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An insight into protection from hepatotoxicity with herbo-mineral formulation: Amlycure DS

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An insight into protection from hepatotoxicity with herbo-mineral formulation: Amlycure DS

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ABSTRACT

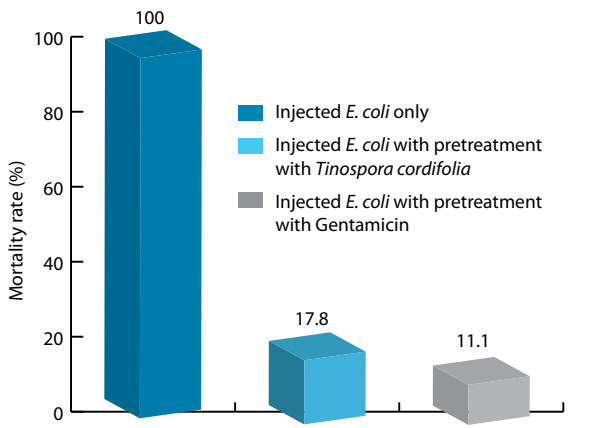
Liver is the largest organ in the body, removing harmful material from the blood, making enzymes and bile that help digest food, and converting food into substances needed for life and growth. The liver is the only organ in the body that is able to regenerate or completely repair damage with new cells. However, long-term complications can occur when regeneration is either incomplete or prevented by progressive development of scar tissue. Although liver disease is stereotypically linked to alcohol or drugs, the truth is that there are over 100 known forms of liver diseases caused by a variety of factors ranging from viruses and genetics to toxins and poor nutrition, affecting everyone from infants to older adults. However, there are herbo-mineral formulations like Amlycure DS which are highly beneficial in such conditions. There have been a number of studies on component herbs and Amlycure DS with very interesting outcome.

EXPERIMENTAL STUDIES WITH COMPONENT HERBS

Picrorhiza kurroa showed regeneration of hepatocytes with stimulation of protein and nucleic acid synthesis in liver cells

Protein, DNA and RNA levels of picroliv from *Picrorhiza kurroa* treated experimental subjects were significantly increased by 20, 55 and 39% respectively, thereby stimulating nucleic acid and protein synthesis in liver. Picroliv caused 65% increase in *in vivo* uptake of leucine and it also showed significant protection (48%) against cycloheximide, a protein synthesis inhibitor. Picroliv has been reported to cause marked enhancement of F_0 F_1 ATPase (ATPase synthase) activity of liver mitochondria both in acute and chronic experimental subjects, suggesting stimulation of ATP synthesis. Low levels of ATP have been attributed to cellular damage.[1]

Figure 1 **Mortality rate with and without pre-treatment using *Tinospora cordifolia* or Gentamicin**



Another study with *Tinospora cordifolia* showed reduction of mortality and improved phagocytosis and intracellular bactericidal capability of neutrophils.

It has been found that pretreatment of experimental subjects with certain plant drugs protects them against *Escherichia coli (E.coli)*, *Staphylococcus aureus* and mixed bacterial species. It has also been found to increase the phagocytic and killing activity of peritoneal macrophages. Giloe (*Tinospora cordifolia*) and gentamicin reduced mortality in mice injected with *E. coli* peritoneally from 100% in controls to 17.8% and 11.1% in cases pre-treated with *Tinospora cordifolia* and gentamicin respectively (Figure 1). *Tinospora cordifolia* treated group showed significantly improved bacterial clearance as well as phagocytic and intracellular bactericidal capacities of neutrophils. In the gentamicin treated mice, although clearance was rapid but polymorph phagocytosis was depressed. *Tinospora cordifolia* did not possess *in vitro* bactericidal activity.[2]

CLINICAL STUDIES WITH AMLYCURE DS

Role of Amlycure in protecting liver from the hepatotoxic effects of anticancer agents and antitubercular therapy: A randomized controlled study[3]

Herbal products like Amlycure DS have been demonstrated to have hepatoprotective action in various studies. Against this background, a study was contemplated to assess the hepatoprotective role of Amlycure DS in patients of breast cancer receiving neo-adjuvant chemotherapy/adjuvant chemotherapy as one group and patients receiving antitubercular therapy in the other group. The effects were compared with a control group consisting of both breast cancer and tubercular patients who did not receive Amlycure DS along with their therapy.

Patient and methods: A total of 61 patients were included in the study (31 patients with tuberculosis of lymph nodes, abdomen etc. and 30 patients with locally advanced breast cancer (LABC)). Diagnosis of breast cancer was confirmed by fine needle cytology (FNAC)/ Tru-cut biopsy and patients received neo-adjuvant chemotherapy (three cycles of cyclophosphamide, adriamycin, 5-fluorouracil in standard doses i.e. CAF regime) after the required investigations including the liver function tests.

Observation and results: Group I - All patients had shown an increase in individual parameters after completion of treatment. When pretreatment LFT parameters were compared with post-treatment LFT, it was found that mean of each individual LFT parameter was increased after treatment and this increase was found to be statistically significant (P <0.05) (Table 1).

Groups II and III: All patients had shown a decrease in individual LFT parameters after completion of treatment. When pretreatment LFT parameters were compared with post-treatment LFT, it was found that mean of each individual LFT parameters decreased after treatment and this decrease in mean was statistically significant (P <0.05) (Tables 2,3).

Primary outcome measure: Amlycure or its constituents have been demonstrated to be effective in checking the antitubercular toxicity. The drug was found to protect against thioacetamide induced toxicity, reverse resultant elevated levels of SGOT, SGPT and alkaline phosphatase in serum and reduce the activity of succinate dehydrogenase and ribonuclease and glucose 6 phosphatase. It was also found to increase the DNA contents due to protective effects of Picroliv. The drug has also been reported to have anticholestatic effects and has also been reported to act as a cardio- and hepatoprotective agent. It has been found to lower LDL/phospholipid ratio.

Secondary outcome measure: The secondary outcome measure was analyzed for the different mechanisms of action of Amlycure DS for the prevention of hepatotoxicity. The proposed mechanism of Amlycure DS with respect to regenerative and anti-degenerative effects on hepatocytes was analyzed. Amlycure DS has been found to:

- *Prevent drug-induced liver cell damage*
- *Exert safe anti-inflammatory action*
- *Exert anti-cholestatic effects*
- *Improve phagocytosis by the liver Kupffer cells*
- *Normalize LFT.*

In view of the multiplicity and complexity of liver proteins, it is obvious that no single test can establish the disturbances of liver fuctions, thus a number of parameters are employed for accurate diagnosis to assess the severity of damage to judge and evaluate the therapy. Amlycure DS or AMD (and its constituents) significantly reduce serum bilirubin and check central necrosis of the hepatocytes due to membrane stabilizing effects. Amlycure DS has also been found to significantly reduce the enzymatic leakage of SGPT, alkaline phosphatase, inhibiting the glutathione depletion by exerting the antioxidant effects of glucosidic contents.

Anti-tubercular drug toxicity inhibition with Amlycure DS: A clinical study[4]

A group of patients suffering from tuberculosis (TB), receiving anti-TB drugs, comprising of rifampicin, isoniazid, pyrazinamide and ethambutol along with hepatoprotective drug, Amlycure DS, showed notable improvement in appetite, while none of them developed jaundice during trial period of 4 months. The SGOT, SGPT levels were also within the normal limits in treated group, while

Table 1 Group I (n=21)

		Mean	Std. Deviation	Std. Error Mean	Correlation	Sign.
Pair 1	PRESB	0.848	0.3156	0.689		
	PSTSB	1.11	0.585	0.128	0.879	0.000
Pair 2	PRESGOT	41.71	16.038	3.500		
	PSTSGOT	58.38	19.418	4.237	0.869	0.000
Pair 3	PRESGPT	39.14	11.612	2.534		
	PSTSGPT	55.10	14.936	3.259	0.555	0.009
Pair 4	PREALK	108.29	88.118	19.229		
	PSTALK	133.29	98.357	21.463	0.952	0.000

Table 2 Group II (n=19)

		Mean	Std. Deviation	Std. Error Mean	Correlation	Sign.
Pair 1	PRESB	1.153	0.6168	0.1415		
	PSTSB	0.97	0.586	0.134	0.949	0.000
Pair 2	PRESGOT	54.42	20.543	4.713		
	PSTSGOT	45.68	16.279	3.735	0.858	0.000
Pair 3	PRESGPT	47.89	17.916	4.110		
	PSTSGPT	37.89	14.110	3.237	0.826	0.000
Pair 4	PREALK	139.21	124.065	28.462		
	PSTALK	96.68	94.242	21.621	0.905	0.000

Table 3 Group III (n=20)

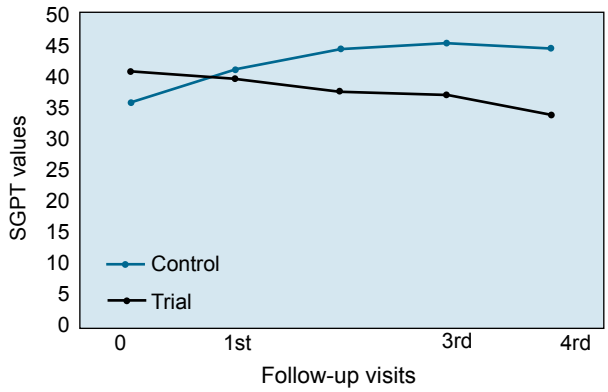
		Mean	Std. Deviation	Std. Error Mean	Correlation	Sign.
Pair 1	PRESB	0.925	0.3740	0.0836		
	PSTSB	0.70	0.152	0.034	0.176	0.459
Pair 2	PRESGOT	61.50	23.654	5.289		
	PSTSGOT	42.85	10.530	2.354	0.726	0.000
Pair 3	PRESGPT	61.10	25.674	5.741		
	PSTSGPT	41.30	11.411	2.552	0.453	0.045
Pair 4	PREALK	135.45	70.657	15.799		
	PSTALK	93.70	36.930	8.258	0.689	0.001

PRESB = Pre-treatment serum bilirubin; PSTSB = Post-treatment serum bilirubin; PRESGOT = Pre-treatment serum glutamic oxaloacetic transaminase (SGOT); PSTSGOT = Post-treatment SGOT; PRESGPT = Pre-treatment serum glutamic pyruvic transaminase (SGPT); PSTSGPT = Post-treatment SGPT; PREALK = Pre-treatment alkaline phosphatase; PSTALK = Post-treatment alkaline phosphatase

Table 4 Pre- and post-treatment statistical values of biochemical investigations in the tuberculosis patients

Parameters	Trial group (ATT + Hepatoprotective drug)					Control group (ATT only)				
	Initial				Follow-up	Initial				Follow-up
	0	1st	2nd	3rd	4th	0	1st	2nd	3rd	4th
Serum Bilirubin ± SD	0.79 ± 0.17	0.78 ± 0.08	0.84 ± 0.09	0.73 ± 0.13	0.77 ± 0.09	0.73 ± 0.18	0.98 ± 0.77	0.79 ± 0.19	0.73 ± 0.12	0.74 ± 0.16
Alkaline Phosphatase ± SD	9.60 ± 2.45	10.78 ± 2.12	11.08 ± 2.00	10.68 ± 1.47	10.10 ± 1.77	10.20 ± 1.79	10.50 ± 2.79	10.60 ± 2.01	13.50 ± 2.63	10.92 ± 1.84
SGOT ± SD	36.46 ± 5.87	34.86 ± 4.07	34.10 ± 3.24	37.38 ± 6.07	35.26 ± 5.06	34.93 ± 5.40	35.14 ± 4.28	36.76 ± 6.01	36.48 ± 7.42	37.90 ± 7.56
SGPT ± SD	40.80 ± 6.66	39.74 ± 6.19	37.64 ± 5.99	37.30 ± 6.46	34.24 ± 5.69	36.20 ± 7.73	41.18 ± 10.70	44.14 ± 14.27	45.32 ± 16.18	44.40 ± 15.82

Figure 2 Changes in SGPT values in the trial and control group



the other group receiving anti-tubercular therapy (ATT), without Amlycure DS developed (four out of 50) icterus and SGOT, SGPT (in 9 out of 50 patients) values were also on higher side (Figure 2, Table 4). Most of the patients were relieved of anorexia, nausea, vomiting, malaise and liver tenderness at the end of third week in the trial group. Mean score of icterus declined significantly in the trial group, improvement in signs and symptoms scores and biochemical values were much better in trial group as compared to control. No significant side effects were observed during the trial.

CONCLUSIONS

The observations of various pre-clinical and clinical studies of Amlycure DS which were conducted at various centers, reinforce the already established hepatoprotective role of Amlycure DS. The well-known hepatotoxic effects of antitubercular drugs and anticancer agents were significantly lower in patients receiving Amlycure DS as compared to their counterparts that did not receive Amlycure DS. There were additional beneficial effects in the form of a generalized well being (euphoria), improvement in appetite and weight, which may be difficult to quantify. There were no deleterious side effects observed in any patient with Amlycure DS. Amlycure DS may be safely recommended along with any potentially hepatotoxic therapy.

REFERENCES

1. *Ind J Expt Biol*. 1992 Jan;30:68-69.
2. *J Postgrad Med* (India). 1992 Jan-Mar;38(1):13-15.
3. The role of Amlycure in protecting liver from the hepatotoxic effects of anticancer agents and antitubercular therapy-a randomized controlled study. Delhi State Chapter. *Journal of Surgery. 2001* November;VI.
4. Antitubercular drug toxicity inhibition with Amlycure DS- a clinical study. *Ind J Cl Prac*. 1996; VII.