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AN OPEN LABEL, NON-COMPARATIVE, MULTI-CENTRE CLINICAL TRIAL OF 'HEPTOVIT S.G.C', A POLYHERBAL FORMULATION, IN THE TREATMENT OF INFECTIVE HEPATITIS.Abha Nagral¹, Anirudh Tripathi² and Ramchandra Joshi³**ABSTRACT**

***HEPTOVIT S.G.C**, a poly herbal Phytomedicine of M/S Millennium Herbal Care Limited was studied for its efficacy and safety in patients with Infective Hepatitis. It contains standardized extracts of herbs judiciously selected from Ayurvedic literature. An open label, multicentric clinical trial was conducted to evaluate its efficacy and safety. Male and female patients above the age of 12 having symptoms of jaundice, fatigue, loss of appetite, nausea, dark coloured urine, abdominal pain, etc. and diagnosed as infective by serological test (type A – E) were included in the study. Patients with Hepatic failure, Hepato-renal failure, Coagulopathy, Cirrhosis of liver, Obstructive jaundice, alcohol dependence, TB, DM, Epilepsy etc., and those with H/o jaundice in the last 6 months, on Hepatotoxic or immunosuppressant drugs, pregnant & lactating women and those on Ayurvedic therapy for the last 6 months were excluded from the study. **HEPTOVIT S.G.C** in a dose of 2 capsules twice a day after meals was given for a maximum period of 6 weeks. Liver function tests, SGPT, SGOT & Bilirubin, were conducted on day 0 and after 1,2,3,4 & 6 weeks to assess its efficacy. CBC, Bilirubin and Blood Urea Nitrogen were estimated as safety parameters before and after treatment. There was a highly significant reduction in the liver function parameters. The SGPT levels reduced by 96.11%, SGOT by 95.87%, Bilirubin (Direct) 81.18% and Bilirubin (Indirect) by 76.98%. There was a highly significant improvement in appetite reduction and abdominal pain. In global assessment, both patients and physician were satisfied with the treatment. **HEPTOVIT S.G.C** is very effective in reducing the symptoms of hepatitis and it did not produce any adverse events hence is very safe.*

Key words: Hepatitis, Liver function test and Safety

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INTRODUCTION

Viral hepatitis (A,B,C,D & E) is a global public health problem, which is responsible for a major portion of morbidity and mortality. It is more endemic in developing countries mainly due to nutritional status. In India viral hepatitis is frequently of prolonged duration with a predisposition to complications like post-hepatitis cirrhosis, chronic cholestasis, sub-acute necrosis and hepatic failure. Hepatitis A is an acute, but benign form of viral hepatitis and is the least serious (self limiting) disease. Acute hepatitis B can range from sub-clinical disease to fulminant hepatic failure and individuals with chronic hepatitis B are at increased risk for the development of hepato-cellular carcinoma. The HDV infection occurs only in the presence of

hepatitis B infection (co-infection or super infection). Hepatitis E virus is clinically indistinguishable from hepatitis A disease and is usually mild except in pregnant women.

In Ayurveda, the Indian traditional system of medicine, several plants have been described to be used for the treatment of liver disorders. A judicious combination of such plants is used for the treatment of hepatitis. **HEPTOVIT S.G.C**, a poly-herbal phytomedicine is one such combination, developed by M/s. Millennium Herbal Care Limited. It is available as softgel capsule and also in syrup form. The product is useful for the treatment of liver disorders such as jaundice, viral hepatitis, drug induced liver damages etc. It can also be used prophylactically as a hepato-protective.

It contains standardised extracts of the following herbs equivalent to:

Bhuiamla	(Phyllanthus niruri)	300 mg
Triphala	(Terminalia chebula, Terminalia balerica, Emblica officinalis)	200 mg
Bhringraj	(Eclipta alba)	200 mg
Daruharidra	(Berbaris aristata)	100 mg
Pittapapda	(Fumaria parviflora)	100 mg
Punarnava	(Boerhavia diffusa)	100 mg
Soonth	(Zingibar officinalis)	100 mg
Chitrakmool	Plumbago zeylanica)	50 mg
Guduchi	(Tinospora cordifolia)	50 mg
Kalmegh	(Endographis paniculata)	50 mg
Kutki	(Picrorrhiza kurroa)	50 mg
Pippali	(Piper longum)	50 mg

The present study was undertaken to assess the efficacy and safety of **HEPTOVIT S.G.C** in patients with infective hepatitis. It was an open label, non comparative trial conducted at two independent centres.

MATERIAL AND METHODS

The study was initiated after obtaining the approval by the Institutional Ethics Committee (IEC). Patients' written informed consent was obtained before enrolling in the study.

Patients

After recording demographic data such as age, sex etc., history, signs, symptoms and clinical examination, patients were selected on the basis of the following criteria.

Male and female patients above the age of 12 having symptoms of jaundice, fatigue, loss of

appetite, nausea, dark coloured urine, abdominal pain etc. and diagnosed as infective by serological test (type A – E) were included in the study. Patients with following disorders were excluded: hepatic failure, hepato-renal failure, coagulopathy, cirrhosis of liver, obstructive jaundice, alcoholic, TB, DM, epilepsy. Patients with H/o jaundice in last 6 months, on hepatotoxic or immunosuppressant drugs, pregnant & lactating women and those on Ayurveda therapy for the last 6 months were excluded from study.

Method

The patients were given 30 capsules at each visit and were asked to take two capsules in the morning after breakfast and two capsules in the evening after dinner for a period of six weeks. Patients were asked to visit centre each week for follow up. Compliance was tested by counting the number of capsules remaining at the end of the each week.

Laboratory investigations like Liver function tests (which included SGPT, SGOT & Bilirubin), were conducted on every visit (day 0 and after 1,2,3,4 & 6 weeks) to assess the efficacy of medication. CBC, Bilirubin and Blood Urea Nitrogen were estimated as safety parameters before starting study and at the end of treatment. Patients were also assessed for clinical signs and symptoms at every visit. Appetite was scored as 1- very poor and 5- very good and abdominal pain was assessed as 1-mild, 2- moderate and 3-severe. Other symptoms were recorded as either present or absent.

Drugs, which are known to produce liver toxicity such as paracetamol, anti-TB drugs etc. were not allowed to be taken during treatment. Other medications were allowed only if it was very essential and name of the drugs and their dosages were recorded in the case report form. Drugs were also allowed to be given to treat the adverse reactions, if any, and were recorded in the ADR form.

The results were analysed using SPSS (V 10.0) statistical package. Descriptive statistics were given as Mean \pm SE. Students 't' test was used for comparing basal and final values. Chi square test with Yale's correction tests were applied to compare the percentage of categorical variables

like sex. Friedman test (non-parametric) were applied to compare overall change considering all time points. Statistical analysis was applied to Per Protocol population or patients who had completed the study. All tests were two tailed. Level of significance was taken as $p \leq 0.001$.

RESULTS

Out of the 50 patients recruited in the study 46 completed the treatment period of 6 weeks. The other 4 patients dropped out of the study for personal reasons. There were 44 male and 2 female patients with an average age of 28.35 ± 1.47 (Mean \pm SE). Almost all the patients had symptoms of jaundice such as loss of appetite, abdominal pain, nausea dark coloured urine etc. Some of them had mild fever, vomiting, malaise, pruritus, restlessness, diarrhoea.

All the liver function parameters which were very high before treatment returned to normal within 6 weeks of treatment. SGPT levels reduced from 1387 ± 177.0 to 53.96 ± 8.53 U/ml, SGOT from 1180.15 ± 199.9 to 48.54 ± 8.24 U/ml, Bilirubin (Direct) from 6.59 ± 0.66 to 1.24 ± 0.28 mg/dl and Bilirubin (Indirect) 4.17 ± 0.27 to 0.96 ± 0.13 mg/dl. The results are statistically highly significant. In the subjective assessment of symptoms Appetite and abdominal pain returned to normal within 3 weeks of treatment. The appetite score increased from 2.00 ± 0.76 to 4.09 ± 0.98 by 3rd week and to 4.60 ± 0.58 by the end of 6 weeks. Similarly the abdominal pain score reduced from 1.57 ± 0.72 to 0.09 ± 0.29 by 3rd week and to 0.00 by the end of 6 weeks. All other signs and symptoms also disappeared within 2 weeks in majority of patients. All these results indicate that the patients were relieved of signs and symptoms within 3 weeks and the liver functions returned to normal within 6 weeks.

All the efficacy parameters were statistically highly significant ($p < 0.001$). The liver function parameters like SGPT, SGOT and Bilirubin returned to normal in all the patients after the completion of treatment (Table.1, Fig.1 & Fig. 2).

There was a highly significant improvement in appetite and reduction in abdominal pain. From mild appetite with a score of 2 it increased to 4.6

indicating a very good improvement. Similarly the abdominal pain reduced from 1.57 to 0 indicating a complete reduction in abdominal pain (Fig.3).

All other signs and symptoms had returned to normal by the end of 2 weeks' treatment. There were no significant differences in the haematological and biochemical parameters after the treatment. **No adverse events were reported by the patients.** In global assessment, both the patients and physician had almost similar opinion about efficacy and safety of **HEPTOVIT S.C.G.**

About 52% of patients said the treatment was very good, 28% said it was good, 11% said it was average and only about 9% said it was poor. According to the physicians, about 41% had very good response, about 41% had good, about 11% had average and only 7% had poor response. Both, patients and investigators said that the drug is safe. Overall, the patients and the physicians appeared to be in agreement with the results (Fig 4).

Table 1: Effect of Heptovit S.G.C on Efficacy parameters (Before and After Treatment)

Efficacy Variable	Day 0 (mean ± S.E)	Day 43 (mean ± S.E)	Reduction	Percentage (%) Reduction to basal
SGPT (U/ml)	1387 ± 177.0	53.96 ± 8.53	1333.51	96.11*
SGOT (U/ml)	1180.15 ± 199.9	48.54 ± 8.24	1131.61	95.87*
Bilirubin (D) (mg/dl)	6.59 ± 0.66	1.24 ± 0.28	5.35	81.18*
Bilirubin (I) (mg/dl)	4.17 ± 0.27	0.96 ± 0.13	3.21	76.98*

*p<0.001

Table 2: Month-wise Effect on Efficacy Variables (Mean ± S.E)

Parameter	Day 0	1 week	2 weeks	3 weeks	4 weeks	6 weeks
SGPT (U/ml)	1387 ± 177.0	447.7 ± 44.5	274 ± 42.58	168.76 ± 9.15	112.65 ± 27.62	53.96 ± 8.53
SGOT (U/ml)	1180.15 ± 199.9	290.96 ± 53.55	180.81 ± 30.81	131.07 ± 27.39	91.52 ± 19.52	48.54 ± 8.24
Bilirubin (D) (mg/dl)	6.59 ± 0.66	4.68 ± 0.71	3.47 ± 0.68	2.45 ± 0.57	1.92 ± 0.45	1.24 ± 0.28
Bilirubin (I) (mg/dl)	4.17 ± 0.27	3.22 ± 0.35	2.64 ± 0.38	2.08 ± 0.34	1.49 ± 0.27	0.96 ± 0.13

Fig 1: Showing the effect of HEPTOVIT S.G.C on SGPT and SGOT

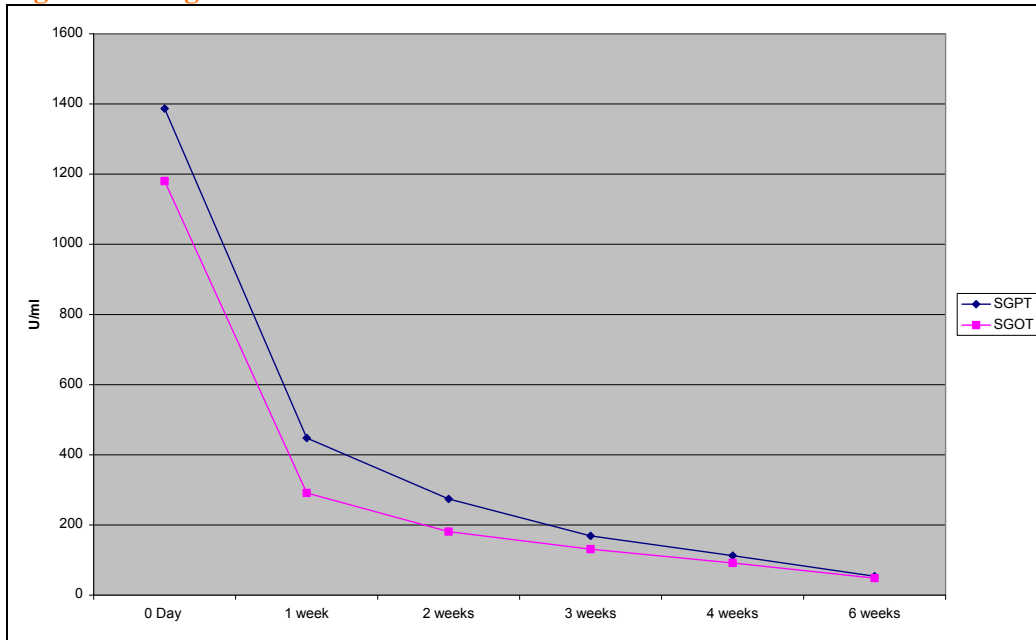


Fig.2: Showing the effect of HEPTOVIT S.G.C on Bilirubin

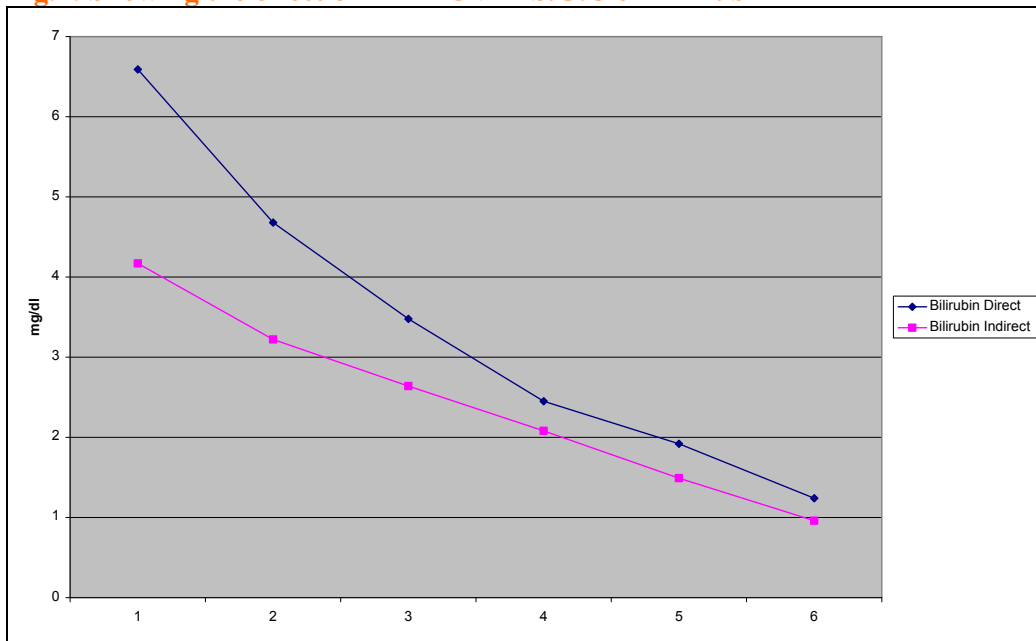


Figure 3: Scoring in appetite change and abdominal pain

Appetite: 1- Very Poor, Poor – 2, Moderate – 3, Good – 4, Very good - 5

Abdominal Pain: 1- Mild, 2-Moderate, 3 – Severe

Fig 3: Showing the effect of HEPTOVIT S.G.C on Appetite and Abdominal Pain

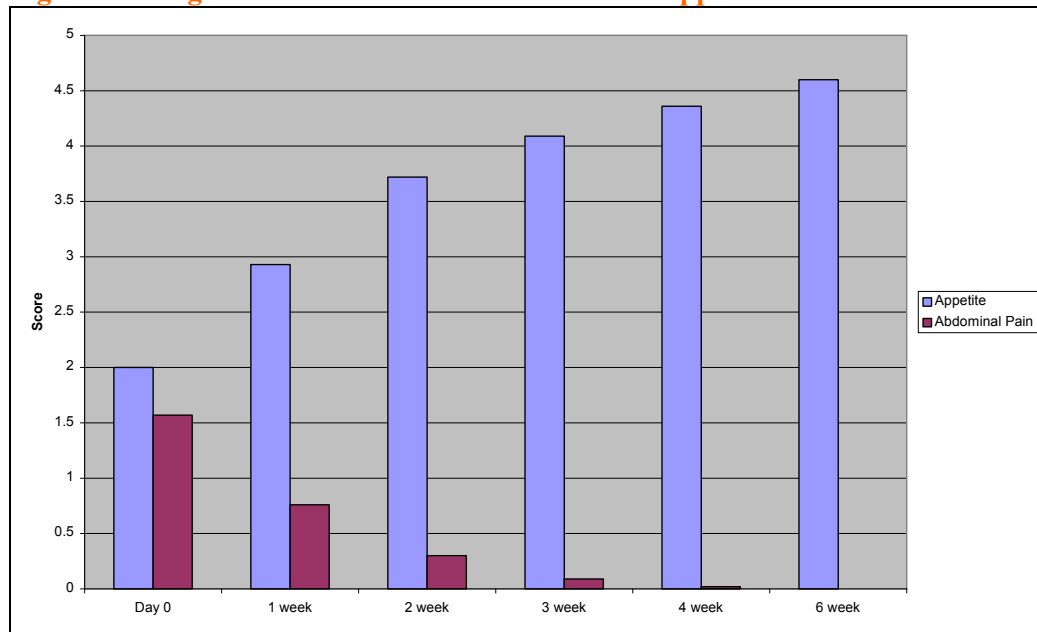
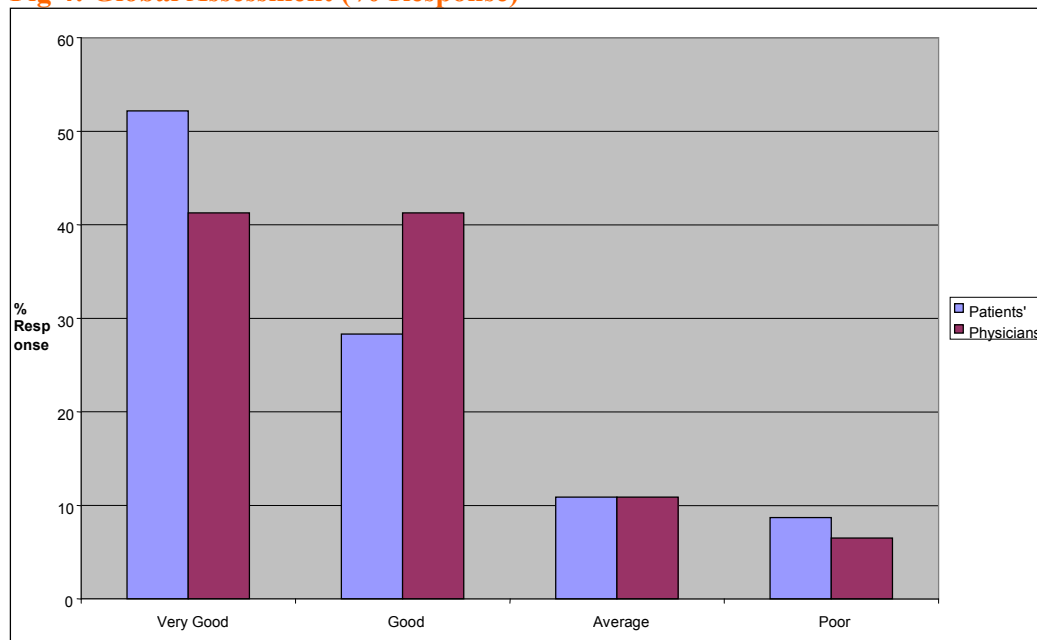


Table 2: Patients' and Physicians' Global Assessment (% Response)

Parameter	Patients		Physician	
	Efficacy	Safety	Efficacy	Safety
Very Good	52.2	43.5	41.3	39.1
Good	28.3	37.0	41.3	43.5
Average	10.9	10.9	10.9	10.9
Poor	8.7	8.7	6.5	6.5

Fig 4: Global Assessment (% Response)



DISCUSSION

Hepatitis is most often viral, due to infection with one of the hepatitis viruses (A, B, C, D, E, F (not confirmed), and G) or another virus (such as those that cause infectious mononucleosis, cytomegalovirus disease). The main non viral causes of hepatitis are alcohol and drugs. Many patients infected with hepatitis A, B, and C have few or no symptoms of illness. For those who do develop symptoms of viral hepatitis, the most common are flu- like symptoms including: loss of appetite, nausea, vomiting, fever, weakness, tiredness and abdominal pain. Treatment of viral hepatitis is dependant on the type of hepatitis.

Viral infection in liver causes destruction of parenchymal cells at the deoxyribonucleic acid (DNA) level, which leads to hepatocellular failure, disturbances in nitrogen metabolism, inflammation, necrosis, and cirrhosis resulting in the obstruction of bile-canaliculi. This obstruction leads to resorbtion of bile into the peripheral bloodstream through the hepatic vein and lymphatics. The process then causes the serum bilirubin level to rise above 2 mg% and is sufficient to be termed clinically as jaundice. ¹

According to Ayurveda, hepatitis (Kamala) is a disease of the circulatory system and is categorized under biliary (*Pitta*) diseases; *ranjaka pitta* is the type of biliary fluid involved in this pathogenesis. ³The liver secretes *Pachaka pitta* (more than 500 cc in a day) and is stored in the gall bladder (*pittashaya*). The stored bile gets reabsorbed and leaves a fraction of original bile (*tyakta drava pitta*). The concentration of original bile in the circulation is critical and any derangement leads to diseases arising out of weak digestive and metabolic activity (*agni vaishamy*). The more dilution of bile in the gall bladder results predominantly in symptoms like nausea, vomiting, and fever. When the concentration is too high, it leads to symptoms like burning sensations, thirst, profused sweating, giddiness, and hemorrhagic conditions. ²

In conventional medication there is no specific treatment for hepatitis. In patients with acute viral hepatitis, the initial treatment consists of relieving the symptoms of nausea, vomiting, and abdominal

pain. Careful attention is given to medications which can have adverse effects in patients with abnormal liver function. Only those medications that are considered necessary are administered since the impaired liver is not able to eliminate drugs normally, and drugs may accumulate in the blood and reach toxic levels. Treatment of chronic infection with hepatitis B and hepatitis C usually involves medication or combinations of medications to eradicate the virus. Medications for chronic hepatitis C infection include: injectable interferon, oral ribavirin and medications for chronic hepatitis B infection include, injectable interferon, oral lamivudine (Epivir), oral adefovir (Hepsera), and oral entecavir (Baraclude).

Inspite of great developments in the treatment of hepatitis, there are still limitations. As a result medical professionals are looking at alternative systems of medications which are considered to be effective and safe. **HEPTOVIT S.G.C** is a Phytomedicine which is a combination of herbs judiciously selected from Ayurvedic texts.

HEPTOVIT S.G.C is an exceptional combination of Ayurvedic herbs, which are used as hepato protective, digestion stimulant, anti inflammatory, etc. It is an excellent recipe of herbs to cure all liver diseases of inflammatory conditions. This product helps removal of toxins from the gastrointestinal tract thereby recuperating liver functions.

In the present study treatment with **HEPTOVIT S.G.C** showed a highly significant improvement in patients with infective hepatitis.

There were no significant changes in vital signs and haematological parameters after treatment with **HEPTOVIT S.G.C** for 6 weeks and also there were no adverse events reported during the trial by any patient, suggesting that the drug is well tolerated and very safe.

There was a highly significant reduction in the liver function parameters. The SGPT levels reduced by 96.11%, SGOT by 95.87%, Bilirubin (Direct) 81.18% and Bilirubin (Indirect) by 76.98%. The reduction in all these parameters shows vast improvement in quality-of-life of patients.

In the Global assessment both the patients and physician had almost similar opinion about the drug's efficacy and safety. More than 52% of patients were of the opinion that the drug is very effective, 28% said it is good, 11% said it is average and only about 9% said it is poor. Physicians' opinion was that it was very good in 41% patients, good in another 41%, average in 11% and poor in about 7% of the patients. Almost similar opinions were recorded for drug safety.

CONCLUSION

In conclusion it may be said that **HEPTOVIT S.G.C**, a phytomedicine, developed by M/S. Millennium Herbal Care Limited, is very effective in treatment of infective hepatitis. All the signs and symptoms disappeared within 2-3 weeks of treatment and all the liver function parameters such as SGPT, SGOT, Bilirubin etc returned to

normal within 4-6 weeks. The drug did not produce any adverse events indicating that it is safe.

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