

Cirrhosis of Liver

Results of Treatment with an Indigenous Drug: Liv.52

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The therapeutic approach for a disorder of unknown aetiology is mainly supportive and with cirrhosis the same holds good. With advancement of modern medicine, improvement has occurred in the field of diuresis, operative management of portal hypertension and haemorrhage, etc.; thus giving the cirrhotics a better scope to deal with complications of the disease like ascites, G.I.T. haemorrhage, etc.; but, there has been no specific contribution towards the revival of deranged hepatocellular function. The ultimate clinical picture of the disease is dependent on the degree of underlying hepatocellular damage as has been described by clinicians working on this problem. [Rickels *et al* (1948), Popper *et al* (1950), Jhingran *et al.* (1965), Dasgupta and Mukerjee (1970)].

Table 1

Name of the components		Acting ingredients	Action	% per tablet
1.	Capparis spinosa	Glucoside Rutin	Diuretic Uricosuric agent	23
2.	Cichorium intybus	Glucoside Cichorin Bitter principle Lactucin	Chloretic, Stomachic Mild diuretic	23
3.	Solanum nigrum	Alkaloids Solanine & Solanidine	Diuretic	12
4.	Terminalia arjuna	Sodium Carbonate Calcium Carbonate Alkaline Chlorides	Stimulant, Astringent, Choleretic, Prevents haemorrhage	12
5.	Achillea millefolium	Glucoside Achillein	Stimulant, Tonic Carminative	6
6.	Tamarix gallica	Tannic acid	Astringent, Tonic Stomachic	6
7.	<i>Mandur bhasma</i>	Ferroso-ferric oxide	Haematinic	12
8.	Cassia occidentalis	Achromine Tannic acid Fatty matters, Sugar etc.	Stimulant, Mild diuretic Stomachic	6

In the absence of drugs for improving hepatocellular function and for prevention of the progress of cirrhosis which involves polyfunctional activities of liver cells, polytherapy or composite therapy by liver extract administration was advocated since olden days. Recently, a fresh scientific evaluation of liver extract therapy in cirrhosis has been done by Toghil *et al* (1969), and based on good results, a strong recommendation has been made by the author.

A combined preparation made from various Indian herbs having poly-directional action on liver cells has been in use in our country for some time. The drug, Liv.52 (The Himalaya Drug Co.) has been observed to have experimental and clinical evidence of preventing hepatocellular damage produced by hepatotoxins like carbon tetrachloride, etc., and also has anabolic, choleretic, stomachic, diuretic and aperient action. [Sule *et al* (1956), Murkibhavi and Sheth (1957), Northover

(1960), Joglekar *et al* (1963), Patel *et al* (1963), Karandikar *et al* (1963), Captain and Syed (1966), Joglekar and Leevy (1970)].

The herbs selected and their active principles as laid down by Nadkarni (1954) and Chopra (1958) are given below:

The combined preparation has already been given clinical trials in hepatic cirrhosis and infective hepatitis in this country and satisfactory results claimed. (Mathur *et al* 1957).

The present paper records an attempt to assess the therapeutic effects scientifically as is done with any other isolated pharmacological principle.

MATERIAL AND METHODS

A group of 42 cases of hepatic cirrhosis was studied and after preliminary confirmation of the diagnosis by needle biopsy of the liver, each case was subjected to periodic observations in the hospital indoor or in the liver clinic. The patients were divided into three groups, i.e.,

Group A: those observed for 3 months;

Group B: for 6 months; and

Group C: for 9 months.

Each group had 2 batches, one on Liv.52 and the other having a placebo. No other drug was used during the period of observation except oral diuretic when indicated. Patients having G.I.T. haemorrhage or hepatic coma were excluded from the study.

Detailed analysis of the patients' symptomatology was made and progress followed up, till the end of the therapy and comparison of the results observed in each group. Liver function tests, namely serum bilirubin, albumin, globulin, alkaline phosphatase, S.G.O.T. and S.G.P.T. were determined in each patient both before and after the course of therapy with drug or placebo, and the results assessed following treatment of change in hepatic function tests. The latter were subsequently subjected to statistical analysis in order to note whether the changes were significant or not.

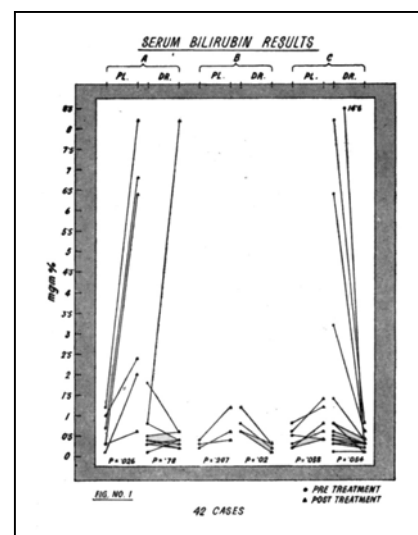
As the most sensitive index of hepatocellular damage, the standard B.S.P. excretion test was also performed in each patient before and after therapy and statistical evaluation made. Chemical determination of B.S.P. was done by following the method of Mateer *et al* (1942). Needle biopsies of the liver were performed in all cases for pre-treatment diagnosis of cirrhosis and for a post-treatment comparative study. Assessment of hepatic cell damage was also done in each biopsy specimen by adopting the criterion mentioned by Popper *et al* (1950).

RESULTS

1. *Clinical*: Symptomatic improvement was noted specially in respect of weakness, anorexia, flatulent dyspepsia and epigastric pain in Groups B and C, having Liv.52 in comparison to those receiving a placebo. A similar observation in general was available regarding physical signs; and in particular, mention may be made of peripheral oedema, ascites, jaundice and hypotension. Hepatosplenomegaly, however, showed no alteration.

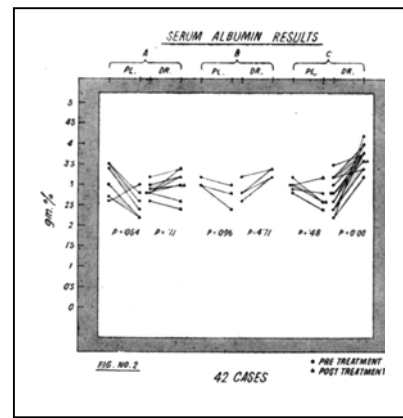
2. *Biochemical*: Results of Liver Function Tests.

(i) *Serum Bilirubin*— Figure 1 shows serum bilirubin values actually increased after therapy in the majority of cases

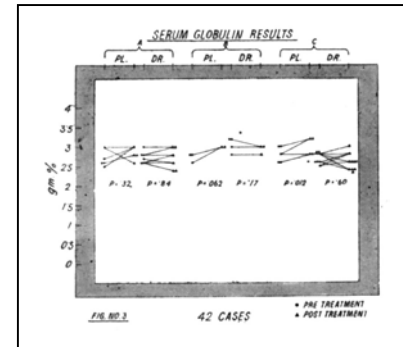


treated with placebo. Statistical values in Group A and Group C went significantly in the opposite direction and were insignificant in Group B. The change in bilirubin values in drug-treated cases shows improvement in all three groups, but statistically the fall of bilirubin values after treatment is significant in Group B and Group C.

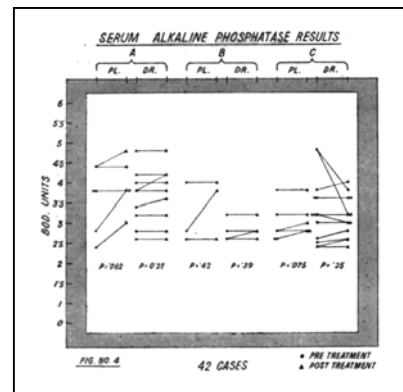
(ii) *Serum Albumin* – The serum albumin values show significant rise after therapy with Liv.52, after treatment for six and nine months respectively, but with placebo there occurred significant deterioration in all groups of cases. Detailed results are shown in Fig.2.



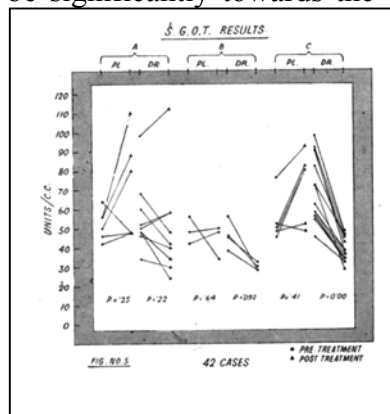
(iii) *Globulin* – The globulin values of placebo-treated cases showed a little alteration towards the high side in all the three groups, but these changes were found to be statistically insignificant (see Fig. 3). Drug-treated cases in all the three groups seemed to show some apparent improvement of globulin values, but statistically these changes were not significant.



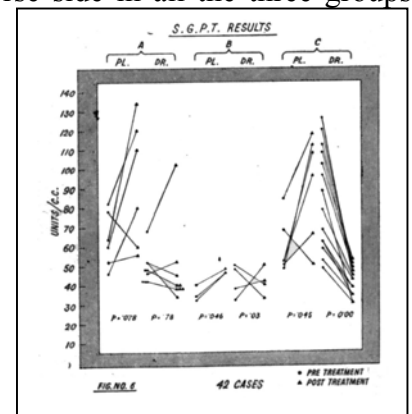
(iv) *Alkaline phosphatase* – Values of Alkaline Phosphatase in placebo-treated cases actually showed deterioration to some extent after therapy, and statistical evaluation showed this change was significantly worse or insignificant (See Fig. 4). The results in drug-treated cases were insignificant in all groups.



(v) *S.G.O.T* – Figure 5 shows the detailed results of S.G.O.T. values, of which the values of placebo-treated cases showed deterioration after treatment to a variable extent in all three groups whereas in treated cases these values are apparently good after therapy. The result in Group C drug-treated cases showed considerable improvement after therapy and statistically the change was found to be highly significant.

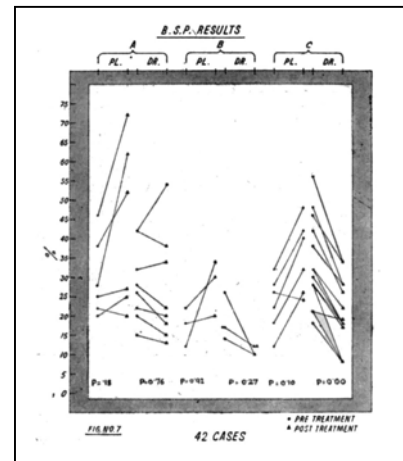


(vi) *S.G.P.T* – The result of this test also among the placebo-treated patients showed deterioration to a variable extent after therapy and on statistically evaluation this deterioration was found to be significantly towards the worse side in all the three groups (See Fig. 6) while in the drug-treated cases the result of this test showed a change for the better, and was found to be statistically significant in Groups B and C.



(vii) *B.S.P* – The alteration of B.S.P. values before and after the therapy was also noted, as in other liver function tests mentioned above and is shown in details in Fig. 7. The result of alteration in B.S.P. values in the placebo-treated

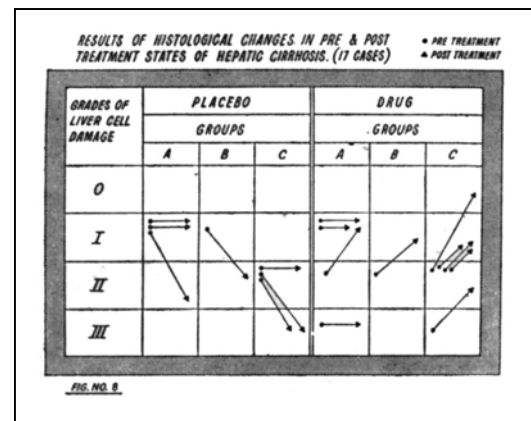
cases was towards the worse side in the majority of the cases. Among-drug-treated cases the alterations of B.S.P. values were found to be for the better in most of the cases of all the three groups and statistical analysis pointed out these changes to be of insignificant value in Groups A and B, but of high significance in Group C.



From the observations of changes in liver function tests mentioned above, it can be clearly pointed out that placebo treatment does not improve the hepatic function. On the contrary, deterioration was noted and emphasised statistically on most occasions. Improvement of hepatic function as very mild in Liv.52-treated cases for a period of three and six months and the result was statistically not always very significant. However, the improvement of hepatic function is found to be of an excellent degree after nine months' therapy with Liv.52 and this was corroborated statistically.

3. Histological observations:

Various degrees of hepatic cell damage were noted in all the 42 pre-treatment liver biopsies, of which nine among 15 placebo-treated cases and 19 among 27 drug-treated cases had evidence of advance degree of hepatic cell damage (grades II and III). Post-treatment histological evaluation could be successfully done in 17 cases (seven amongst placebo and 10 amongst drug-treated cases).



The detailed results of pre- and post-treatment histological comparison from the standpoint of degree of hepatic cell damage, are shown in a tabular form in Fig. 8.

From this figure it will be evident that in a majority of placebo-treated cases hepatocellular damage actually advanced with therapy, i.e. in four out of seven cases. On the other hand, seven specimens out of 10 of the drug-treated cases showed definite degrees of histological improvement, mostly amongst Group C cases (i.e. those treated for nine months). In this aspect the histological results also confirm the results drawn from various liver function tests.

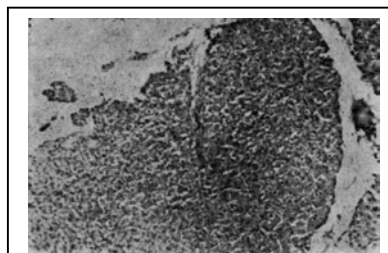


Figure 9A:
Figure 9A shows pre-treatment biopsy picture of liver in a placebo-treated case showing cirrhosis with grade I hepatic cell damage.

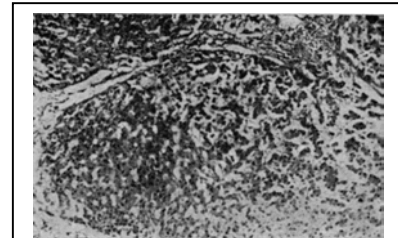


Figure 9B:
Figure 9B shows post-treatment biopsy picture of the same with advancement of cirrhotic process where cell damage deteriorated to grade II degree.

A few of the histologic appearances before and after therapy are shown in Fig. Nos. 9A and 9B, 10A and 10B and 11A and 11B.

DISCUSSION

The clinical aspect of the results noted from this study showed that drug treatment was beneficial in ameliorating symptoms like anorexia and weakness. This probably is due to the anabolic effect of

Liv.52 reported previously (Kale *et al*, 1966; Damle and Deshpande, 1966). Liv.52 has also been shown to increase appetite and relieve anorexia following various ailments. (Athavale, 1966). This is a definite advantage while treating cases of cirrhosis.

Epigastric pain, another common but confusing symptom of cirrhosis was also relieved satisfactorily in the majority of drug-treated cases, but not in placebo-treated ones. This symptom is difficult to explain and some authorities believe that it is due to associated gastritis and is particularly noted in alcoholic cirrhosis (Sherlock, 1968). But, in any way, persistence of these symptoms mentioned above leads to depression amongst cirrhotics as they think that the disease is regressing. But an advantage on this point was noted in patients treated with Liv.52, as it helped in keeping up a high morale by relieving the above mentioned symptom.

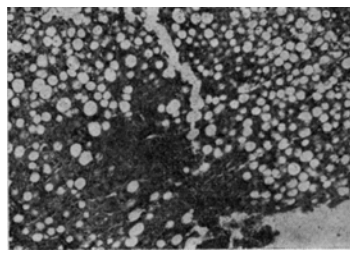


Figure 10A:
Figure 10A shows a picture of nutritional cirrhosis with extensive fatty changes and grade II hepatic cell damage.

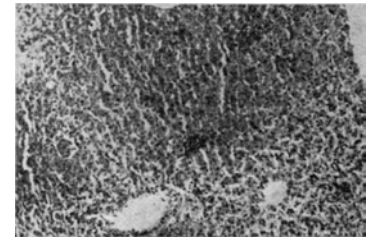


Figure 10B:
Post-treatment improvement (9 months' drug therapy) in the same is shown in Figure 10B, where liver structure is completely normal.

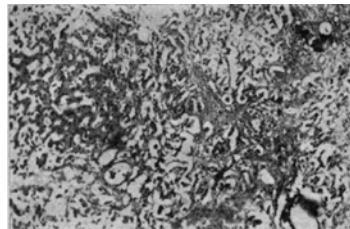


Figure 11A:
Figure 11A shows picture of post-necrotic cirrhosis with grade III cell damage.

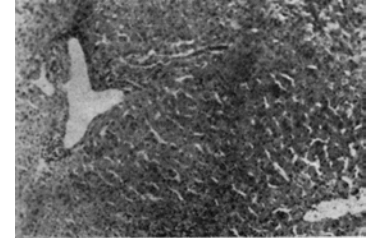


Figure 11B:
Post-treatment (9 months' drug therapy) biopsy picture of the same is shown in Figure 11B, where the cell damage has improved to grade II and regeneration nodule formation is also evident.

Various liver function tests were employed in this study in order to assess the result of therapy. From the results observed it will be noted that overall improvement of liver function was noted clearly in six and nine months' drug-treated cases, but on statistical evaluation of the same only the nine months' result with the drug showed excellent and highly significant results. Placebo treatment in all groups and drug treatment in other groups was not statistically significant for claiming success in therapy. Here again not all the tests employed in this study did serve this purpose; the result of albumin, S.G.O.T. and S.G.P.T. was very helpful for the purpose of assessment, besides results of B.S.P. test.

Alkaline phosphatase and globulin values have got no direct and significant role in the assessment of drug therapy. Thus, the question of selective liver function tests in clinical application is once more proved. In this respect, follow-up results of treatment in cirrhosis could be done by noting changes in serum albumin, S.G.O.T. and S.G.P.T.

B.S.P. is a highly sensitive test and undoubtedly the best, but is very costly for routine use.

Improvement of hepatocellular damage was also clearly noted in drug-treated cases from post-treatment liver biopsy specimens, mostly in the group treated for nine months. Placebo treatment was followed by histological deterioration in some cases. Thus the results of hepatic function tests and needle biopsy specimens of liver demonstrated definite improvement of hepatocellular function with composite treatment of cirrhosis of the liver. In this respect, a prolonged treatment for at least nine months was necessary. The additional advantage of treatment with Liv.52 is due to its anabolic and diuretic effects which lead to amelioration of most distressing features like weakness, flatulent

dyspepsia, ascites, etc., giving the clinician an advantage in keeping the morale of the patient very high. On the other hand, definite improvement of hepatocellular function is also ensured to cirrhotics on Liv.52.

SUMMARY

A controlled study was carried out with an Indian indigenous drug Liv.52 and a placebo on a total of 42 needle biopsy confirmed cases of hepatic cirrhosis. The result of therapy was assessed from the clinical standpoint and determination of liver function tests like serum bilirubin, albumin, globulin, alkaline phosphatase, S.G.O.T., S.G.P.T. and standard B.S.P. tests. Post-treatment needle biopsy of the liver was also done in 17 cases. The cases were divided into three groups viz. A, B and C, according to the period of therapy for three, six and nine months, respectively.

The overall result including B.S.P. test, showed definite and statistically highly significant degree of improvement of hepato-cellular function following therapy with Liv.52 for nine months. Placebo treatment showed deterioration of results in all three groups of cases. Drug treatment for three and six months did not have highly significant results.

Liv.52 dosage used 2 t.d.s.

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