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PHARMACOLOGICAL ANTI-HEPATOTOXIC ASSESSMENT OF POLYHERBAL FORMULATIONS LIV-AMRIT SYRUP, LIVAYU LIVER CARE CAPSULES, AND LIVOMAP SYRUP

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ABSTRACT

In present investigation, anti-hepatotoxic activity of Liv-Amrit Syrup (Patanjali), Livayu Liver Care Capsules (Dr Vaidya's) and Livomap Syrup (Maharishi Ayurveda) against rifampicin and atratyloside was undertaken. Livayu Liver Care Capsules (560 mg/capsule) was found to contain 16 Medicinal Herbs (188 SPMs) as herbal ingredients which produced synergism. Subsequently, Liv-Amrit Syrup (456 mg/15ml) was found to contain 14 medicinal plants (164 SPMs) as herbal ingredients. Further, Livomap Syrup was found to contain 13 Herbal Drugs with 142 SPMs. In anti-hepatotoxic activity, R-CIN in combination with ATR produced severe hepatic necrosis, degeneration, with elevated in LFTs due to necrosis. Oral administration of Liv-Amrit Syrup, Livayu Liver Care Capsules produced significant alleviation of LFTs parameters, reversal effects. Silymarin (standard) induced better alleviation of LFTs. and finally Livayu Liver Care Capsules and Liv-Amrit Syrup polyherbal formulations induced significant anti-hepatotoxic activity (comparatively lesser anti-hepatotoxic effects then standard reference drug i.e. Silymarin). In thiopentone sodium sleep induced analysis it was found that in toxic control animals, R-CIN in combination with ATR induced hepatotoxicity exhaust glutathione stores, reduced onsetof sleep and increased duration of sleep and liver-weight ratio was also increased.

KEYWORDS: Rifampicin, Atractyloside, glutathione, Liv- Amrit Syrup, Livomap Syrup, Livayu Liver Care Capsules, Liv-Amrit Syrup, Secondary Plant Metabolites, Silymarin,

INTRODUCTION

Allen (2002), liver is sizable most essential organ, cone shaped, dark reddish-brown (rubbery texture), one of the largest solid glandular organ (about 3 pounds / weighing about 1.5 Kg; approx. 2.5% of body weight) and master chemist of body. Moore, 2006 stated that liver is located in the right upper quadrant of the abdomen. Kogure *et al*, 2007, liver holds about 13% of the body's total blood and divided into two lobar segments (right and left; right lobe larger than left lobe), and two accessory lobes (further subdivided into eight couinaud segments; consist of 1,000 lobules (small lobes). Yang *et al*., 2010, liver is most regenerative part after skin that plays an astonishing vital functions / essential role in detoxification and metabolism of various endogenous and exogenous injurious substances. Sutherland *et al*., 2002, liver secretes bile (digestive fluid), metabolise proteins, carbohydrates, fats; stores glycogen, vitamins, other substances; synthesizes blood-clotting factors; removes wastes / toxic matter from blood; regulates blood volume; destroys old red blood cells.

Hepatotoxicity

Nilesh *et al*., 2012, hepatotoxicity is a term for hepatic damage and chemicals (hepatotoxins) which cause liver injury. Drug-induced liver injury (DILI) is responsible for 5% of all hepatic patients and 50% of all acute hepatic failures. Besides, more than 1000 drugs, toxins, and toxic herbs have been reported to cause liver injury, and drugs account for 20-40% of liver failure.

Types of hepatotoxicty

Drug induced hepatotoxicity

Mohit *et al*., 2011, Drug-induced hepatotoxicity cause of acute liver failure (leading cause for termination of drug development in preclinical and clinical phases). It affects a huge population across the globe as liver is the main organ for metabolism of exogenous compounds (highly vulnerable to damage by drugs and toxic metabolites).

Risk factors for drug induced hepatoxicity

- Race: Example - Blacks and Hispanics are more susceptible to isoniazid (INH) toxicity. P-450 enzymes vary from individual to individual.
- Age: Infections and multiple drug therapies, high risk of hepatotoxicity, poor hepatic blood-flow, drug-binding variation, drug-drug-interactions;
- Sex: Females more prone than males;

- Alcohol ingestion: Due to depletion of glutathione, alcoholics are more prone to drug induced hepato-toxicity;
- Liver disease: Patients under treatment for HIV infection and hepatitis B or C.
- Other co-morbidities: Low glutathione - more susceptible to drug reactions.
- Drug formulation: Long-acting drugs;
- Host factors: Susceptibility to drugs induced liver disease

Pathophysiology of drug induced hepatotoxicity

The pathophysiologic mechanisms of hepatotoxicity include both hepatocellular and extracellular mechanisms. The following are some of the mechanisms that have been described:

- Disruption of the hepatocyte;
- Disruption of the transport proteins;
- Cytolytic T-cell activation;
- Apoptosis of hepatocytes;
- Mitochondrial disruption;
- Bile duct injury;
- Drug toxicity mechanisms;
- Intrinsic or predictable drug reactions;

Mohit *et al*., 2011 stated that hepatotoxins (e.g. carbon- tetrachloride, alcohol, pyrrolizidine alkaloids, mycotoxins and bacterial toxins) or drugs (e.g. paracetamol, anti-tuberculosis drugs e.g. rifampicin) in overdoses / prolonged therapy induce hepatotoxicity. Dianzani *et al*., 1991 illustrated that Chemical / Drug Induced Liver injury (DILI) affects a huge population (Davies, 1997)

Hepatotoxicants

Thonda *et al*., 2012 revealed that hepatotoxins cause liver damages (in transforming / clearing highly toxic chemicals / medications when taken in high quantity).

Biomarkers of hepatotoxicity

Table 1: Hepatotoxicity Markers. (Singh *et al*. 2011)

Biochemical parameter	Histopathological Lesion	Reason of Abnormality
Alanine aminotransferase (ALT/SGPT)	• Hepatocellular necrosis	• Leakage from damaged tissue
Albumin	• Hepatic dysfunction	• Decreased synthesis
Alkaline phosphatise	• Hepatobilary injury • Choleastasis	• Overproduction, releases in blood
Arginase	• Hepatocellular	• Release from hepatocytes
Aspaertate aminotransferase (AST/SGOT)	• Hepatocellular necrosis	• Damaged tissue leakage
Bile acids	• Hepatobiliary disease	• Regurgitation into blood
Glumate dehydrogenase	• Hepatic necrosis	• Leakage / damaged tissue
Glutathione S-transferase	• Necrosis of hepatocytes	• Rapidly leaks from hepatocytes
Lactate dehydrogenase	• Hepatocytes's necrosis	• Leaking damaged tissue
Malate dehydrogenase	• Necrosis of liver cells	• Damaged tissue / leakage
Sorbitol dehydrogenase	• Liver cell necrosis	• Damaged tissue leaking
Total bilirubin	• Hepatobiliary injury as well as cholestasis	• Hepatic clearance is decreased
Total protein	• Hepatic dysfunction	• Reduced synthetic capacity

Hepatoprotection

Jesika *et al*., 2016, hepatoprotection is important as it plays a critical role in metabolism and overall health (Chattopadhyay *et al*., 2007)

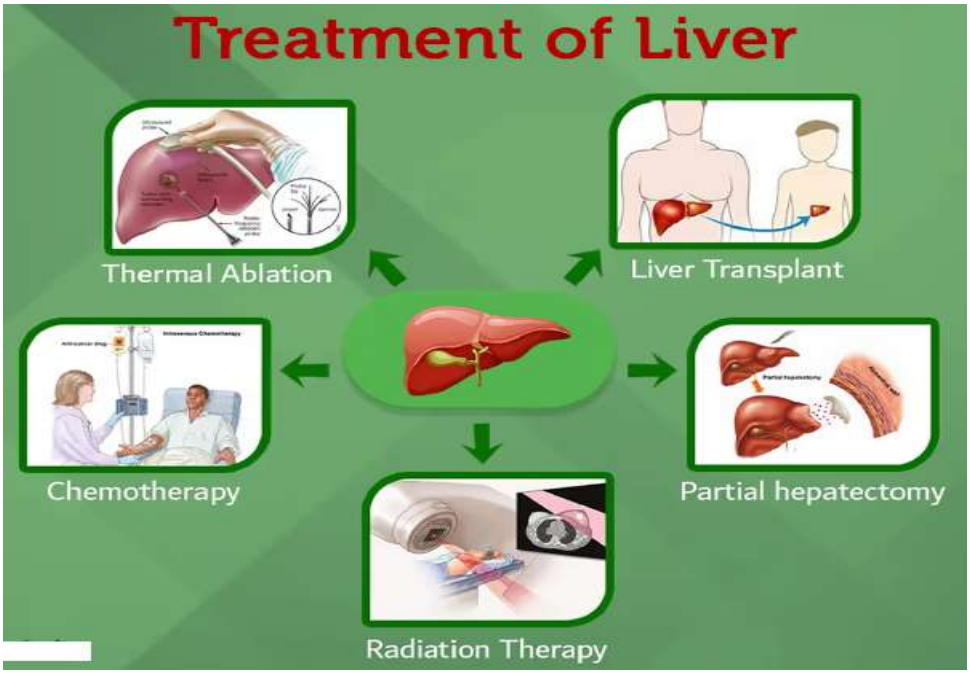

Fig. 1: Treatment of liver diseases.

Hepatoprotective drugs

Allopathic drugs: Ursodeoxycholic acid (Ursodiol)

Gupta *et al.*, 2009 found that ursodeoxycholic acid decreases intestinal absorption decreased expression of hepatocyte cell surface membrane. Gustav *et al.*, 2003 reported that it is used to treat idiopathic hepatitis; alcoholic hepatitis.

Role of herbals

Varshaw *et al.*, 2011, about 160 phytotherapeutic agents (SPMs) isolated from 101 plants possess hepatoprotective activity. In Indian market, more than 90 plants are used in 750 patented and proprietary multi ingredient phytoformulations. In spite of the tremendous advances made, no significant and safe hepatoprotective agent is available in modem therapeutics. Therefore currently in many laboratories in India, stress is laid on development of plant based natural products / herbal formulations as liver protecting agents.

Hepatoprotective polyherbal formulations

Schuppan *et al.*, 1999 reported that several herbals produce therapeutic activity in treating hepatic disorders.

Table 2: Plant drugs with activity against liver disease. (Saumendu *et al.*, 2012)

Plant Name / Family	Chem. Constituents	Uses
Silybum marianum (Asteraceae)	Flavonolignans: silybin, silydianin and silychristine, betaine	Hepatoprotective (Anil *et al.*, 2012)
Eclipta alba (Asteraceae)	Alkaloid known as ecliptin, nicotin, glucoside	Viral hepatitis, liver disorder, memory disorders (Zafar *et al.*, 2000)
Picrorrhiza Kurrora (Scrophulariaceae)	Iirridoid bitter substance picroside and kutkoside	Bitter tonic, in jaundice
Andrographis paniculata (Acanthaceae)	Andrographolides, kalmeghin (upto2.5%), deoxyandrographolide	Antipyretic, tuberculosis, anti-hepatotoxicity (Varshaw *et al.*, 2011)
Curcuma longa (Zingiberaceae)	Diaylheptanoids curcumin, volatile oil, curcuminoids,	Anti-inflammatory (Varshaw *et al.*, 2011)
Tephrosia purpurea (Fabaceae)	Tephrosin, deguelin and quercetin	In liver and spleen diseases. (Anil *et al.*, 2012)
Solanum nigrum (Solanaceae)	Solamargrine, andsolasonine	Hepatoprotective, diuretic, antiseptic.
Taraxacum officinale (Asteraceae)	Taraxecerin, taraxcin, sesquiterpene lactones.	Hepatic and biliary disorders, kidney stones
Cichorium intybus (Asteraceae)	Bitter glucoside, cichorin	Liver protection
Peumus boldus	Alkaloids, volatile oils,	Choleretic, diuretic,

(Monimiacee)	flavonols and their glycosides	stomachic, mild sedative. (Saumendu *et al*., 2012)

Liv-Amrit Syrup (Patanjali)

Liv-Amrit Syrup is a polyherbal formulation for better health of liver (improve appetite, and useful in indigestion, reduces flatulence, bloating (digestive disorder) and disorders of liver/ spleen.

Liv-Amrit Syrup formulation contains *Phyllanthus niruri* Linn., *Boerhavia diffusa* Linn., *Eclipta alba* Linn., *Solanum nigrum* L., *Terminalia arjuna* Roxb., *Triphala, Tephrosia purpurea* (L.) Pers., *Tinospora cordifolia* Miers., *Glycyrrhiza glabra* L., *Picrorhiza kurroa* Royle., *Berberis aristata* DC., *Cassia fistula* Linn., *Andrographis paniculata* Nees., *Saccharum officinarum* L., sodium methyl paraben (preservative), sodium propyl paraben (preservative), sodium benzoate (preservative) and citric acid (preservative) etc.

Fig. 2: Liv-Amrit Syrup (Patanjali) and its composition.

Livayu Capsules (Dr. Vaidya's)

Fig. 3: Livayu capsules (Dr. Vaidya's) and its composition.

Livomap Syrup (Maharishi Ayurveda)

Fig. 4: Livomap Syrup (Maharishi Ayurveda) and its composition.

Livomap Syrup is a 100% Ayurvedic formulation made with a judicious combination of highly effective and potent natural herbs that protects the liver and energises the liver. It is a clinically tested natural remedy that can be consumed regularly.The herbs in the syrup protect the liver from seasonal infections and promote overall health.Livomap is a herbal infusion that improves gut health. It helps in the removal of toxins and stimulates appetite and metabolism.

Rifampicin: Toxicology and Adverse effects of Rifampicin

Masters *et al*., 2005, it is an intensely red solid which impart red-orange color to the urine, sweat and tears. The toxicity of Rifampicin has been determined by Sridhar *et al*., 2012 co-administration of rifampicin with other drugs that are metabolized through these cytochrome P-450 enzymes may accelerate the metabolism and reduce the activity of these other drugs. (Riss *et al*., 2008)

Atractyloside

Van *et al*., 2002 showed that ATR is an extremely toxic glycoside, obtained from the rhizomes of the Mediterranean thistle *Atractylis gummifera*, that produces hypoglycemia and convulsions in animals.

Atractyloside poisoning is an infrequent but often fatal form of herbal poisoning, which occurs worldwide but especially in Africa and the Mediterranean regions. Belitz *et al*., 2009 the results show that the ATR content in the herb is 8.98 thousand ppm, the ATRactylodes ATR content to 9230 ppm. Karl *et al*., 2006 *Atractyloside* (ATR), the toxic principle is commonly found in South Africa plant *Callilepis laureola.* Candy *et al*., 1977, ATR is also

found in *Coffea arabica* Linn. (Family Rubiaceae) / coffee beans. Watson *et al*., 1979, *Callilepis laureola*, cause fatal liver necrosis, nephrotoxic and hypoglycaemic. Sudipta *et al*., 2012, it has been found that no significant and safe allopathic drug is available. In this research investigation an attempt was made to perform research on comparative pharmacological assessment of polyherbal formulations Liv-Amrit Syrup (Patanjali), Livayu Liver Care Capsules (Dr Vaidya's) and Livomap Syrup (Maharishi Ayurveda). So, objectives of the study were as follows:

- Qualitative analysis of Herbal Formulation
- Antioxidant activity by SOD, catalase and peroxidise activity.
- Pharmacological investigations of Liv-Amrit Syrup, Livayu Liver Care Capsules and Livomap Syrup for anti-hepatotoxic activity against rifampicin and atractyloside.
- Effect of polyherbal formulations on thiopentone sodium induced sleeping time in rifampicin and atractyloside induced hepatotoxic rats.
- To establish the pharmacodynamics involved in anti-hepatotoxic activity.

MATERIALS AND METHODS

- Estimation of Superoxide-dismutase (SOD), Catalase, and Peroxidase
- SGPT, SGOT, AKLP, protein, albumin, billirubin, alkaline phosphatase etc., histopathological analysis.
- Sleeping time analysis.

Pharmacognostical and Pharmacological Comparison of Formulation

Table 3: Pharmacognostical and Pharmacological Comparison of Polyherbal formulations.

Parameter	Liv-Amrit Syrup	Livayu Liver Care Capsules	Livomap Syrup
Constituents	164 SPMs from 14 Medicinal Plants	198 SPMs from 16 Medicinal Herbs	142 SPMs from 13 Herbal Drugs
Constituents Medicinal Plants	*Phyllanthus niruri*	*Andrographis panniculata*	*Boerhaavia diffusa*
	Boerhaavia diffusa	*Tephrosia purpurea*	*Trichosanthes Cucumerina*
	Eclipta alba	*Phyllanthus niruri*	*Zingiber officinale*
	Solanum nigrum	*Tinospora cordifolia*	*Picrorhiza kurroa*
	Terminalia arjuna	*Embelia Officinalis*	*Tinospora cordifolia*
	Triphala	*Berberis aristata*	*Cedrus deodara*
	Tephrosia purpurea	*Picrorhiza kurroa*	*Moringa oleifera*

	Tinospora cordifolia	*Terminalia chebula*	*Terminalia chebula*
	Glycyrrhiza glabra	*Eclipta alba*	*Crataeva religiosa*
	Cichorium intybus	*Solanum nigrum*	*Berberis aristata*
	Picrorhiza kurroa	*Boerhaavia diffusa*	*Artemisia absinthium*
	Berberis aristata	*Aloe barbadensis*	*Tephrosia purpurea*
	Cassia fistula	*Adhatoda vasika*	*Phyllanthus niruri*
	Andrographis panniculata	*Fumaria officinalis*	
		Plumbago zelanica	
		Embelia ribes	
Medicinal Uses	disorders of liver / spleen; Hepatocyte repair & regeneration; detoxify hepatotoxins; increase hepato-biliary secretions; fat digestion reduces flatulence, indigestion, bloating (digestive disorder)	Detoxify hepatotoxins; increase appetite; Anti-viral; anti-inflammatory; liver cells regeneration; liver toxicity due to allergic foods and alcohol consumption; enhance digestion;	Energizes liver; stimulates appetite; improves bile flow; viral hepatitis; anti-HBs Ag activity; prevents gall stones formation; liver infection and inflammation; regeneration of liver cells; hepatoprotective;
Dose	10-15 ml TID;	1 Capsule BID	10-15 ml TID;
Toxicity Profile	Safe dose: 3000 mg/kg bw Toxicity absent.	Safe dose: 2000 mg/kg bw Toxicity absent.	Safe dose: 2500 Toxicity absent.
Side Effects	Absolutely safe and no side effects.	No side effects	No side effects.

Qualitative Chemical Tests for Detection of PPMs and SPMs

Polyherbal Formulation (Liv-Amrit Syrup, Livayu Liver Care Capsules and Livomap Syrup) were used for preliminary phytochemical screening using different polar and non-polar solvent extracts for of detection of different phytoconstituents using standard procedures described by Harborne, Khandelwal and Kokate.

Anti-hepatotoxic activity

IAEC of IEC-GI Institution as per CPCSEA guidelines approved the Form B IEC/IAEC/2023/08 proposal was approved by IAEC (02-11-2023) (Registration No.–1332/PO/Re/S/10/CPCSEA). Animals were received from Central Laboratory Animal Resources (CLAR, JNU), Delhi.

Table 4: Groups of animals for anti-hepatotoxic assessment.

Group	Drug treatment
I	Normal Control (Vehicle / Water Control)
II	Toxic Control: Rifampicin (RCIN; 1gm/kg)+Atratyloside (ATR; 100 mg/kg b.w. p.o.) for 1 week
III	R-CIN+ATR (1 week) + Liv-Amrit Syrup (114 mg/kg p.o.) for 3 weeks
IV	R-CIN+ATR (1 week) + Liv-Amrit Syrup (228 mg/kg p.o) for 3 weeks
V	R-CIN+ATR (1 week)+Livayu Liver Care Capsules (140 mg/kg) (3 weeks)
VI	R-CIN+ATR (1 week) +Livayu Liver Care Capsules (280 mg/kg; 3 weeks)
VII	R-CIN+ATR (1 week) + Livomap Syrup (1 ml/kg p.o.) for 3 weeks
VIII	R-CIN+ATR (1 week) + Silymarin Syrup (140 mg/kg p.o; 3 weeks)

Group I: Animals were given water *ad libitum* / vehicle control. On 8th day biochemical parameters of liver were estimated. The blood samples for the LFT estimations were collected from retro-orbital sinus. Further, liver sections were taken out for histopathological studies.

Group II: Animals of Group II were served as toxic control group (R-CIN+ATR) and animals were given R-CIN (1gm/kg)+ATR (100 mg/kg b.w./day) for 01 weeks and then biochemical parameters of liver (LFTs) were estimated on 8th day.

Group III to VIII: Animals of Group II to VIII were served as models for R-CIN + ATR induced hepatotoxicity.

Animals of Group II to VIII were given R-CIN (1gm/kg)+ATR (100 mg/kg b.w./day) for 01 week to induce hepatotoxicity followed by treatment with polyherbal Syrup formulation Liv-Amrit Syrup (114 mg/kg; Group III), Liv-Amrit Syrup polyherbal formulation (228 mg/kg; Group IV), Livayu Liver Care Capsules (140 mg/kg; Group V), Livayu Liver Care Capsules (280 mg/kg; Group VI), Livomap Syrup (1ml/kg; Group VII), and Silymarin (standard drug; 140 mg/kg; Group VII) for 03 weeks. Finally, on 21st day animals were sacrificed, blood was collected from retro-orbital sinus under anesthesia induced by Ketamine 80-85 mg/kg i.p. in combination with Xylazine 8-10 mg/kg of the body weight. The serum was separated by using refrigerated centrifuge and used for the assay of marker enzymes viz., SGOT, SGPT, AKLP, Albumin and Bilirubin. Anti-hepatotoxic effects were compared with Silymarin (Standard). Blood samples were analysed for biochemical parameters like SGPT / ALT, SGOT / AST, Abumin, Total proteins, alkaline phosphatase and Billirubin were estimated (Gornal *et al*., 1949; Lowry *et al*., 1949; Godfried *et al*., 1935).

Effect on Thiopentone sodium Induced sleeping-time and liver weight

Kulkarni (1999), reported that barbiturates are extensively metabolized in the liver and damaged liver suffers with delay in barbiturates clearance (thiopentone sodium 40 mg/kg i.p; cause longer duration of hypnotic effect. (Gujrati *et al*., 2007)

Grouping of animals

Table 5: Groups of animals for sleeping time effect.

Group	Drug treatment
I	Normal Control (Vehicle / Water Control)
II	Toxic Control: Rifampicin (RCIN; 1gm/kg) + Atratyloside (ATR; 100 mg/kg b.w. p.o.) + Thiopentone sodium (40 mg/kg i.p)
III	R-CIN+ATR + Thiopentone sodium + Liv-Amrit Syrup (228 mg/kg p.o)
IV	R-CIN+ATR+Thiopentone sodium+Livayu Liver Care Capsules (280 mg/kg)
V	R-CIN+ATR + Thiopentone sodium + Livomap Syrup (1 ml/kg p.o.)
VI	R-CIN+ATR+Thiopentone sodium+Silymarin Syrup (140 mg/kg p.o)

Group I: Animals were given water *ad libitum* / vehicle control.

Group II: Toxic control group animals were given R-CIN and ATR.

Group III to V: Animals of Group II to V were served as models for R-CIN and ATR induced hepatotoxicity. Animals of Group II to V were given R-CIN and ATR to induce hepatotoxicity followed by treatment with Liv-Amrit Syrup, Livayu Liver Care Capsules and Livomap Syrup and Thiopentone sodium (40 mg/kg i.p) (Group III and V) and Silymarin (standard drug, 140 mg/kg) with Thiopentone sodium (40 mg/kg i.p) (Group VI).

***In-vivo* antioxidant effects**

The present investigation was conducted on experimental animals in accordance with the international principles for laboratory animals' use and care as found in the guidelines (Council of European Communities, 1986). The study protocol was approved by the CPCSEA Form B IEC/IAEC/2023/08 on 02-11-2023. Superoxide dismutase (SOD) activity: Determined by method of Habbu *et al*., 2008 and results were expressed as SOD Units/ mg. Catalase activity: Catalase was determined by an adaptation of the method of Aebi, 1984.

Safety & Toxicity evaluation

Following the rules set forth by the Organisation for Economic Cooperation and Development (OECD), we investigated the toxicity of Liv-Amrit Syrup and Livayu Liver Care Capsules in albino wistar rats in this investigation.

Animals: 05 Groups (6 animals/group)

I: Distilled water.

II: Liv-Amrit Syrup (LAS)114 mg/kg.

III: LAS 114 mg/kg

IV: Livayu Liver Care Capsules (LLCC)140 mg/kg.

V: LLCC 280 mg/kg.

Sub-acute toxicity study

Rats in groups II and III were given Liv-Amrit Syrup (114 and 256 mg/kg), while groups IV and V were given Livayu Liver Care Capsules (140 and 280 mg/kg). Various blood parameters were analysed (Bretaudiere *et al*., 1976; Wu and Hoak, 1974; Dacie and Lewis, 2001; Pla and Fritz, 1971; Crosby *et al*., 1954; Dacie and Lewis, 1991; Spencer, 1986; Thinder, 1969).

RESULTS AND DISCUSSIONS

Research work was started with procurement of Liv-Amrit Syrup, Livayu Liver Care Capsules and Livomap Syrup from genuine commercial sources. It was found that Livayu Liver Care Capsules contains 16 Medicinal Herbs (188 SPMs; 560 mg/capsule) as herbal / medicinal ingredients which produced synergism with drug concentration. Liv-Amrit Syrup contains 14 plants (164 SPMs; 456 mg/15ml) as herbal ingredients. Besides, Livomap Syrup (Maharishi Ayurveda) contains 13 Herbal Drugs (142 SPMs). On the basis of composition, Livayu Liver Care Capsules contains better and more scientific anti-hepatotoxic herbals drugs than Liv-Amrit Syrup and Livomap Syrup.

Alkaloids, phenolic chemicals, anthraquinones, flavanoids, terpenoids, found in Liv-Amrit Syrup, Livayu Liver Care Capsules, and Livomap Syrup during phytochemical screening. In anti-hepatotoxic activity, rifampicin (R-CIN; 1 gm/kg) in combination with atractyloside (ATR; 100 mg/kg) produced severe liver damage / hepatic necrosis, degeneration, steotosis, with increase in SGPT and SGOT, total protein, total billirubin and alkaline phosphatase due to necrosis and breakdown of hepatic cells. Elevated biochemical parameters were assessed and compared with hepatic lesions, damaged anatomical architecture; centilobular necrosis, cytoplasmic vacuoles, lymphocytic infiltration, fatty degeneration. Oral administration of Liv-Amrit Syrup (Group III-IV), Livayu Liver Care Capsules (Group V-VI) produced significant alleviation of LFTs parameters. These polyherbal syrup formulations showed reversal effects. Silymarin (standard / reference drug) produced better alleviation of LFTs (biochemical parameters). Finally, Livayu Liver Care Capsules and Liv-Amrit Syrup

polyherbal formulations induced significant anti-hepatotoxic activity but comparatively lesser anti-hepatotoxic effects then standard reference drug i.e. Silymarin. Mechanism of pharmacological anti-hepatoxic effects include attenuation of depletion of glutathione, anti-oxidant, hepatocyte membrane stabilization, anti-inflammatory, inhibition of phopholipase A2, enhanced proteins synthesis (RNA repair).

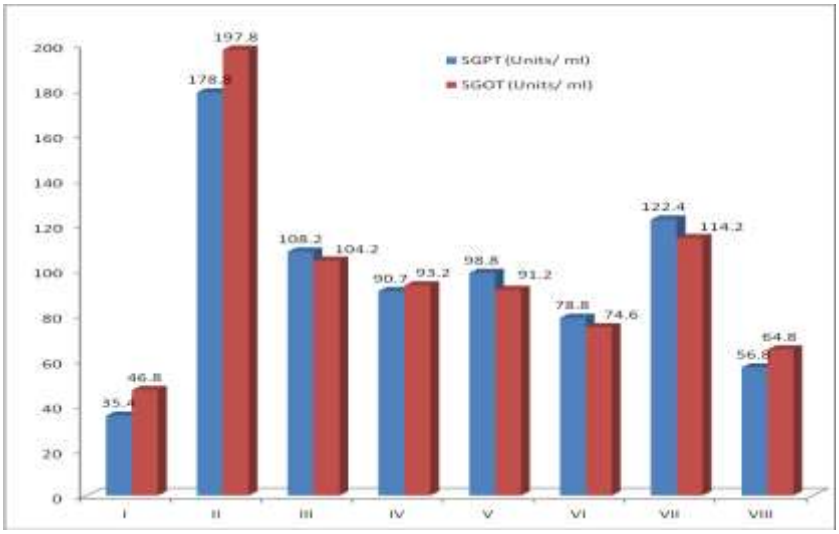

Fig. 5: Effect of formulations on SGPT and SGOT.

Subsequently, in thiopentone sodium sleep induced analysis it was found that sleeping time pattern was normal in Group-I (normal control). In Group-II (toxic control) animals, RCIN in combination with ATR and Thiopentone sodium induced hepatotoxicity exhaust glutathione stores, caused hepatic necrosis and liver-weight ratio were also increased (reduced onset of sleep and increased duration of sleep). Finally, reduction in sleeping-time was recorded with Liv-Amrit Syrup, Livayu Liver Care Capsules and Livomap Syrup and Silymarin (standard) when compared to toxic control group.

Table 6: Effect of Extracts on thiopentone induced sleeping time & liver weight.

Group	Thiopentone sod. induced sleeping time		Liver wt (g/100g bw)
	Onset (s)	Duration (min)	
Group I (Normal control)	204.52 ± 4.92	76.64 ± 4.92	3.94 ± 0.50
Group II (Toxic Control)	54.32 ± 4.24a	242.36 ± 4.72a	6.44 ± 0.30a
Group III (Liv-Amrit Syrup)	138.36± 4.62	162.12 ± 5.62	5.72 ± 0.16
Group IV (Livayu Liver Care Capsule)	163.22 ± 3.86***	135.34 ± 5.46***	5.26 ± 0.12*
Group V (Livomap Syrup)	114.32 ± 4.24	202.62 ± 4.72	5.94 ± 0.30
Group V (Silymarin)	176.34 ± 7.26***	120.46 ± 6.34***	4.80 ± 0.14*

Values are mean ± SEM of 6 animals /group

aP < 0.001 relative to control gp; ***P < 0.001 relative to toxic control group

*P < 0.05 relative to toxic control group

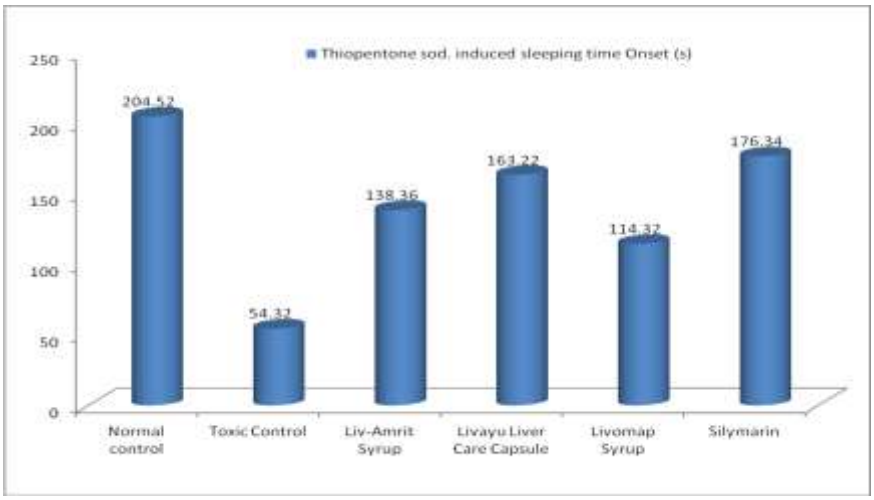

Fig. 6: Effect of Thiopentone sodium on onset of sleeping time.

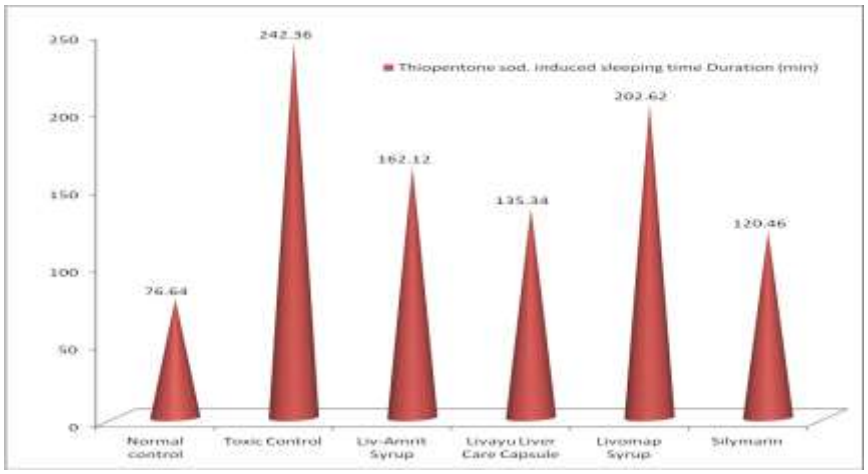

Fig. 7: Effect of Thiopentone sodium on duration of sleeping time.

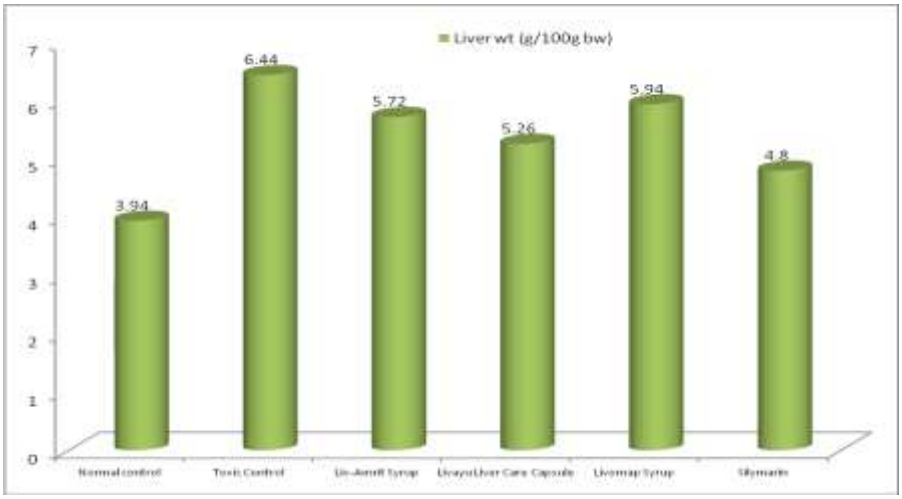

Fig. 8: Effect of thiopentone sodium on liver weight.

In antioxidant activity, the administration of R-CIN and ATR for one week induced severe hepatotoxicity (acute liver damage due to decreased levels of catalase, glutathione, peroxidase, glutathione reductase, SOD). Liv-Amrit Syrup, Livayu Liver Care Capsules and Livomap Syrup were found to possess antioxidant potential with significant superoxide radical scavenging activity. Liv-Amrit Syrup, Liv-Amrit Syrup and Livomap Syrup induced important role in restoration of NAD, cytochrome, and glutathione (scavenging hydrogen peroxide).

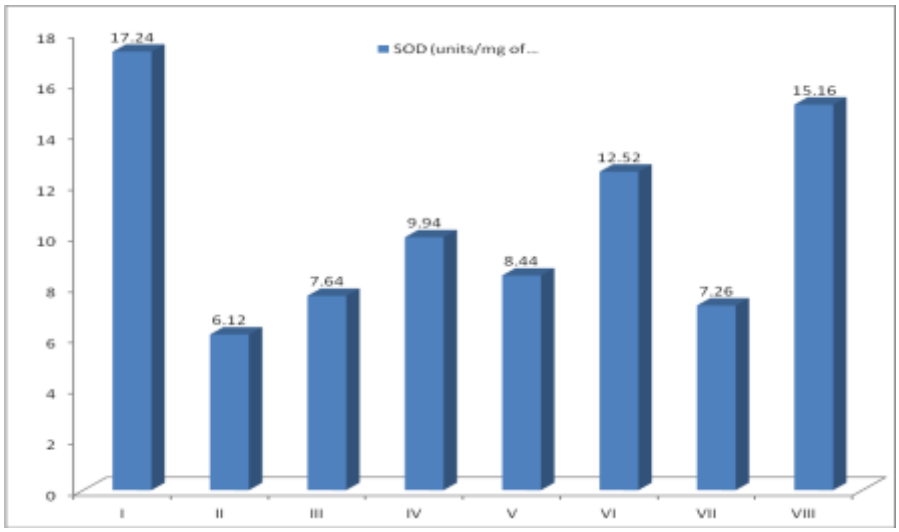

Fig. 9: Effects of the polyherbal formulations on SOD.

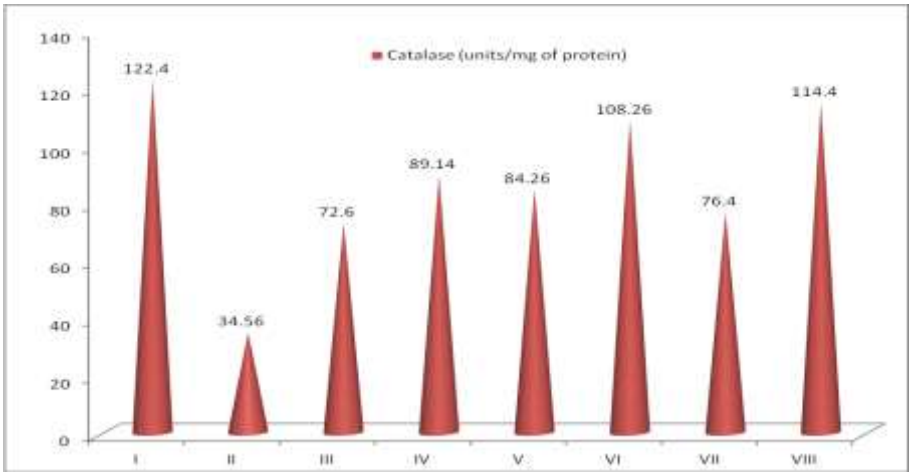

Fig. 10: Effects of the polyherbal formulations on Catalase.

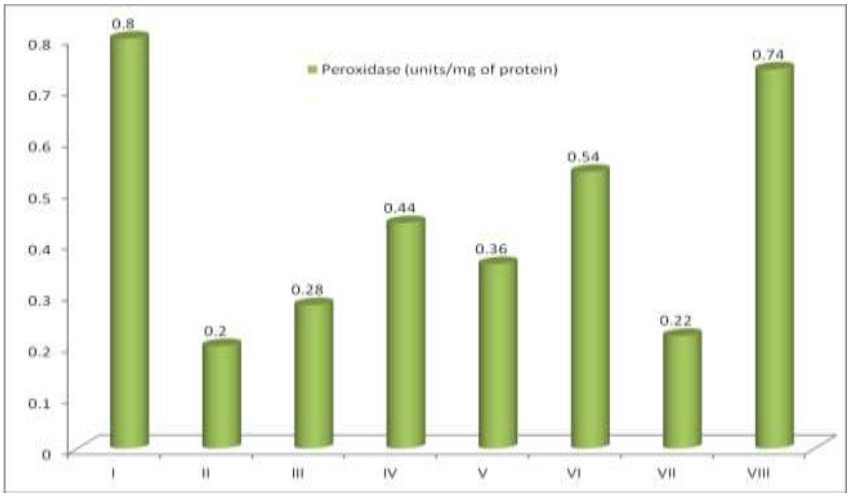

Fig. 11: Effects of the polyherbal formulations on Peroxidase.

Then, in safety and toxicity evaluation, polyherbal formulations caused no death in rats not even when administered at doses of up to 2000 mg/kg/b.wt. However, several changes in behaviour were seen, including ataxia and diminished ability to move. Haematological indicators did not significantly change when using Liv-Amrit Syrup and Livayu Liver Care Capsules. Liv-Amrit Syrup and Livayu Liver Care Capsules have a very broad safety margin and are categorised as Safe. Further studies are proposed for isolation and characterization of pharmacologically active principles of these formulations.

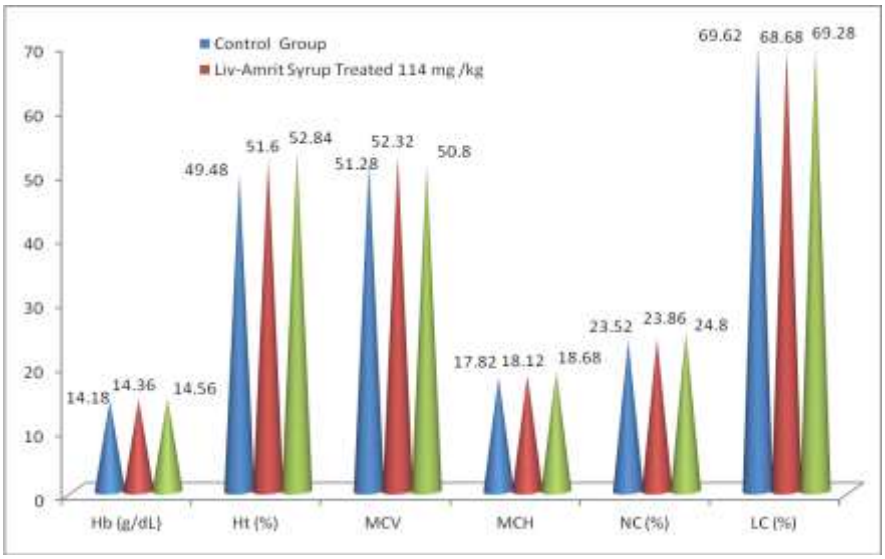

Fig. 12: Effects of Liv-Amrit Syrup on blood parameters.

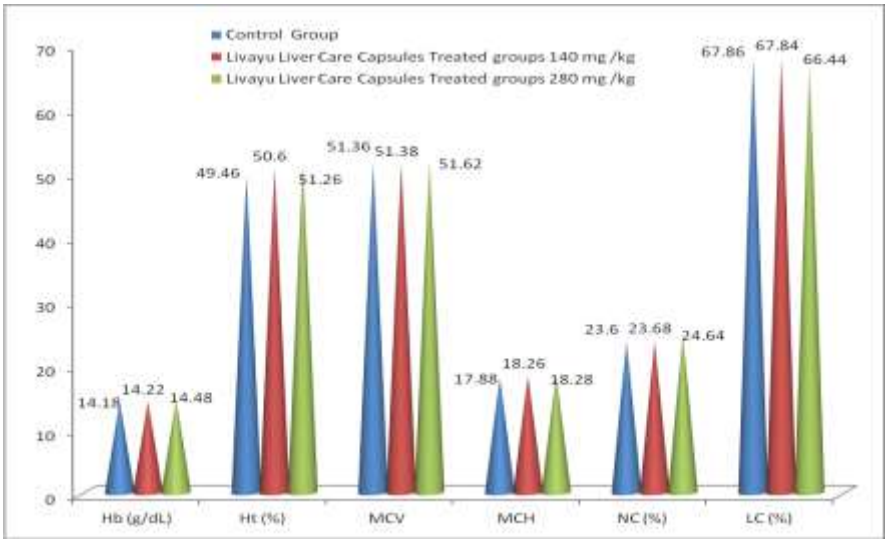

Fig. 13: Effects of Livayu Liver Care Capsules.

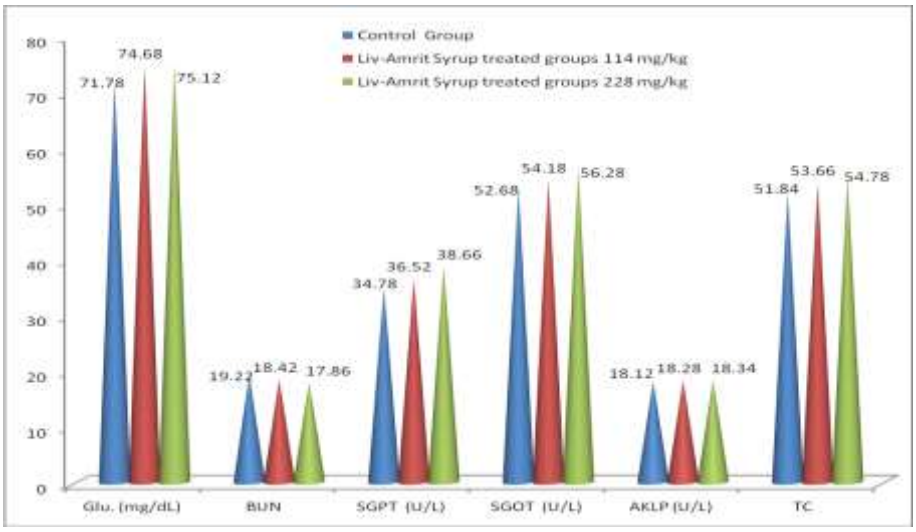

Fig. 14: Effect of Liv-Amrit Syrup.

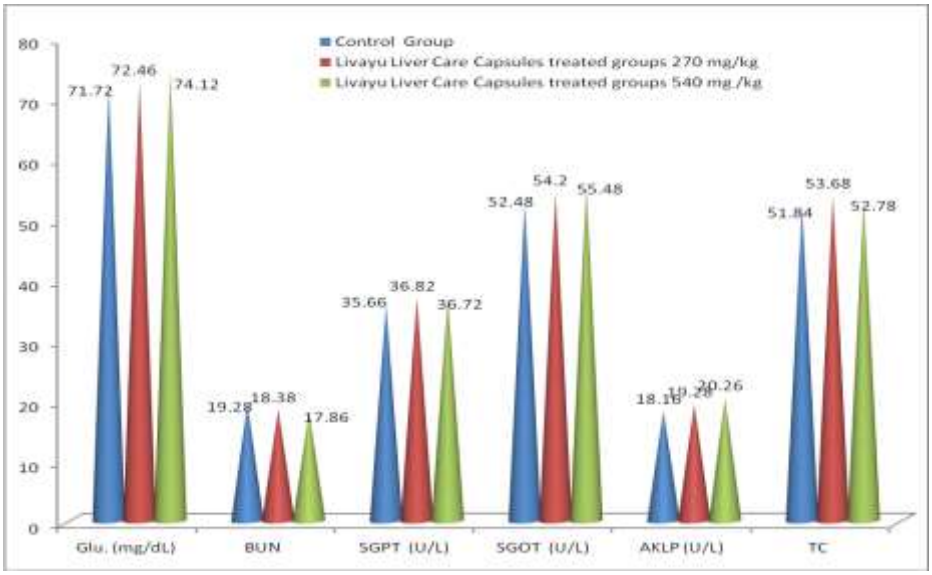

Fig. 15: Effect of livayu liver care capsules.

CONCLUSIONS

Livayu Liver Care Capsules and Liv-Amrit Syrup polyherbal formulations induced significant anti-hepatotoxic activity. In thiopentone sodium sleep induced analysis it was found that in toxic control animals, R-CIN in combination with ATR induced hepatotoxicity exhaust glutathione stores, reduced onset of sleep and increased duration of sleep and liver-weight ratio was also increased. Finally, Liv-Amrit Syrup, Livayu Liver Care Capsules and Livomap Syrup and Silymarin reduced sleeping-time. Liv-Amrit Syrup, Livayu Liver Care Capsules and Livomap Syrup were found to possess antioxidant potential with significant superoxide radical scavenging activity. Further studies are proposed for isolation and characterization of pharmacologically active principles of these formulations.

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