Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Der Pharmacia Lettre, 2010, 2(6): 52-59
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-5071
USA CODEN: DPLEB4

Comparative evaluation of hepatoprotective activity of *Andrographis paniculata* and Silymarin in ethanol induced hepatotoxicity in albino wistar rats

S.Vetriselvan*, Victor Rajamanikkam[1], Parimala Devi[1] Subasini[2], G. Arun[3]

**Rural College of Pharmacy, Devanahali, Bangalore, India*
[1]Sastra University, Thanjavur, India
[2]Vivekanantha College of Pharmacy, Thiruchankodu, India
[3]E. G. S. College of Pharmacy, Nagapattinam, India

ABSTRACT

The effect of Andrographis Paniculata extract was studied on ethanol induced hepatic damage in rats.Treatment with aqueous extract of A.Paniculata (50mg/kg,100mg/kg,200mg/kg body weight)was found to protect the rat from hepato-toxin action of ethanol an evidenced significant reduction in the elevated serum transaminase levels.Histopathological studies showed marked reduction in fatty degeneration and centrizonal necrosis in animals receiving different doses of A.Paniculata along with ethanol as compared to the control group. The rat administered silymarin(50mg/kg) used for comparative evaluation, showed a significant reduction in serum enzyme activity and normal liver.It is stipulated that the extract treated groups were partially protected from hepatocelur damage caused by ethanol.

Key words: *Andrographis paniculata*, Silymarin, Ethanol, Albino wistar rats.

INTRODUCTION

Liver disease is a worldwide problem. Liver is a organ of paramount importance as a plays an essential role in maintaining the biological equilibrium of vetabrates. The spectrums of functions(20) include: metabolism(31)and disposition of chemicals (4,5)(xenobiotics) to which the organ is exposed directly or indirectly: metabolism of lipids,carbohydrates and proteins; blood coagulation and immunomodulation(9,10,11,12).

Treatment options for common liver diseases such as cirrhosis(19), fatty liver and chronic hepatitis are problematic. The conventional drugs used in the treatment of liver diseases(21,22,23) viz., corticosteroids,antiviral and immunosuppressant(16,17,18) agents are sometimes inadequate and may lead to serious adverse effects. Paradoxically, these may themselves cause hepatic damage. Eg: cholestatic jaundice with azathioprine and elevation of serum transaminases(6,7,8) by interferon and virazole. It is therefore imperative to search alternative drugs for the treatment of liver disease(13,14,15)to replace the currently used drugs of doubtful efficacy and safety.

The present work deals with preclinical evaluation of aqueous extract of *A.paniculata* and silymarin for hepatoprotective activity.

MATERIALS AND METHODS

Plant Material:
The aqueous extract of *A.paniculata* and standard drug of *silymarin* have been provided by Natural Remedies Pvt.LTD. Bangalore.

Experimental animals:
Albino wiatar rats(100-120gm) of male sex were obtained from the central animal facility, natural remedies pvt,LTD.Bangalore and housed six animals in polypropylene cages(32×24×16cm) with paddy husk as bedding.Animals were housed at temperature of 25±2ċ and relative humidity of 30-60%. A 12:12h light and dark cycle was followed.The animals had free access to feed(Mfd.by:Gold mohur foods and feed Ltd.Bangalore.) and UV purified water add libitum .

Experimental method:Experimentally induced hepatotoxicity
Ethanol is one of the most commoly used hepatotoxin in the experimental study of liver diseases.alcohol(24,25) dependency is a major health and soscio economic proplem throught the world.liver is among the organs most susceptible to the toxic effects(26,27,28) of ethanol.almost all ingested ethanol is metabolized in the liver and ethanol abuse can lead to acute and chronic liver diseases.ethanol induces changes in membrane lipid composition and fluidity,which may eventually,effect celluar functions(29,30) in addition,a group of metabolic products called free radicals can damage liver cells and promote inflammation.the body's natural defenses against free radicals(antioxidants)are inhibited by ethanol(1,2,3) consumption.

Experimental design:
Albino wistar rats were divided into seven groups of six animals in each group as follows:
Group i: *Animal of this group received distilled water,p.o. for 28 days*
Group ii: *Animal of this group received ethanol induced hepatotoxicity,20%v/v in dm water.*
Group iii: *Standard group:animal of this group received silymarin 50mg/kg/day, p.o. for 28 days.*
Group iv: *Test group: Animal of this group received extact of Andrographis paniculata 50mg/kg/day, p.o for 28 days.*
Group v: *Test group: Animal of this group received extract of Andrographis paniculata 100mg/kg/day, p.o for 28 days.*
Group vi: *Test group: Animal of this group received extract of Andrographis paniculata 200mg/kg/day, p.o for 28 days.*

RESULTS AND DISCUSSION

Table 1: Effect of silymarin and extract of *A. paniculataon* on serum glutamic oxaloacetic transaminase (SGOT) in albino Wistar rats orally administered with Ethanol (20% v/v; 24gm/kg) for 28 days

Treatment Groups	SGOT
	Day 28
I Vehicle control (10 ml/kg)	66.74 ± 2.81
II Intoxicated control Ethanol (24gm/kg)	96.87 ± 2.87 [a]
III Silymarin (50gm/kg)	70.13 ± 4.59 [b]
IV Extract of A.paniculata (50 mg/kg)	86.56 ± 4.86
V Extract of A.paniculata (100 mg/kg)	76.32 ± 2.91 [b]
VI Extract of A.paniculata (200 mg/kg)	73.96 ± 4.59 [b]

Values are expressed as mean ±SEM; n=8, [a] $p \leq 0.05$ Ethanol control Vs Vehicle control.
[b] $p \leq 0.05$ Silymarin / Extract of A.paniculata Vs Ethanol control.

Table 2: Effect of silymarin and extract of *A. paniculata* on serum glutamic pyruvic transaminase (SGPT) in albino Wistar rats orally administered with Ethanol (20% v/v; 24gm/kg) for 28 days

Treatment Groups	SGPT
	Day 28
I Vehicle control (10 ml/kg)	23.28 ± 1.39
II Intoxicated control Ethanol (24gm/kg)	30.47 ±1.21 [a]
III Silymarin (50gm/kg)	24.46 ± 1.49 [b]
IV Extract of A.paniculata (50 mg/kg)	27.70 ± 0.77
V Extract of A.paniculata (100 mg/kg)	23.72 ± 4.11 [b]
VI Extract of A.paniculata (200 mg/kg)	**24.38 ± 1.83 [b]**

Values are expressed as mean ±SEM; n=8, [a] $p \leq 0.05$ Ethanol control Vs Vehicle control,
[b] $p \leq 0.05$ Silymarin / Extract of A.paniculata Vs Ethanol control.

Table 3: Effect of silymarin and extract of *A. paniculata* on lactate dehydrogenase (LDH) in albino Wistar rats orally administered with Ethanol (20% v/v; 24gm/kg) for 28 days

Treatment Groups	LDH
	Day 28
I Vehicle control (10 ml/kg)	1180.21 ± 130.22
II Intoxicated control Ethanol (24gm/kg)	2000.84 ± 55.10 [a]
III Silymarin (50gm/kg)	1209.60 ± 128.41 [b]
IV Extract of A.paniculata (50 mg/kg)	1645.75 ± 116.12
V Extract of A.paniculata (100 mg/kg)	1422.66 ± 89.12 [b]
VI Extract of A.paniculata (200 mg/kg)	1315.79 ± 136.78 [b]

Values are expressed as mean ±SEM; n=8, [a] $p \leq 0.05$ Ethanol control Vs Vehicle control.
[b] $p \leq 0.05$ Silymarin / Extract of A.paniculata Vs Ethanol control.

Table 4: Effect of silymarin and extract of *A. paniculata* on alkaline phosphatase (ALP) in albino Wistar rats orally administered with Ethanol (20% v/v; 24gm/kg) for 28 days

Treatment Groups	ALP
	Day 28
I Vehicle control (10 ml/kg)	172.55 ± 13.57
II Intoxicated control Ethanol (24gm/kg)	333.14 ± 7.45 [a]
III Silymarin (50gm/kg)	192.78 ± 13.69 [b]
IV Extract of A.paniculata (50 mg/kg)	256.74 ± 23.51
V Extract of A.paniculata (100 mg/kg)	202.53 ± 18.01 [b]
VI Extract of A.paniculata (200 mg/kg)	197.52 ± 20.07 [b]

Values are expressed as mean ±SEM; n=8, [a] $p \leq 0.05$ Ethanol control Vs Vehicle control [b] $p \leq 0.05$ Silymarin / Extract of A.paniculata Vs Ethanol control

Table 5: Effect of silymarin and extract of *A. paniculata* on total bilirubin in albino Wistar rats orally administered with Ethanol (20% v/v; 24gm/kg) for 28 days

Treatment Groups	Total bilirubin
	Day 28
I Vehicle control (10 ml/kg)	0.118 ± 0.03
II Intoxicated control Ethanol (24gm/kg)	0.413 ± 0.13 [a]
III Silymarin (50gm/kg)	0.155 ± 0.026 [b]
IV Extract of A.paniculata (50 mg/kg)	0.187 ± 0.04 [b]
V Extract of A.paniculata (100 mg/kg)	0.151 ± 0.015 [b]
VI Extract of A.paniculata (200 mg/kg)	0.143 ± 0.08 [b]

Values are expressed as mean ±SEM; n=8, [a] $p \leq 0.05$ Ethanol control Vs Vehicle control. [b] $p \leq 0.05$ Silymarin / Extract of A.paniculata Vs Ethanol control.

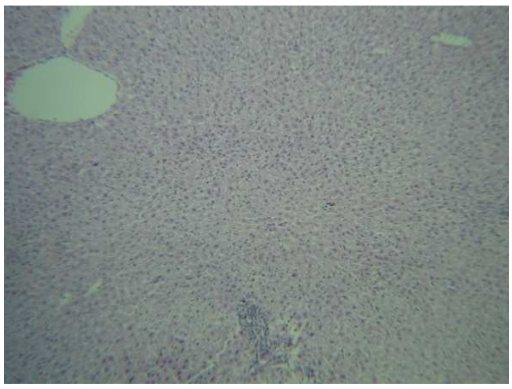
Table 6: Effect of silymarin and extract of *A. paniculata* on direct bilirubin in albino Wistar rats orally administered with Ethanol (20% v/v; 24gm/kg) for 28 days

Treatment Groups	Direct bilirubin
	Day 28
I Vehicle control (10 ml/kg)	0.086 ± 0.015
II Intoxicated control Ethanol (24gm/kg)	0.278 ± 0.016 [a]
III Silymarin (50gm/kg)	0.089 ± 0.01 [b]
IV Extract of A.paniculata (50 mg/kg)	0.155 ± 0.041
V Extract of A.paniculata (100 mg/kg)	0.096 ± 0.016 [b]
VI Extract of A.paniculata (200 mg/kg)	0.092 ± 0.007 [b]

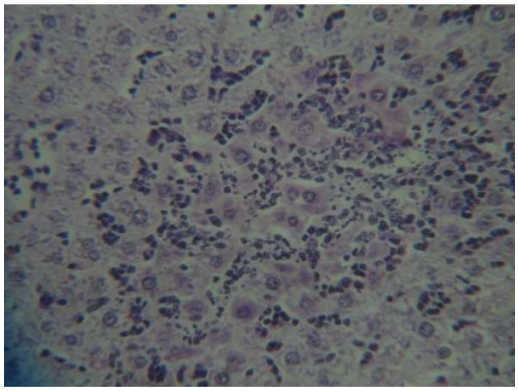
Values are expressed as mean ±SEM; n=8, [a] $p \leq 0.05$ Ethanol control Vs Vehicle control. [b] $p \leq 0.05$ Silymarin / Extract of A.paniculata Vs Ethanol controll.

Statistical Analysis:
All values were expressed as mean±S.E.M. A 'p' value less than 0.05 was considered statistically significant.

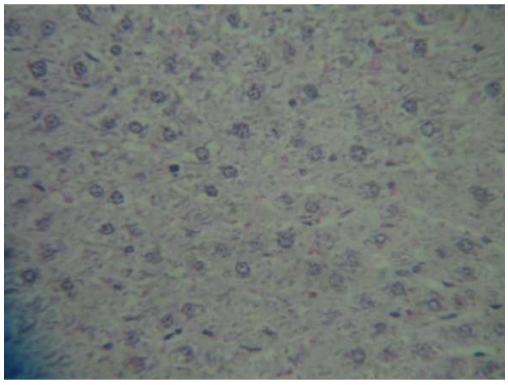
Histopathological Examination



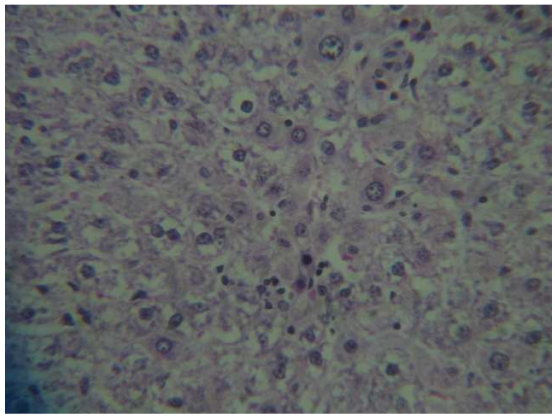
(Normal control 10ml/kg DM water)
FIGURE 1: Control rat liver section revealing normal hepatic parenchyma with a central vein at the top corner. HE x 5



(Intoxicated control 24gm/kg Ethanol)
FIGURE 2: A focus of intense necrotic hepatitis in the diseased control revealing nuclear pyknosis, karyolysis/karyorhexis and intense cellular infiltration. HE x 10

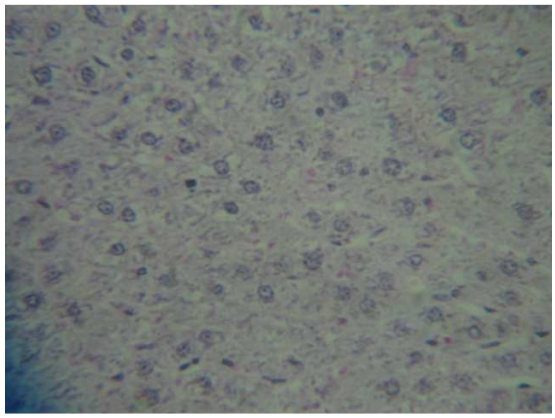


(Standard- silymarin 50mg/kg)
FIGURE 3: Standard drug treated liver section revealing relatively normal hepatic parenchyma comparable to that of the control. HE x 10



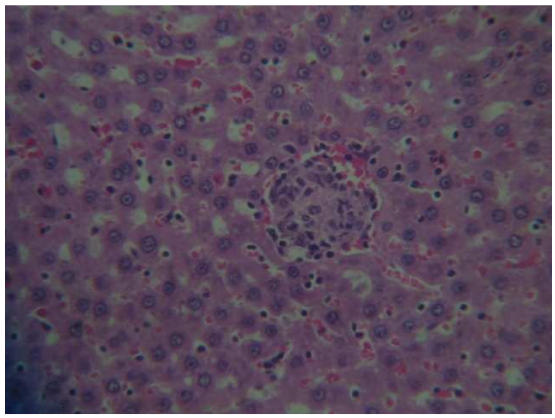
(Ethanol 24gm/kg + A.paniculata 50mg/kg)

FIGURE 4: Higher magnification of control rat liver section revealing swollen hepatocytes with decreased sinusoidal spaces. HE x 5



(Ethanol 24gm/kg + A.paniculata 100mg/kg)

FIGURE 5: Higher magnification of control rat liver section revealing swollen hepatocytes with decreased sinusoidal spaces. HE x 5



(Ethanol 24gm/kg + A.paniculata 200mg/kg)

FIGURE 6: High dose rat liver section revealing comparatively normal hepatic parenchyma with a single focus of spotty necrosis. HE x 5

Hepatoprotective activity of herbal formulation containing different proportion of *Andrographis Paniculata* and Silymarin were evaluated using hepatotoxicity(32,33,34) model. Ethanol induced

toxicity model was taken as prototype of exudative. The extracts of *Andrographis Paniculata* and *Silymarin* successive water extracts showed significant hepato protective effect.From the above experimental study we conclude that: The extract of *Andrograrphis Paniculata* produces adequate hepatoprotective activity on albino wistar rats. The extract of *Andrograrphis Paniculata* produces adequate hepatoprotective activity on albino wistar rats. Silymarin is the superior extracts from *Silybum Marianum as* compare to two extracts. It showed potent hepatoprotective activity.

Ethanol induce hepatotoxicity when administered into the body. In the present study, the comparative evaluation has been carried out extract's of *Andrographis Paniculata* and *Silymarin* *Silymarin* has been already evaluated for its hepatoprotective activity. Our experiment showed the extract of Andrographis Paniculata successive water extracts posses the good hepatoprotective activity.

The dose levels selected for studies were, *A.Paniculata* extract of 50 mg/kg, 100mg/kg and 200mg/kg for Successive water extract. Compare with standard drug of *silymarin*50mg/kg significantly act within our test drug of *Andrographis Paniculata* as the experimental study.

REFERENCES

[1] Schumann G.,et.al., *clin.chem.Lab.med*., 40,725(**2002**)
[2] Bergmeyer H.U.,et.al.,*clin.chem*., 23/5. (**1977**)
[3] Mess D.W., Henderson,A.K.Clinical Enzymdogy in Tietz Textbook of clinical chemistry, 3rd ed.,.C.A.Buritis and E.R.Ashwood, Eds.W.B. Saunders, Philadephia, **1994**,P.617-721.
[4] Murray R.L., Enzymes, in clinial chemistry; Theroy, anaysis and co-relation, L.A.KaPlan and A.J.Pesece, Eds.C.V.Mesby, Toronto, **1994**, P1079-1134.
[5] Young D., In Effect of Pcanalytical Variables on clinical Laboratory Tests, 2nd ed., AACE Press, Washington, **1997**, P4-489.
[6] Bergeyer H.U. et.al., *clin.chem*., 24/1 58(**1978**).
[7] Rej.R., et./al., *clin.chem*.,27/2, 213(**1981**).
[8] Enzymes, Kaplan A., Lavemel L.S., In clincal Chemistry; Interpretation and Techniques, 2nd ed., lea and Febiger, Ph8iladelphia, **1983**, P219-296.
[9] Essani.N.A. Fisher,M.A.Fathood,A.Manning,A.M.Smith C.W. and Pcssayre,D.(**1995**) , 1632-1639.
[10] Essabu,N.A. Bajit,.M.L.Farhood,.A. VonderfeehtS.L. and Jaschke. H. (**1997**). *J.Immaunol*.1458, 5941-5948.
[11] Kestersib,J.W. Graneman.G.R., and Machinist,J.M. (**1984**). *Hepatology* 4, 1143-1152.
[12] kassahun, K., and abbott, F. (**1993**). *Drug Metab. Dispos.* 21, 1098-1106.
[13] Jaeschke, H., Smith, C.W.Clemens, M.G., Ganey, P.E., and Roth, R.A. (**1996**). *APPL. Pharmacol.* 139, 213-226
[14] Jaeschke, H., and Smith, C.W. (**1997**). *J.Leukoc. Biol.* 61, 647-653.
[15] Laskin, D.L., and Laskin, J.D.(**2001**). *Toxicology* 160,111-118
[16] Laskin,D.L., and Pendino.K.J.(**1995**) *Taxicol* 35,655-677.
[17] Lawson.J.A., Fisher, M.A,. Simmons, C.A., Farhood,A/., and Jaschekle, 14, (**1998**) Parenchyamal cella poptosis as a singal for sinusoidal sequetration.
[18] Hinson,J.A.,Pike, S.L.Pujford, N.R., and Mayeux,P.R (**1998**) *ChemRes,.Toxicol* 11,604-607.
[19] Jacschke,H(**2000***) J.Gastroenterol Hepatol* 15, 718-724.
[20] Jacschke, H(**1997**) *Am.J.Jhysiol*.273 G602-C611.

[21] Pessayre.D.Berson,A.Fromently,B. and Mansouri,A (**2001**) *SeminlLiverDis* 21,57-69.
[22] Mari.MWu.D.NictoN.and Cederbaum,.A.I.(**2001**).*J.Biomed.Sci*.8, 52-58.
[23] Lewis,W. and Dalakas,M.C.(**1995**), *Nature Med*.1, 417-422.
[24] Morimoto,M.Zern.M.A.Hegbjork,AL. ingelman, Sundberg.M. and French,S.W. (**1994**) *Proc.Soci.Exp.Biol.Med*.207, 197-205.
[25] Patel,T.Roberts, L,.R.Jones,.B.A.and Gores,G.J.(**1998**) *Semin Liver Dis*.18, 105-114.
[26] Formently B. and Pescayre,D (**1995**) *Pharacol.Ther*.67,101-154.
[27] Friedman S.L. (**2000**) *J. Biol Chem*,275, 2247-2250.
[28] Bilzer,M.Jacschie,H.Vollmar,A.M. Paumgartner,G. and Gerbes,A.L.(**1999**) *AmJ.Physiol*. 276,G.1137-G1144,
[29] Chen.Q.and CederbaurunA.I.(**1998**) *Mol.Pharmacol* 53. 638-648.
[30] KNIGHT,t.r. Kurtzm A Bajit.M.L.Hinson J.A. and Jacchke,H.(**2001**) *Toxicol.Sci*.62. 212-220.
[31] Koop.D.R. (**1992**) Oxidative and reductive metabolism by cytodrome P4502E1, FASEB J.6, 724-730.
[32] Goldin,R.D. Ratnayak.I.D.Breach.C.S Brown I.No. and Wckramasinghc.S.N. (**1996**) *J.Pathol*,.179, 432-435.
[33] Laskin.DL.Garner,C.R. Price,.V.F. and Jollow, D.J. (**1995**) *Hepatology* 21, 1045-1050.
[34] Lawson J.A.Fathoo,A.Hopper R.D. Bajit.M.L. and Jaschke, H. (**2000b**), *Taxicol.Sci*.54. 509-516.