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Studies with Liv.52 in the Treatment of Infective Hepatitis, Chronic Active Hepatitis and Cirrhosis of the Liver

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INTRODUCTION

Amongst the wide spectrum of liver diseases prevalent all over the world, incidence of Infective Hepatitis, Chronic Active Hepatitis and Cirrhosis of the Liver comprises a very large group which is responsible for a high rate of mortality and morbidity amongst the population at large all over India. Various causes have been ascribed to the significantly higher morbidity and mortality from this group of diseases in our country and also in other underdeveloped and developing countries. Amongst them, under nutrition and/or malnutrition, specially protein malnutrition, widely prevalent infections, particularly viral infections, liver injuries caused by parasitic infections, and recognised or unrecognised toxins etc. have been considered important factors in explaining the higher incidence, a more severe course, and a rather unsatisfactory prognosis in this group of diseases. While the aetiology in certain clinical entities of the group e.g. viral hepatitis, post-hepatitis cirrhosis etc. has been well recognised and well established and this has helped clinicians towards a better understanding of the disease process, certain entities of the clinical spectrum still remain ill-understood, in spite of extensive studies of the conditions. Mostly the aetiology of these conditions still remains a matter of conjecture, rather than a scientific truth, e.g. juvenile cirrhosis of India, classical portal cirrhosis etc.

The other important aspect of the problem regarding this group of diseases is the relatively unsatisfactory response to therapy and prognosis. This remains so in spite of the spectacular progress made during last 3-4 decades in the therapy of other diseases, infective or otherwise. Though one entity of the group, viz. Infective (Viral) Hepatitis is more or less a self-limiting disease, mostly resolving itself in 4-6 weeks' time, the others of the group tend to be relentlessly progressive either ending fatally, or leading to morbidity over a prolonged period. Even in case of the first category viz. Viral hepatitis, though the prognosis is stated as excellent in most of the advanced countries, in India it is a common experience that the disease runs a more prolonged course, some times severe and fulminant, leading to hepatic failure, and the mortality from the disease is not insignificant. Moreover, many cases are left behind with a stage of chronic and more prolonged activity (cholestatic hepatitis, chronic active hepatitis etc) which ultimately may lead to post-hepatitis cirrhosis, following a progressive course and with resultant morbidity and mortality. Since there is no specific treatment for the conditions until now, the therapeutic regimen followed in these cases up to the present moment is by and large symptomatic and at best palliative. Different regimens have been tried at different times by different authorities and institutions, not without controversial arguments in favour of or against a particular regimen and the available literature is replete with claims and counterclaims. In spite of the not-too-happy a situation, attempts are perpetually being made to find out some effective therapy for the conditions. A better than before understanding of the aetiopathogenesis and progress of the disease, both pathological and clinico-biochemical, has encouraged workers in different parts of India and abroad to renew and augment the search for a better remedy for these conditions than was available until a few years back. Unfortunately, no "Specific" treatment for these conditions has been available till date, and clinicians and others concerned have to be satisfied with the best sort of symptomatic and palliative

regimen available, along with the much needed reassurance and explanation of the situation to the unfortunate sufferers from the diseases.

To be an ideal remedy in the aforesaid disease states, it must at least fulfil the following criteria, viz. (1) the remedy must be able to control the infection or counter the noxious and injurious elements, if these are aetiological factors, (2) it should be able to protect the liver parenchyma from the ravages of the factors in (1), (3) it should enable the healing process of the damaged parenchyma of the liver to revert to a structurally normal or near normal state, (4) it must help the liver parenchymal cells to regain their multifarious functional capabilities to normal or as near normal as possible, (5) by virtue of the above effects, it should be able to prevent complications, short-term or long-term, leading to mortality and morbidity. Unfortunately, virtually all of the therapeutic schedules followed at present still lag far behind the above ideals in many respects.

During the last decade and a half, an indigenous proprietary preparation "Liv.52" marketed by The Himalaya Drug Co., for the therapy of different liver diseases, has been claimed by the manufacturers to have properties which to some extent fulfil and approach the ideal requirements of a remedy of this nature. During the same time, a good number of clinicians and allied workers in the field have tried the preparation in liver diseases of different types. Their results, both by the clinical and biochemical parameters, as also in pathological and long-term prognostic aspect, have been recorded mostly in Indian medical literature[1-12].

The preparation is claimed to possess the following major properties:

(i) Hepatic stimulant and choleretic, leading to increased functional efficiency.
(ii) Protects the hepatic parenchyma against the effect of toxi-infective noxious agents.
(iii) Accelerates cellular metabolic activity and promotes regeneration of damaged liver cells.

Also it is claimed to be a good appetiser, stimulator of haemopoiesis and a pronounced anabolic agent.

Different workers have recorded their observations by different parameters, and on the whole, the main theme harped upon by most of the workers in the available literature on the use of the remedy has been on the lines that the preparation has a definite beneficial effect on the liver diseases. Since there is no truly "specific" remedy available for the conditions, the preparation has been considered a definite advance towards palliative therapy and effective control of mortality and morbidity in our population from the ravages of the diseases.

In consideration of the foregoing facts, and bearing in mind the claims and at times counterclaims about the efficacy of the preparation in different liver diseases, it was decided to observe for ourselves in the Department of Medicine, Medical College, Calcutta the claimed efficacy or otherwise of the preparation by conducting a controlled trial in the commonly available case material of the group viz. (i) Acute Infective (Viral) Hepatitis, (ii) Chronic Active Hepatitis and (iii) Cirrhosis of the Liver.

The full requirements of the preparation for the trial were supplied by The Himalaya Drug Co. The preparation Liv.52 is available in three forms, viz. drops, syrup and tablets.

COMPOSITION

Each Liv.52 tablet contains:

Capparis spinosa	65 mg
Cichorium intybus	65 mg
Solanum nigrum	32 mg
Cassia occidentalis	16 mg
Terminalia arjuna	32 mg

Achilla millefolium	16 mg
Tamarix gallica	16 mg
Mandur bhasma	33 mg

Processed in Eclipta alba, Phyllanthus niruri, Boerhaavia diffusa, Tinospora cordifolia, Berberis aristata, Raphanus sativus, Phyllanthus emblica, Plumbago zeylanica, Embelia ribes, Terminalia chebula, Fumaria officinalis.

MATERIAL AND METHODS

The trial was started in the Medical College and Hospital, Calcutta in the month of June 1974, after receiving permission from local authorities and from the Drugs Controller, Directorate General of Health Services, India. The trial was conducted from June 1974 to August 1977. During this period 165 (one hundred sixty five) patients were included initially in the trials. Children below 10 years were excluded. Patients were selected both from Indoor and Outdoor Section of the Hospital. Sixty one patients were excluded from the final analysis, 44 for the lack of proper follow-up and 17 due to death from hepatic coma within 24-72 hours of admission. Of the remaining one hundred four cases who could be followed up, seventy three patients were on Liv.52 and 31 patients belonged to Control Group. The number of cases in each category is given in Table I.

Table I: Categories of liver disease studied

		Liv.52 group	Control group
(a)	Infective Hepatitis	30	15
(b)	Chronic Active Hepatitis	24	8
(c)	Cirrhosis	19	8
		73	31

Table II: Age distribution

		Liv.52 group				Control group			
		10-30 years	31-45 years	46-60 years & above	Total	10-30 years	31-45 years	46-60 years & above	Total
(a)	Infective hepatitis	20	7	3	30	9	5	1	15
(b)	Chronic active hepatitis	10	12	2	24	3	5	0	8
(c)	Cirrhosis	3	8	8	19	2	3	3	8
		33	27	13	73	14	13	4	31

Table III: Sex distribution

		Liv.52 group			Control group		
		Male	Female	Total	Male	Female	Total
(a)	Infective hepatitis	22	8	30	10	5	15
(b)	Chronic active hepatitis	16	8	24	5	3	8
(c)	Cirrhosis	14	5	19	6	2	8
		52	21	73	21	10	31

Out of admitted cases in the Hospital only those cases who had not received any treatment beyond general measures were included in the study. After selection of the patients, all were clinically examined and the findings recorded in a proforma prepared for the purpose. The cases were then placed in the clinical categories indicated earlier.

Haematological and biochemical investigations were then carried out and recorded in respect of each patient. They were repeated every week to every month and every third month, as warranted by the category of cases. Haemogram included Hb, TC, DC, ESR, BT, CT and prothrombin time.

Blood biochemical studies included blood sugar, urea, Serum bilirubin, Total protein, Albumin/Globulin ration, Protein Electrophoresis, Alkaline phosphatase, SGOT and SGPT in each case. B.S.P. excretion test was done in 20 cases in the two groups of patients viz. Chronic Active Hepatitis and Cirrhosis, taking 5 Control and 5 Liv.52 cases from each group. HBsAg was tested in all cases. Skiagram of the chest, Barium-swallow of oesophagus and in some, Barium-meal X-ray of stomach and duodenum were done in cases of Cirrhosis.

Periodic liver biopsy was done in patients of each clinical category, excepting Infective Hepatitis. Liver scientigram could be done only on six cases and had to be discontinued due to some unavoidable problems.

The patients were put on Liv.52 tab. (4 tablets, t.i.d. irrespective of age and sex) after thorough investigations, and the improvement in the patients were assessed clinically, haematologically, biochemically and histopathologically at periodic intervals. Haemogram and biochemical studies were repeated in each patient every month, and liver biopsy was repeated at intervals of 3 to 6 months.

After their discharge from the hospital, patients were directed to attend a special follow-up clinic of the trial at O.P.D. at periodic intervals, where they were reviewed and received the supply of drugs. They were readmitted from time to time for further investigations and assessment.

In both groups of cases (viz. Liv.52 Group and Control Group) patients received supportive treatments in the form of rest, nutritious diet, Vitamin B-complex, Glucose drinks and drip etc. Frusemide and spironolactone were used as and when indicated for the relief of oedema and/or ascites, but steroids were not used in any patient of either group.

The efficacy of the treatment was assessed by the improvement of subjective symptoms and objective signs, the degree of improvement in various Liver Function Tests, as well as the degree of histopathological improvement of liver.

OBSERVATIONS AND RESULTS

Group A: Infective Hepatitis: In the present study of 45 cases of Infective Hepatitis, 30 patients were put on Liv.52 and 15 cases served as Controls.

Symptoms in these cases included fever, anorexia, nausea, vomiting, right hypochondriac/epigastric pain, yellow coloration of urine and conjunctivae, prostration, boneache, headache, insomnia, flatulence and in some, clay-coloured stools.

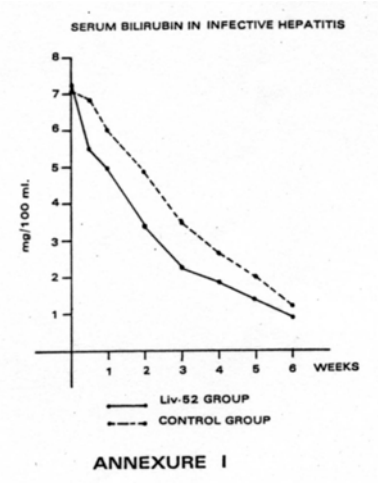
All of them had slight to severe degree of jaundice and enlarged tender liver ranging from 1" and 2½" below right costal margin.

Clinical and biochemical improvements were observed in majority of cases earlier in Liv.52 Group than in Control Group.

1. *Clinical*: Symptomatic improvement was observed specially in respect of fever, anorexia, nausea, weakness, boneache, headache, insomnia, flatulence and epigastric pain earlier in Liv.52 Group than in Control Group. Disappearance of yellow coloration of urine and conjunctivae was also much earlier in Liv.52 Group than in Control Group. Similar improvement in physical signs like enlarged tender liver, jaundice etc. was observed in the Liv.52-treated cases.

2. *Biochemical (Liver Function Tests)*

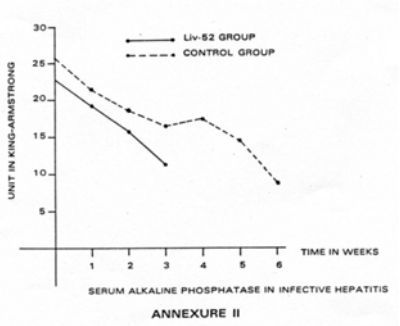
(i) *Serum Bilirubin*: The improvement in the level of Serum bilirubin in majority cases of Liv.52 Group was observed very early i.e. within 7 days' of treatment and the value of Serum bilirubin became normal to near-normal within 2-3 weeks in majority of cases (73.33%) in Liv.52 Group, whereas the improvement in the level of Serum bilirubin in Control Group was observed much later i.e. after 2-3 weeks, in majority of cases. Serum bilirubin became normal only after 3-6 weeks in this group. The trend of changes in Serum bilirubin is depicted in Table IV and Annexure I.



ANNEXURE I

Table IV: Serum bilirubin level in infective hepatitis (in mg)								
	On admission	3rd day	1st week	2nd week	3rd week	4th week	5th week	6th week
Liv.52 group (Mean: 30 cases)	7.23	6.49	4.98	3.31	2.24	1.85	1.34	0.98
Control group (Mean: 15 cases)	7.19	6.86	6.00	4.87	3.50	2.64	2.00	1.23

(ii) *Alkaline Phosphatase*: Values of Alkaline phosphatase in the Liv.52 Group of cases showed earlier improvement in majority of cases (73.33%) than in Control Group (26.66%). Improvement was observed within 2-3 weeks in Liv.52 Group whereas in Control Group, majority of patients took 3-6 weeks to show improvement. The trend of changes in Alkaline phosphatase is depicted in Table V and Annexure II.



ANNEXURE II

Table V: Serum alkaline phosphatase in infective hepatitis (in King-Armstrong Units)							
	On admission	1st week	2nd week	3rd week	4th week	5th week	6th week
Liv.52 group (Mean: 30 cases)	22.97	19.20	15.8	11.14	–	–	–
Control group (Mean: 15 cases)	25.78	21.36	18.89	15.98	17.10	14.70	8.90

(iii) *SGOT / SGPT*: In the Liv.52 Group 22 out of 30 patients (73.33%) showed earlier improvement in 2-3 weeks, whereas 4 out of 15 (26.66%) patients in Control Group showed the same response within that time, and rest of the cases in Control Group took 3-6 weeks to become normal (Table VI).

Table VI: Serum GOT and GPT in infective hepatitis (in Karmen Units)														
	On admn.		1st week		2nd week		3rd week		4th week		5th week		6th week	
	GOT	GPT	GOT	GPT	GOT	GPT	GOT	GPT	GOT	GPT	GOT	GPT	GOT	GPT
Liv.52 group (Mean: 30 cases)	73.7	152.5	70.4	137.7	47.4	81	28.9	48.2	–	–	–	–	–	–
Control group (Mean: 15 cases)	89.6	154.9	74.1	123.3	60.9	100	46.8	75.9	48.5	78.5	43	63.5	21.5	31.5
(Normal: less than 40 units)														

(iv) *Total Protein / Albumin / Globulin*: In Liv.52 Group the Serum albumin values showed significant early rise in majority of cases than in Control cases (Table VII).

Table VII: Serum total protein, Albumin: Globulin ration in infective hepatitis (in gm%)															
	On admn.			3rd day			1st week			2nd week			3rd week		
	TP	A	G	TP	A	G	TP	A	G	TP	A	G	TP	A	G
Liv.52 group (Mean: 30 cases)	5.6	3.0	2.6	5.7	3.2	2.5	5.8	3.4	2.4	6.1	3.7	2.4	6.3	3.8	2.5
Control group (Mean: 15 cases)	5.2	2.9	2.3	5.1	2.9	2.2	5.1	3.0	2.1	5.3	3.2	2.1	5.7	3.5	2.2
(Normal: Serum albumin 3.5 to 5: Serum globulin 2 to 3.5) (T.P. =Total protein; A = Albumin; G = Globulin)															

The distribution of cases showing duration for improvement of subjective symptoms and objective signs as well as in biochemical profiles in cases of Infective Hepatitis both in Liv.52 Group (30 cases) and Control Group (15 cases) is summarised in Table VIII.

Table VIII: Period taken for clinical and biochemical improvement in infective hepatitis (in weeks)						
Age group	Liv.52 group (30 cases)			Control group (15 cases)		
	1-3 weeks	4-6 weeks	Above 6 weeks	1-3 weeks	4-6 weeks	Above 6 weeks
10-30 years	17	5	1	4	5	–
31-45 years	3	1	–	–	5	–
46-60 years and above	2	1	–	–	–	1
	22	7	1	4	10	1
%	73.33	23.33	3.33	26.66	66.6	6.6

Thus in 45 cases of Infective Hepatitis following observations in respect of results of treatment have been made:

		Liv.52 group	Control group
(i)	Good	22 (73.33)	4 (26.66)
(ii)	Fair	7 (23.33)	10 (66.66)
(iii)	Poor	1 (3.33)	1 (6.66)
		30	15

Criteria for Assessment of Results as “Good”, “Fair” and “Poor” in Infective Hepatitis:

Good : Improved clinically and biochemically within a period of 1-3 weeks.
Fair : Improved clinically and biochemically within a period of 4-6 weeks.
Poor : Improved clinically and biochemically only after 6 weeks or showing indifferent or no improvement.

Group B: Chronic Active Hepatitis: In the present study of 32 cases of Chronic Active Hepatitis, 24 patients were put on Liv.52 and the remaining 8 received only conventional therapy (minus steroids) and served as Control Group.

The major symptoms and signs of the cases, number of cases involved and their age and sex-wise distribution both in the Liv.52 and Control Groups are presented in Table IX.

Table IX: Symptoms, signs, age, sex distribution in chronic active hepatitis								
	Liv.52 group (24)				Control group (8)			
	10-30 years	31-45 years	46-60 years & above	Total	10-30 years	31-45 years	46-60 years & above	Total
Fever (20)	6	8	1	15	3	2	–	5
Anorexia (32)	10	12	2	24	3	5	–	8
Weakness (28)	10	12	–	22	2	4	–	6
Weight loss (16)	5	8	1	14	1	1	–	2
Flatulence (18)	6	7	2	15	1	2	–	3

Yellow urine (32)	10	12	2	24	3	5	–	8
Joint pain (3)	2	1	–	3	–	–	–	–
Dyspepsia (32)	10	12	2	24	3	5	–	8
Jaundice (32)	10	12	2	24	3	5	–	8
Hepatomegaly (32)	10	12	2	24	3	5	–	8
Splenomegaly (5)	1	2	1	4	1	–	–	1
Pedal oedema (6)	1	2	1	4	1	1	–	2
Ascites (2)	–	1	–	1	–	1	–	1
Spider naevi (1)	–	1	–	1	–	–	–	–
Palmar erythema (2)	–	1	–	1	–	1	–	1
Gynaecomastia (1)	–	1	–	1	–	–	–	–
Figures in parenthesis indicate number of cases								

RESULTS

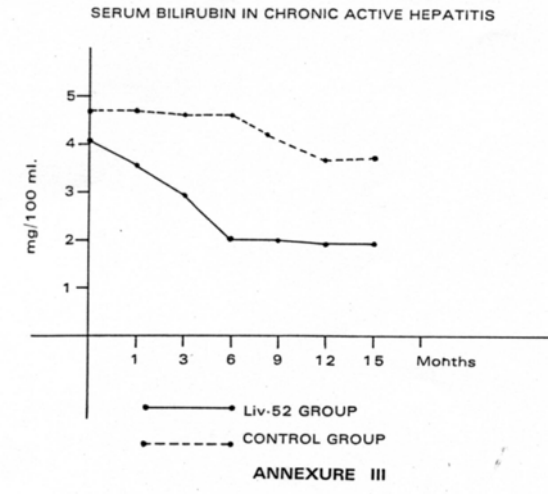
Chronic Active Hepatitis

1. *Clinical*: Clinical improvement in respect of fever, anorexia, yellow urine, weight loss, flatulence, dyspepsia, jaundice etc. was observed early in majority of cases of Liv.52 Group, as compared to Control Group (Table X).

Table X: Period taken for clinical improvement in chronic active hepatitis

Age group	Liv.52 group			Control group		
	3-6 months	7-12 months	13-24 months & above	3-6 months	7-12 months	13-24 months & above
10-30 years	5	5	–	–	2	1
31-45 years	4	6	2	–	2	3
46-60 years & above	–	1	1	–	–	–
	9	12	3	–	4	4
%	37.5	50	12.5	–	50	50

No improvement could be achieved in 12.5% of cases in the Liv.52 Group, even after following up the cases for 36 months, whereas 50% of cases in Control Group failed to improve; rather many of them deteriorated in the same period.



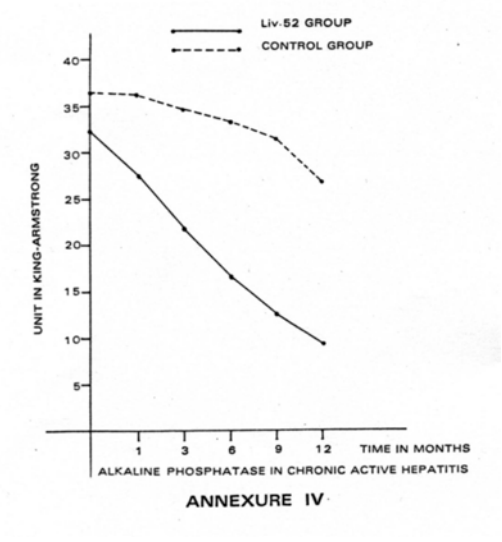
2. *Biochemical*:
   (i) *Serum bilirubin*: Table XI and Annexure III depict the trend of changes in Serum bilirubin in the 2 groups. It was observed that in 9 cases of Liv.52 Group, Serum bilirubin began to decrease very early and the levels came down to normal or near normal in 6 months' time, whereas no case in Control Group showed any such improvement within that period.

Table XI: Serum bilirubin in chronic active hepatitis (in mg/100 ml)

	On admission	1st month	3rd month	6th month	9th month	12th month	15th month
Liv.52 group (Mean: 24 cases)	4.1	3.6	2.9	2.2	2.6	1.9	1.9
Control group (Mean: 8 cases)	4.7	4.7	4.6	4.6	4.2	3.9	4.0

Twelve cases of Liv.52 Group started to show lowering of Serum bilirubin after 6 months, which became almost normal in 12 months' time, whereas only 4 cases of Control Group showed a similar improvement.

Three cases out of 24 patients i.e. 12.5% in Liv.52 Group, Serum bilirubin showed no improvement, rather the levels increased, whereas in Control Group 4 cases out of 8 patients (i.e. 50%) showed no improvement and became worse.



ANNEXURE IV

(ii) *Alkaline Phosphatase*: Table XII and Annexure IV depict the trend of changes in Alkaline phosphatase in the Liv.52 Group and Control Group of Chronic Active Hepatitis. It was observed that in 9 cases of the Liv.52 Group, there was an early improvement in the values of Alkaline phosphatase which became normal in 6 months whereas no such improvement was observed in any case of Control Group within that period.

Table XII: Alkaline phosphatase in chronic active hepatitis (in King Armstrong Units)

	On admission	1st month	3rd month	6th month	9th month	12th month
Liv.52 group (Mean: 24 cases)	32.5	27.4	21.9	16.6	12.6	9.4
Control group (Mean: 8 cases)	36.4	36.1	34.9	33.2	31.6	26.7
(Normal: 4-13 units)						

Twelve other Liv.52-treated cases showed moderate improvement and their values became normal in 12 months' time. The values remained normal during the period of the next 12 months also, with only half the dose of Liv.52 i.e. 6 tablets daily in 3 equal doses, whereas 4 cases out of the 8 patients in Control Group showed only some improvement during the same period.

Three cases out of the 24 Liv.52-treated cases and 4 out of 8 Control cases failed to show any improvement in Serum alkaline phosphatase values, even after 36 months.

(iii) *Serum Total Protein/Albumin*: *Globulin*: The trend of changes in Serum Total Protein/Albumin: Globulin is depicted in Table XIII.

Table XIII: Serum total protein, Albumin : Globulin in chronic active hepatitis

	On admn.			1st month			3rd month			6th month			9th month			12th month		
	TP	A	G	TP	A	G	TP	A	G	TP	A	G	TP	A	G	TP	A	G
Liv.52 group (Mean: 24 cases)	6.2	2.8	3.4	6.2	2.9	3.3	6.3	3.3	3.0	6.4	3.6	2.8	6.4	3.6	2.8	6.4	4.0	2.4
Control group (Mean: 8 cases)	5.9	2.4	3.5	5.9	2.1	3.8	5.9	2.0	3.9	5.9	2.1	3.8	6.0	2.4	3.6	6.1	2.7	3.4
The observations on albumin and globulin in Chronic Active Hepatitis are summarised in Table XIV.																		

Table XIV: Albumin : Globulin

	No. of cases improved in 6 months	No. of cases improved in 12 months	No. of cases not improved after 36 months	No. of cases significantly improved in 6-12 months	No improvement
Liv.52 group (Mean: 24 cases)	9 (37.5%)	12 (50%)	3 (12.5%)	21 (87.5%)	3 (12.5%)
Control Group (Mean: 8 cases)	0 (0%)	4 (50%)	4 (50%)	–	–

(iv) *Serum GOT and GPT*: The trend of changes in SGOT and SGPT is depicted in Table XV.

Table XV: SGOT/SGPT in chronic active hepatitis

	On admn.		1st month		3rd month		6th month		9th month		12th month	
	GOT	GPT	GOT	GPT	GOT	GPT	GOT	GPT	GOT	GPT	GOT	GPT
Liv.52 group (Mean: 24 cases)	73.79	118.5	70.4	115.4	64.2	104.1	47.1	74.6	40.0	65.3	23.2	37.5
Control group (Mean: 8 cases)	69.8	130.2	81.2	127.8	80.8	126.5	75.6	123.3	67.0	111.6	51.7	80.3

It was observed that 21 out of 24 patients (87.5%) on Liv.52 showed total improvement in respect of SGOT/SGPT results in 12 months' time, as against a slight improvement in 4 out of 8 cases of the Control Group during the same time.

It was noteworthy that GOT/GPT reverted to normal in only 6 months' time in 9 out of 24 patients (37.5%) in the Liv.52 Group against NIL in the Control Group.

(v) *BSP Study*: There had been marked clearance in BSP in all the 5 cases of Liv.52 Group in 12 months' time as against only one case in the Control Group.

(vi) *Protein Electrophoresis*: Quantitative immunoglobulin determination by Electrophoresis method revealed an elevation of all types with a marked increase in IgG at the initial 1st and 2nd investigations on admission and after 6 months respectively, both in Liv.52 Group and Control Group. But on subsequent investigations at 9th and 12th months, 21 patients (87.5%) of the Liv.52 Group showed almost normal range of immunoglobulins with a slightly higher level of IgG, whereas in the Control Group, only 4 out of 8 (50%) patients showed a similar improvement.

(vii) *Histopathological Investigation*: Nine cases (37.5%) in Liv.52 Group showed marked improvement in respect of regeneration and repair of liver cells in 6 months' time, whereas none in the Control Group showed any significant improvement during the same period.

However, in 12 months' time regressive changes in respect of liver cell damage were observed in 12 cases (50%) and 4 cases (50%) of the Liv.52 and Control Groups respectively.

Three cases (12.5%) of the Liv.52 Group showed no improvement of liver cell pathology, rather they became worse, in spite of intensive therapy (12 tablets of Liv.52 daily for 3 years). Two patients out of these 3 were HBsAg +ve. Four patients (50%) of the Control Group failed to improve histopathologically, ultimately attaining a picture of cirrhosis.

Thus, in 32 cases of Chronic Active Hepatitis, the above inferences have been made in respect of results of treatment (See Table XVI).

Table XVI: Results of treatment in chronic active hepatitis

		Liv.52 group	Control group
(i)	Good	9 (37.5%)	Nil (0%)
(ii)	Fair	12 (50%)	4 (50%)
(iii)	Poor	3 (12.5)	4 (50%)
		24	8

Group C: Cirrhosis of the Liver: Cases of Cirrhosis of the Liver were selected from the Medical wards of Medical College Hospital, Calcutta during the period from June 1974 to February 1975. 27 of them who could be followed up for 2-3 years were included in the present study for analysis. Nineteen patients of these 27 belonged to the study group with Liv.52, and 8 patients served as Controls. Four out of these 27 cases were chronic alcoholics for ± 20 years, and 21 had a history of recurrent (±3) jaundice, 4 out of whom were found to be HBsAg positive.

Clinical features and findings of investigations in all the cases were recorded in the proforma, as in cases of Infective Hepatitis and Chronic Active Hepatitis. B.S.P. excretion studies could be done in 10 cases only (5 Liv.52 and 5 Controls). Histopathological studies were performed in all cases and were repeated at 6 monthly intervals.

Table XVII shows the distribution of the cases age-wise and sex-wise, based on histopathological diagnosis in both Liv.52 and Control Groups.

Table XVII: Age and sex distribution in cirrhosis cases

Age group	Liv.52 group (19)						Control group (8)					
	Post-necrotic cirrhosis		Portal cirrhosis		No discernible cause		Post-necrotic cirrhosis		Portal cirrhosis		No discernible cause	
	M	F	M	F	M	F	M	F	M	F	M	F
10-30 years	2	1	–	–	–	–	1	1	–	–	–	–
31-45 years	5	2	1	–	–	–	2	1	–	–	–	–
46-50 years and above	3	1	2	–	1	1	2	–	1	–	–	–
	10	4	3	–	1	1	5	2	1	–	–	–

All the 21 cases (14 on Liv.52 and 7 Controls) showing post-necrotic cirrhosis, histopathologically, had a history of recurrent jaundice. The 4 patients showing histopathological picture of portal cirrhosis had a history of consumption of alcohol in the form of country liquor over prolonged periods (±20 years).

The major symptoms and signs, number of cases involved, and their distribution, age and sex-wise in the Liv.52 and Control Groups are presented in Table XVIII.

Table XVIII: Age/sex distribution, symptoms and signs in cirrhosis of liver

	Liv.52 group (19 cases)							Control group (8 cases)						
	10-30 years		31-45 years		46-60 years & above		Total	10-30 years		31-45 years		46-60 years & above		Total
	M	F	M	F	M	F		M	F	M	F	M	F	
Symptoms:*														
Anorexia (27)	2	1	6	2	6	2	19	1	1	2	1	2	1	8
Flatulence (25)	2	1	6	1	5	2	17	1	1	2	1	2	1	8
Dyspepsia (16)	1	1	4	1	4	1	12	–	1	1	1	1	–	4
Weakness (26)	2	1	6	1	6	2	18	1	1	2	1	2	1	8
Weight loss (20)	–	1	6	–	6	2	15	–	–	2	1	2	–	5
Malaise (22)	2	1	6	1	5	2	17	1	1	2	–	1	–	5
Fatiguability (21)	2	1	6	1	4	2	15	1	1	1	1	1	–	5
Low-grade fever (10)	1	–	2	1	2	–	6	1	1	1	1	–	–	4
Bulging of abdomen (25)	2	1	5	2	5	2	17	1	1	2	1	2	1	8
Diarrhoea (6)	–	–	1	1	1	1	4	1	–	1	–	–	–	2
Yellow urine (12)	2	–	2	1	2	1	8	1	–	2	–	1	–	4
Yellow conjunctivae (12)	2	–	2	1	2	1	8	1	–	2	–	1	–	4
Haematemesis (6)	–	–	2	–	2	–	4	–	–	1	–	1	–	2
Malaena (6)	–	–	2	–	2	–	4	–	–	1	–	1	–	2

Epigastric Pain(12)	1	1	3	1	1	1	8	1	1	1	1	–	–	4
Breathlessness (2)	–	–	–	–	1	–	1	–	–	–	–	–	1	1
Signs:*														
Hepatomegaly (27)	2	1	6	2	6	2	19	1	1	2	1	2	1	8
Splenomegaly (27)	2	1	6	2	6	2	19	1	1	2	1	2	1	8
Ascites (23)	1	1	5	2	4	2	15	1	1	2	1	2	1	8
Oedema (23)	1	1	5	2	4	2	15	1	1	2	1	2	1	8
Wasting (22)	1	1	4	2	4	2	14	1	1	2	1	2	1	8
Clinical Jaundice (12)	2	–	2	1	2	1	8	1	–	2	–	1	–	4
Spider Argiomas (8)	1	–	2	1	1	1	6	–	–	1	–	1	–	2
Palmar erythema (14)	1	1	3	1	4	1	11	1	–	1	1	–	–	3
Gynaecomastia (4)	–	–	1	–	1	–	2	–	–	1	–	1	–	2
Testicular atrophy (3)	–	–	1	–	1	–	2	–	–	–	–	1	–	1
Parotid swelling (2)	–	–	1	–	1	–	2	–	–	–	–	–	–	–
Clubbing (1)	–	–	1	–	–	–	1	–	–	–	–	–	–	–
Purpura (1)	–	–	–	–	–	–	–	–	–	–	–	1	–	1
*Figures in parenthesis indicate number of cases.														

RESULTS

Cirrhosis of Liver

1. *Clinical*: Clinical improvement in respect of different symptoms and signs was observed earlier in majority cases of Liv.52 Group, in comparison to that of Control Group, where the improvement was delayed, and only 50% cases showed such an improvement. The clinical improvements which were observed in different age-groups both in Liv.52 Group and Control Group have been summarised in Table XIX.

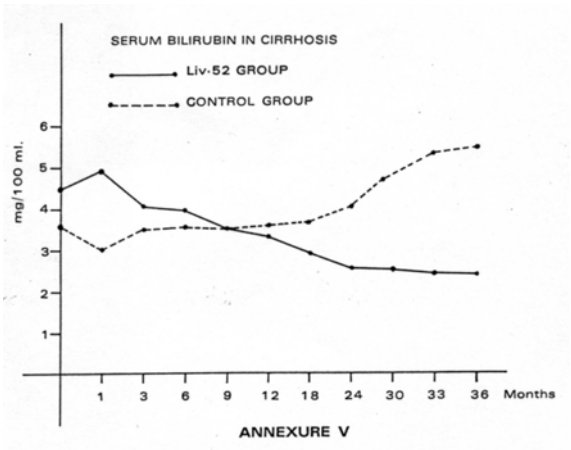
   Table XIX shows that out of 19 patients in the Liv.52 Group, 4 improved clinically in 12 months' time and another 10 in 24 months' time.

Table XIX: Clinical improvement in cirrhosis patients

Age group	Liv.52 group (19 cases)					Control group (8 cases)				
	6-9 months	9-12 months	12-18 months	18-24 months	No improvement in 36 months	6-9 months	9-12 months	12-18 months	18-24 months	No improvement in 36 months
10-30 years	1	–	1	–	1	–	–	–	1	1
31-45 years	–	2	2	3	1	–	–	1	1	1
45-60 years & over	–	1	2	2	3	–	–	–	1	2
	4		10		5	–		4		4

2. *Biochemical*:

   (i) *Serum Bilirubin*: (1) Level of Serum bilirubin came down to normal range from its initial level in 12 months in 13 cases on Liv.52 and remained within normal range for full period of follow-up (36 months) whereas only one patient in the Control group showed a similar response. (2) One patient in the Liv.52 Group (1/19) and 2 patients in the Control Group (2/8) took 24 months for the reversion of Serum bilirubin to normal level. (3) Five patients of Liv.52 Group (5/19) and in five patients of Control Group (5/8) failed to show any improvement even after 36 months.

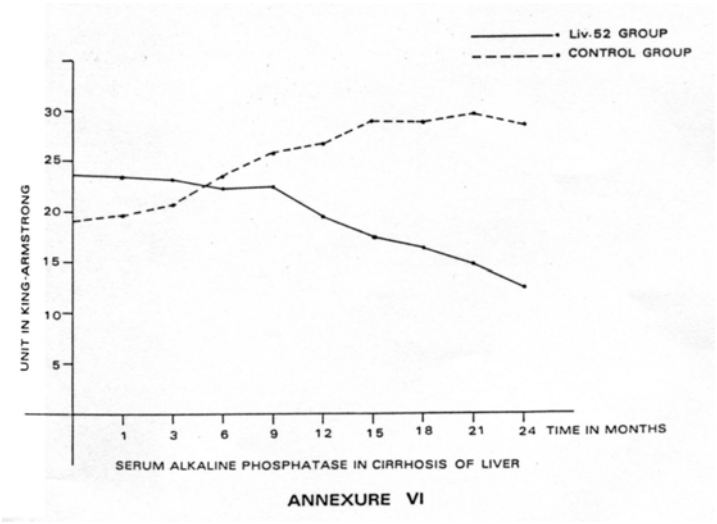


ANNEXURE V

Table XX and Annexure V show the mean values and the trend of changes in serum bilirubin in the two groups.

Table XX: Serum bilirubin in cirrhosis of the liver (mg/100 ml)														
	On admn.	1st month	3rd month	6th month	9th month	12th month	15th month	18th month	21st month	24th month	27th month	30th month	33rd month	36th month
Liv.52 group (Mean: 19 cases)	4.5	4.9	4.1	3.9	3.5	3.3	3.2	2.9	2.7	2.6	2.5	2.5	2.4	2.4
Control group (Mean: 8 cases)	3.6	3.5	3.5	3.6	3.6	3.6	3.7	3.7	4.0	4.1	4.4	4.7	5.3	5.4

(ii) *Alkaline Phosphatase*: (1) In 4 cases on Liv.52, values of Alkaline phosphatase showed early improvement which became normal in 9 to 12 months; whereas no case in the Control Group showed a similar improvement during the same period. (2) In 10 cases on Liv.52, Serum Alkaline phosphatase showed moderate initial improvement, the values becoming normal within 18 to 24 months, and remaining normal for the next 12 months of observation, as against only 3 cases of Control Group showing only slight improvement in 24 months' time. (3) Five patients on Liv.52, 5 of the Control Group failed to show any improvement in the Alkaline phosphatase level, even in 36 months.



ANNEXURE VI

Table XXI and Annexure VI show the Mean values and the trend of changes in Alkaline phosphatase (K.A. units) in the Liv.52 and Control Group.

Table XXI: Alkaline phosphatase in Cirrhosis of liver (in K.A. units)										
	On admn.	1st month	3rd month	6th month	9th month	12th month	15th month	18th month	21st month	24th month
Liv.52 group (Mean: 19 cases)	23.8	23.2	23.1	22.07	20.4	19.4	17.3	16.2	14.6	12.6
Control group (Mean: 8 cases)	19.0	19.8	21.5	23.3	25.6	26.3	28.7	28.7	29.3	28.4

(iii) *Serum Albumin*: Majority of the patients on Liv.52 showed significant improvement of hypoalbuminaemia, which was a marked feature in all cases of cirrhosis. (1) In four (4/19) cases on Liv.52, the Serum albumin values became normal in 12 months' time, as against none in the Control Group. (2) In ten (10/19) patients on Liv.52, Serum albumin values attained normal levels in 18 to 24 months' time, as against 3 out of 8 of the Control Group showing similar result during the same period. (3) Five patients on Liv.52 and 5 patients of the Control Group failed to show any improvement in their

albumin level, even after 36 months, rather some of the Control Group showed deterioration.

(iv) *Serum Globulin*: Hyperglobulinaemia was a common feature in almost all cases of cirrhosis liver in the series. (1) In four cases on Liv.52, Serum globulin levels became normal in 12 months' time, as against none in the Control Group. (2) In 10 cases on Liv.52, Serum globulin level attained normal level in 18 to 24 months, as against 3 patients of Control Group who showed a slight improvement during the same period. (3) Five cases on Liv.52 (5/19) and 5 cases of Control Group (5/8) failed to show any improvement in their Serum globulin level, even in 36 months.

Table XXII shows the Mean values and the trend of changes in the Total protein, Albumin and Globulin in the two groups of cases.

Table XXII: Serum total protein, Albumin : Globulin in cirrhosis of the liver (in gms/100 ml)

	On admission			3 months			6 months			9 months		
	TP	AL	GL	TP	AL	GL	TP	AL	GL	TP	AL	GL
	1			2			3			4		
Liv.52 group (Mean: 19 cases)	6.2	2.3	3.9	6.3	2.5	3.8	6.4	2.7	3.7	6.5	3.0	3.5
Control group (Mean: 8 cases)	5.6	1.8	3.8	5.7	1.7	4.0	6.0	1.8	4.2	6.1	1.9	4.2

12 months			15 months			18 months			21 months			24 months		
TP	AL	GL	TP	AL	GL	TP	AL	GL	TP	AL	GL	TP	AL	GL
5			6			7			8			9		
6.6	3.1	3.5	6.6	2.9	3.7	6.7	3.2	3.5	6.8	3.5	3.3	6.8	3.7	3.1
6.2	2.1	4.1	6.3	2.2	4.1	6.4	2.3	4.1	6.6	2.4	4.2	6.8	2.4	4.4

(v) *SGPT / SGPT*: Serum GOT and specially GPT were found to be high in almost all cases of cirrhosis of the liver in the series. (1) As in cases of other biochemical profiles, Serum GOT as well as GPT levels in 4 cases on Liv.52 became normal in 12 months and remained normal for the next 24 months; no case in the Control Group showed such improvement in 12 months. (2) In 10 cases on Liv.52 Serum GOT and GPT levels became normal to almost normal in 18-24 months and remained normal in subsequent 12 months as against 3 cases (3/8) of the Control Group showing slight improvement during that period. (3) Five cases on Liv.52 (5/19) and 5 cases in the Control Group (5/8) failed to show any improvement in their SGOT and SGPT levels, rather they gradually worsened, even after treatment for 36 months.

Table XXIII shows the Mean values and the trend of changes in Serum GOT and GPT in Cirrhosis of the liver in both in the Liv.52 Group and the Control Group.

Table XXIII: Serum SGOT and SGPT in cirrhosis of the liver (in Karmen units)

	On admn.		3rd month		6th month		9th month	
	GOT	GPT	GOT	GPT	GOT	GPT	GOT	GPT
	1		2		3		4	
Liv.52 group (Mean: 19 cases)	21.1	47.7	21.9	48.4	21.0	47.0	19.9	45.4
Control group (Mean: 8 cases)	31.2	53.7	23.2	57.8	25.2	67.0	26.0	63.6

12th month		15th month		18th month		21st month		24th month	
GOT	GPT	GOT	GPT	GOT	GPT	GOT	GPT	GOT	GPT
5		6		7		8		9	
18.3	43.3	17.8	43.1	21.6	53.0	19.2	48.1	15.8	40.9
37.1	69.8	29.6	72.1	28.7	72.8	32.2	71.8	31.2	69.8

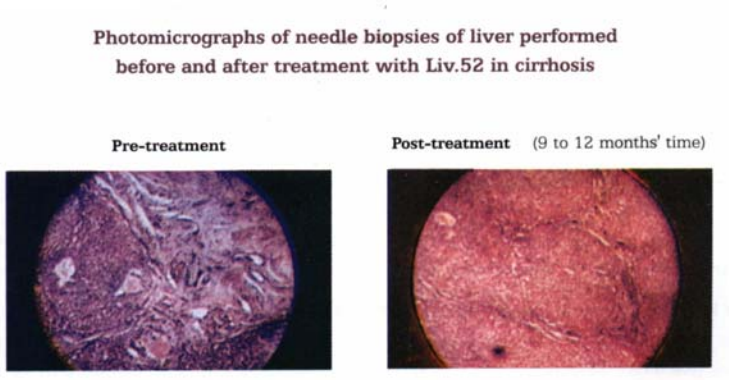
(vi) *BSP Studies*: BSP excretion studies could be performed on only 5 cases on Liv.52 and 5 cases of the Control Group. Four cases on Liv.52 (4/5) showed greater excretion of BSP in 12-18 months as against only one case of the Control Group.

(vii) *Protein Electrophoresis*: Increased level of all fractions of immunoglobulin, particularly IgG, was found in all cases of Cirrhosis patients before treatment.

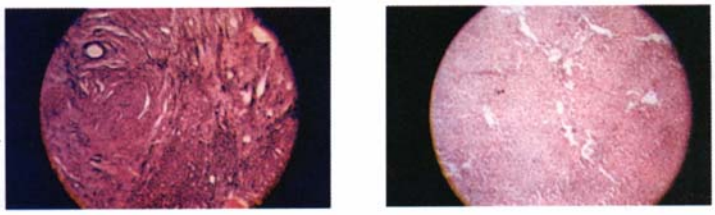
IgG became normal in 14 cases on Liv.52 after 18-24 months. In no case was there any improvement in the IgG level in the all cases of Cirrhosis patients before treatment.

IgG became normal in 14 cases on Liv.52 after 18-24 months. In no case was there any improvement in the IgG level in the Control Group. In fact, in 5 cases it rose to a higher level.

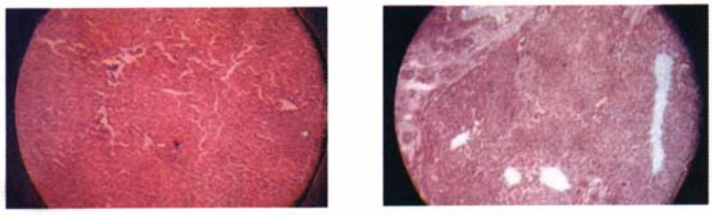
(viii) *Histopathological Examination*: (1) Four cases on Liv.52 showed remarkable improvement in 12 months the picture showing almost normal liver structure with minimal fibrosis, and remained so until 24 months later. None of the Control Group revealed any remarkable changes in histopathology from that in the initial stage (even after 9-12 months' treatment). (Annexure VII, VIII and IX). (2) Ten cases on Liv.52 (10/19) showed moderate improvement in the liver architecture in 18 to 24 months and the fibrosis did not progress in subsequent 12 months' follow-up, whereas 3 cases in Control Group (3/8) showed early similar improvement in 24 months, but the fibrosis was more pronounced, when examined 12 months later. (3) Five cases on Liv.52 (5/19) who had marked destruction of the liver architecture with pronounced fibrosis showed no improvement, even after 36 months of intensive therapy. Five cases of the Control Group (5/8) behaved in a similar manner, rather the histopathological picture deteriorated further at the end of the study.



Case No. 4 – Annexure VII



Case No. 11 – Annexure VIII



Case No. 2 – Annexure IX

Inference

Analysing the 27 cases of Cirrhosis of the Liver 19 belonging to Liv.52 Group and 8 belonging to Control Group clinically, biochemically and histopathologically, the following inferences may be drawn as regards results, presented in Table XXIV.

Table XXIV: Results of treatment in cirrhosis of the liver

		No. of cases	
		Liv.52 group (19 cases)	Control group (8 cases)
(a)	Good	4 (21.05%)	Nil (0%)
(b)	Fair	10 (52.63%)	3 (37.50%)
(c)	Poor	5 (26.32%)	5 (62.50%)

Criteria for Results: 'Good', 'Fair' and 'Poor' in Chronic active hepatitis and Cirrhosis of the liver.

Good: Improved clinically, biochemically and histopathologically in 6-12 months and remained so up to subsequent 36th month of follow-up.

Fair: Improved clinically, biochemically and histopathologically in 18 to 24 months and remained so up to 36th month as follow-up.

Poor: No improvement/deterioration in 24 to 36 months.

DISCUSSION

Hepatic damage in any form is a difficult condition to treat. Though the liver has great reserves and a good power of regeneration, it frequently happens that if and when the initial insult in severe and/or the pathological process is prolonged, permanent and irreversible, changes may occur undermining the capability of the organ to maintain its multifarious normal functions, thereby leading to a significant morbidity and often mortality affecting the unfortunate victims. No "Specific" treatment has so far been evolved for the treatment of the spectrum of cases selected for the present study, viz., Viral Hepatitis, Chronic Active hepatitis and Cirrhosis of the Liver, and the different regimes of treatment advocated have remained mostly symptomatic and at the most palliative as has been expressed earlier in the introductory comments. It would appear imperative, therefore, for every clinician and research worker to look for a drug that would help these difficult and trying maladies, or at least minimise the ravages and complications associated with or precipitated by them.

Keeping the above basic facts in mind it would appear from the results of the present study that the indigenous preparation Liv.52, though not a "Specific" remedy, has a definite beneficial effect on the foregoing conditions, much more than what could be achieved by other conventional therapies tried so far. The study also provides a good corroboration of the earlier findings of other workers in the field (*loc. cit.*) who have tried the preparation over a number of years with highly encouraging results.

The efficacy of the drug may now be highlighted category-wise in the three conditions where it was tried in the present study:

(1) *Infective Hepatitis*: Though in itself this is mostly a self-limiting disease resolving itself within a few weeks, experience in India reveals that the disease tends to assume a more severe form with a rather prolonged course with a attendant greater propensity for serious complications than encountered in other advanced countries as pointed out earlier. Therefore, the aim in the treatment should be to cut short the course and prevent the complications of the

disease as far as possible. This target appears to have been achieved in the present study corroborating the findings of other workers.

(a) *Clinical*: Majority of the cases treated with Liv.52 had significantly earlier resolution of the symptomatology, viz., fever, anorexia, nausea, epigastric pain, jaundice, hepatomegaly etc. than in the Control Group. The findings in the present study compare well with the findings of Sule *et al.* (1965)[1], Ramalingam *et al.* (1971)[2], Mukherjee *et al.* (1970)[6], Patel *et al.* (1972)[10] and Mehrotra *et al.* (1973)[11] and others all of whom have reported uniformly good and earlier resolution of the symptomatology in majority of their cases.

(b) *Biochemical (Liver Function Tests)*: (i) *Serum Bilirubin*: In the present study, 73.33% of cases had an earlier clearance of Serum bilirubin (within 2-3 weeks) than in the Control Group. The corresponding finding in the literature reports are: Sule *et al.*[1] – 76%, Ramalingam *et al.*[2] – 80%, Patel *et al.*[10] – 74% and Mehrotra *et al.*[11] – 77.14%. The high percentage of cases showing significantly earlier clearance of Serum bilirubin in these cases may encourage one to use the preparation specially in cases with cholestasis in preference to steroids, in consideration of the comparative safety of the former as against the possible hazards of the latter. Steroids, however, were not used in any of the cases under study.

(ii) *Alkaline Phosphatase*: As observed in respect of Serum bilirubin, this elevated serum enzyme also showed an early clearance in 73.33% as against only 26.66% of the Control Group. Dave *et al* (1972)[3] made similar observations in 68.2% of his cases, Sule *et al.*[1] in 71.5% and Patel *et al.*[10] in 63%. Gupta *et al.* (1972)[4] however reported no significant clearance of the enzyme in a limited number of cases in his study.

(iii) *SGOT* and *SGPT* showed earlier clearance in the Liv.52 Group in 73.33% of cases comparing favourably with the findings of Sule *et al.*[1]: 78.4%, Patel *et al,*[10]: 77.8%, Gupta *et al,*[4] also reported similar findings.

(iv) *Serum Total Protein / Albumin: Globulin* showed significant earlier improvement in their values in the Liv.52 treated cases but references were inadequate for comparison.

Histopathological studies were not undertaken in this category of cases.

All in all, the use of Liv.52 in cases of Infective Hepatitis in our study have shown significant advantages over other conventional therapies in ensuring an earlier all round clinical and biochemical improvement, and these findings compare well with the findings of other workers, and in the absence of a "Specific", or for that matter even a better drug at the present moment, the preparation Liv.52 can safely be recommended for use in cases of Infective Hepatitis, specially in consideration of its being absolutely free from any side effects.

(2) *Chronic Active Hepatitis*: The syndrome of Chronic Active Hepatitis is usually a progressive condition, the aetiology of which may be diverse but mostly leading to a common denominator, viz., immunological disturbances affecting the organ. The condition may have a diverse symptomatology as listed in the text of this paper earlier, biochemical evidences of gross liver dysfunction and often pathognomonic histopathological changes in the liver biopsy material.

The overall result of treatment by conventional therapy is usually unsatisfactory, the condition ultimately leading to Cirrhosis of the Liver or early hepatic failure. The situation being so, it was decided to treat 24 patients of Chronic Active Hepatitis with Liv.52 and study its efficacy in the condition. Earlier Das Gupta and Mukherjee (1971)[7] reported the results of treatment in 7 cases with this drug, keeping another 3 cases as Controls. They reported good clinical response with marked improvement in Liver Function Tests done at the end of one and a half to two year. Histopathological evidence of improvement of piecemeal necrosis and arrest of progress of lobular distortion were also reported in their cases. Overall, all the Liv.52 treated cases were reported as "improved" with in 1½ to 2 years, while the 3 control cases expired within one year. The present study more or less corroborates the findings of the above workers as will be evidenced by:

(a) *Clinical improvement*: in 87.5% cases within one year as against 50% in the Control Group. Das Gupta and Mukherjee, noted clinical improvement in all the 7 cases within 1½ to 2 years.

(b) *Biochemical improvement*: in Liver Function Tests, viz., Serum bilirubin, Serum Alkaline phosphatase, Serum Total protein/Al: Gl, SGOT, SGPT, BSP excretion studies–all showed early improvement in 6 months to 12 months' time in 87.5% of cases which compares well with the results obtained by Das Gupta and Mukherjee who found improvement in these parameters in all their cases.

(c) *Protein Electrophoresis*: Quantitative immunoglobulin determination revealed elevation of all types with marked increase in IgG which came down to normal or almost normal within 12 months in 87.5% of the Liv.52-treated cases, and this finding tallies well with those of the above workers.

(d) *Histopathological study*: Das Gupta and Mukherjee observed disappearance or clearing of piecemeal necrosis of liver cells, evidence of hepatic cell regeneration and arrest of progressive hepatic architectural distortion within 1½ to 2 years in all their 7 cases. In the present study, a comparable result was obtained in 87.5% of cases treated with the drug.

Though the long-term prognosis is considered to be bad in most of the cases, the overall results in the Liv.52 Group were "Fair" to "Good" at the end of 3 years. Cook *et al* (1970)[13] reported good response in 22 out of 49 patients treated with steroids for 3 to 6 years. None of the patients in the present study received steroids, and the overall results appear nearly similar or even better than what was obtained with long-term steroid therapy without the hazards of the latter being involved. It appears worthwhile to plan a regime of combined Liv.52 + steroids therapy in this condition in a representative series of case to see whether the combination will further improve the long-term prognosis.

(3) *Cirrhosis of the Liver*: Though the aetiology of Cirrhosis of the liver is multifactorial, the net result of the liver injury and the ultimate clinical course of the disease are by and large similar, having a more or less progressively downhill course over a prolonged period. The conventional therapy is often unsatisfactory, and is usually only helpful for some degree of palliation. The present study shows that prolonged treatment of cases of Cirrhosis of the Liver using a comparatively high dose of the drug, Liv.52 (4 tab. t.i.d.), not only produces a better and earlier palliation of the symptomatology, but there is also marked improvement in the biochemical profile as revealed by periodical Liver Function Tests. There was also good evidence to show that, the drug helps regeneration of the hepatic cells and controls the cirrhotic process thus giving a more useful and prolonged life to the unfortunate sufferers

from the disease. Only a very long-term follow-up will show whether the disease can be completely "cured" by the drug. The observations of Gupta *et al*. (1972)[4,5] and Mukherjee and Das Gupta (1971)[8] are also similar and compare well with the results of the present study. Mukherjee and Das Gupta also stressed the need to continue the therapy with the drug for a minimum period of 9 months for obtaining good results.

Some of the results of the present study may now be highlighted.

(a) *Clinical*: Improvement of symptomatology was observed in 12-24 months in 73.68% of the cases treated with the drug as against 50% in the Control Group.

(b) *Liver Function Tests*:

(i) Serum bilirubin, serum Alkaline phosphatase, serum Total protein/Al: Gl, SGOT and SGPT all reverted to normal or near normal in 73.68% of the Liv.52 treated cases within 12-24 months as against only 37.5% of cases of the Control Group within the same period.

(ii) B.S.P. Excretion studies done in a limited number of cases (5 Liv.52 and 5 Control) showed a much greater excretion in 4 out of 5 of the Liv.52 treated cases as against only 1 out of 5 of the Control cases.

Mukherjee and Das Gupta also reported a highly significant improvement in all the above parameters when the cases were treated with the drug for a minimum period of 9 months.

(iii) Protein Electrophoresis showed an increase in all the fractions of globulin in cirrhosis in all the cases with predominance of IgG, which came down to normal within 18-24 months in 73.68% of the cases of the Liv.52 Group against none in the Control Group, 5 of the 8 latter cases showing a further progressive increase in the component within the same period.

(c) *Histopathological Studies*: Four cases of the Liv.52 Group (as against none in the Control Group) showed a remarkable improvement in 12 months showing a normal liver architecture with minimal fibrosis, and remained so after another 24 months. Another 10 cases showed a fair degree of improvement in liver architecture with arrest of the progress of fibrosis, as against progressive fibrosis and further distortion of the liver architecture in most of the cases of the Control Group.

Mukherjee and Das Gupta, and others also reported more or less similar findings after prolonged treatment of their cases with Liv.52.

Considering the clinical, biochemical and histopathological parameters, the present study revealed "Fair to Good" results in 73.68% of the cases treated with Liv.52 as against only 37.5% of the cases in the Control Group.

A series of long-term experimental studies carried out by different workers substantiate the protective and regenerative action of Liv.52 on the liver against a battery of hepatotoxins (Murkibhavi and Sheth, 1957[14], Sheth *et al,* 1960[15], Joglekar *et al*[16], Patel *et al*[17], Karandikar *et al*[18], 1963, Qazi, 1965[19], Captain and Syed,[20] (1966); Joglekar and Leevy, 1970[21]. Clinically also the drug has been tried extensively by different workers in various liver disorders and allied conditions, and by using different parameters of Liver Function Tests for assessment, as also by studying histopathological changes by serial liver biopsies. These workers have consistently confirmed that

Liv.52 accelerates the clinical and biochemical recovery and also improves/arrests the progress of the histopathological changes (vide list of references). The present study adds strong support to and corroborates the findings of earlier workers. It may be said with confidence that in the absence of the availability of any better drug for the treatment of various liver disorders at the present moment, Liv.52 stands out on its own merit as a highly useful adjunct to the present-day therapeutic armamentarium against the ravages of the unfortunate diseases affecting the human liver.

SUMMARY AND CONCLUSIONS

A controlled study was undertaken to observe the efficacy of an indigenous drug Liv.52 introduced and marketed by The Himalaya Drug Co., Bombay on liver diseases. The present study covered a total of 104 cases of which 73 were treated with the above drug, 31 serving as Controls and belonged to the categories given below:

		Liv.52	Control
(1)	Infective (Viral) Hepatitis	30	15
(2)	Chronic Active Hepatitis	24	8
(3)	Cirrhosis of the Liver	19	8

The parameters chosen for assessment and analysis of the cases after follow-up of up to 3 years were (i) Clinical improvement, (ii) Improvement in the Biochemical profile, specially Liver Function Tests and (iii) Histopathological improvement (in the second and third categories).

On analysis of the data obtained after the full study, the results were graded as "Good", "Fair" and "Poor" according to criteria already indicated in the text.

The following observations and conclusions were then arrived at:

Category (1) *Infective Hepatitis*: The results of treatment with Liv.52 were considered "Good" in 73.33%, "Fair" 23.33% and "Poor" in 3.33% of cases as against 26.66%, 66.66% and 6.66% respectively in the Control Group, both groups being analysed by the above parameters excepting histopathological studies which were not undertaken in this category of cases.

Category (2) *Chronic Active Hepatitis*: The results with Liv.52 were considered "Good" in 37.50%, "Fair" in 50.00% and "Poor" in 12.50% of cases as against 0%, 50% and 50% respectively in the Control Group analysed on the basis of all the three parameters.

Category (3) *Cirrhosis of the Liver*: The results with Liv.52 were considered as "Good" in 21.05% "Fair" in 52.63% and "Poor" in 26.32% of cases as against 0%, 37.5% and 62.5% respectively analysed by all the parameters of study.

No deleterious side effects were noted in any of the cases treated with the drug, even in those who failed to improve and in this respect the drug was considered absolutely safe.

In conclusion, it may be said with some confidence that since the studied categories of liver diseases which are so common in our country producing a significant degree of morbidity and mortality there being no "Specific" treatment for the conditions, the results of treatment with the indigenous drug Liv.52 appear highly encouraging, at least as a good palliative if not curative, to give the unfortunate sufferers an early improvement and a more prolonged, active and useful life. The drug may be considered as a significant advance, at least by one step, towards successful therapy of these chronic liver diseases.

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