_4 control**								
	Range	**251-286**	**241 -249**	**4.1-4.7**	**2.6-3.1**	**188 – 193**	**168-179**	**5.2-5.67**	**3.16 - 3.89**
	Mean ±SE	**270.2±3.74**	**245 ± 3.28**	**4.40±0.25**	**2.85 ±0.57**	**190.5 ±1.67**	**173.5 ±4.24**	**5.43 ± 0.32**	**3.52 ±0.19**
3	**ilymarin+CC l_4**								
	Range	**148.3-152**	**143-149**	**4.96 -5.19**	**2.76- 3.89**	**118.3-122**	**118-129**	**5.69-5.88**	**3.54 -3.96**
	Mean ±SE	**150.20±1.67**	**145±4.24**	**6.80±0.32**	**3.32 ± 0.19**	**120.15±1.67**	**125±4.24**	**6.80±0.32**	**3.75 ± 0.19**
4	**H+CCl_4**								
	Range	**128- 137**	**129-172**	**3.83- 4.17**	**2.77- 3.13**	**190-215**	**209-225**	**3.65-4.16**	**3.04-3.27**
	Mean ±SE	**132±1.16**	**170±2.13**	**4.02±0.41**	**2.97± 0.44**	**199±3.14**	**213±4.15**	**3.87± 0.62**	**3.11±0.11**
5	**M+CCl_4-1**								
	Range	**165- 179**	**190-194**	**3.64 -4.01**	**3.08-3.41**	**213– 221**	**216-262**	**2.85- 3.29**	**2.30– 2.48**
	Mean ±SE	**171±3.12**	**192±1.14**	**3.77±0.52**	**3.12±0.33**	**217±3.13**	**240±6.18**	**3.03± 0.12**	**2.37± 0.17**
6	**L+CCl_4-1**								
	Range	**240-251**	**237-243**	**2.67-3.14**	**3.03-3.24**	**177-185**	**160-178**	**4.87-5.19**	**2.87-3.19**
	Mean ±SE	**244±2.15**	**240±2.19**	**2.88±0.64**	**3.11±0.17**	**181±2.14**	**168± 0.14**	**4.59±0.47**	**3.01±0.18**

While this different dose of *Echinacea* extracts (600, 450 and 300 mg/kg/day) with high dose of CCl_4 (3 mg/kg) show that, (220.20±1.67, 250.20±1 257.7±1.67 .67IU/L) ,(225±4.24, 125±4.24, 261.5±4.24 IU/L),(4.31±0.32, 6.80±0.32, IU/L) (6.80±0.32 g/dl) and (3.75±0.19 g/dl).

different doses of carbon tetrachloride treated group.

The effect of *Echinacea purpurea* and *Stevia rebaudiana* may be Because it have some important secondary metabolits. The *Echinacea* herb has many constituents including glycoproteins, alkamides, polyacetylene flavonoids, caffeic acid derivatives, polysaccharides, and volatile oils. The concentration of the active ingredients. **(Bauer 1998; Bauer and Woelkart2005)**. The chemical composition of *Echinacea* may be responsible for the obtained results. *Stevia* aqueous extracts showed hepatoprotective effect may be due to secondary metabolites to confirm that we need subjected *Stevia* aqueous extracts to phytochemical screening.

Conclusion

It can be concluded that aqueous extracts of some *Astereace* plants (*Stevia eebaudiana* and *Echinacea purpurea*) have moderate hepatoprotective activity against CCl_4 inducing liver toxicity.

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Tabe 2. Showed that.

Aqueous extract of *Stevia rebaudiana* at different dose levels of (550, 375 and 275)mg/kg/day with low dose of CCl_4 (1 mg/kg) were evaluated. Oral administration resulted show that, Alanine aminotransferase, Aspartate transaminase, Total protein and Albumin (199±3.14, 217±3.13, 181±2.14 IU/L),(213±4.15, 240±6.18, 168±0.14 IU/L),(3.87±0.62, 3.03±0.12, 4.59±0.47 g/dl) and (3.11±0.11, 2.37±0.17, 3.01±0.18 IU/L) compared with CCl_4 control group (190.5±1.67 IU/L) ,(173.5±4.24 IU/L) ,(5.43±0.32 g/dl) and (3.52±0.19 g/dl) but silymarine group (120.15±1.67 IU/L), (125±4.24 IU/L) ,(6.80±0.32 g/dl) and (3.75±0.19 g/dl).

while this different doses of plant extracts (550, 375 and 275 mg/kg/day) with high dose of CCl_4 (3 mg/kg) show (132±1.16, 171±3.12, 244±2.15 IU/L),(170±2.13, 192±1.14, 240±2.19 IU/L),(4.02±0.41, 3.77±0.52, 2.88±0.64 g/dl) and (2.97±0.44, 3.12±0.33, 3.11±0.17 g/dl) comparing with CCl_4 control group (270.2±3.74 IU/L) ,(245±3.28 IU/L) ,(4.40±0.25 g/dl) and (2.85±0.57 g/dl) but sylimarin group (150.20±1.67 IU/L), (145±4.24 IU/L) ,(6.80±0.32 g/dl) and (3.32±0.19 g/dl). On other hand the result of normal control group show that (21.50±1.76 IU/L),(32.8±1.25 IU/L),(7.20±0.26 g/dl) and (4.10±0.17 g/dl).

Discussion

The present study investigated the effect of a different doses of *Echinacea purpurea* and *Stevia rebaudiana* extracts in a model of hepatotoxicity induced by CCl_4 in rats. Findings of the present study indicated that the administration of the different doses *Echinacea* and *Stevia* extracts to CCl_4-treated rats showed moderate protective effect by lowering the liver marker enzymes Compared with

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