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An Evaluation of Potential Hepato–Protective Properties of *Hylocereus Undatus* Fruit in Experimental Rat Model

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ABSTRACT

Detoxifying organ liver is used to conduct various metabolic functions. A broad spectrum of poisonous substances is associated with liver damage. *Hylocereus undatus* have been used to treat a wide range of diseases. In our study, we assessed the hepatoprotective activity of *C. grandis*. The ethanolic extract of *Hylocereus undatus* significantly restored the pathological state of some biological markers such as SGOT, SGPT, ALP, creatinine, total cholesterol, LDL, triglycerides level which was altered due to the destructive effects of CCl4-injection. hepatic toxicity containing rodents ($p< 0.05$). Consequently, the extract reversed the marred level of proteins, like Y-GT, MDA, LDH, SOD, and CAT which are closely associated with hepatic function. The study evidenced that various doses of *Hylocereus undatus* extract deliver significant hepatoprotective activity in rats suffering from CCL4 induced hepatotoxicity. Thus, more investigations are needed to detect the responsible mechanism to exert desired activity.

Abbreviations: CLD: Chronic Liver Diseases; ALD: Alcoholic Liver Disease; NASH: Non–Alcoholic Steatohepatitis; HCC: Hepatocellular Carcinoma; SGOT: Serum Glutamic–Oxaloacetic Transaminase; GGT: Gamma–Glutamyl Transferase; MDA: Malondialdehyde

Introduction

The liver is the body's largest, most complex internal organ [1-3] accounting for 2–3% of total body weight [4] of an adult human. An estimated 1.5 billion people [5-7] suffer from Chronic Liver Diseases (CLD) worldwide; the percentage has increased by 31% in the USA among people aged 45–64 yrs [8]. There is large evidence that oxidative stress plays a key role in the pathophysiology of various liver diseases such as Alcoholic Liver Disease (ALD), Non–Alcoholic Steatohepatitis (NASH), Hepatitis Type C and Hepatocellular Carcinoma (HCC) [9,10]. The liver is particularly susceptible to cellular injuries due to an elevation in ROS activity OH, H_2O_2., O_2. [11] since excessive consumptions of alcohol, drug overdose, exposure to certain toxic chemicals, viral or parasitic infection [12] can generate and activate free radicals (ROS). ROS molecules have a role in cell signaling process including apoptosis, gene expression, and the activation of metabolic cascades [13]. Oxidative stress and ROS formation are predominantly generated through the induction of cytochrome P450–2E1 (CYP2E1), causing DNA adducts, cleavage of phosphodiester bonds [14], breakage of double strand thus damaging the DNA structure, causing chromosomal alterations , genetic mutations [15] causing conditions such as fibrosis/ cirrhosis and eventually progressing towards Hepatocellular Carcinoma (HCC) There were over 840,000 new diagnosed cases of liver cancer and 780,000 related deaths were recorded in 2018 [16,17] '/However, about 80% of liver diseases can be prevented through early–stage diagnosis, [18] regular and effective use of medications and the necessary lifestyle regulations.

A common drug in use is L–glutathione (L–cysteine, glycine and L–glutamate), a low molecular weight, water–soluble tripeptide, that acts as a free–radical scavenger often combined with ascorbic acid as oral dietary supplementation, they have valuable detoxifying and anti–oxidant properties and are known to strengthen immune responses [19-22] and protect the body against oxidative stress. However, they have certain adverse effects such as digestive disturbances, abdominal cramps, bloating, diarrhea, breathing difficulties due to bronchial constriction and allergic symptoms such as rash. Plants play a pivotal role in the process of new drug discovery and synthesis; they serve as a rich, diverse and abundant source of naturally–occurring medicinal compounds [23]. These may either work as a safer, more effective alternative of the existing drug molecule or be explored further through research for their enormous, yet undiscovered therapeutic potentials [24,25]. Approximately 65–70% of the human population is largely dependent on the plant kingdom for their primary healthcare needs. A single plant usually contains thousands of active compounds that help to cure different specific diseases; moreover, the concentrations of the necessary constituents can be altered through genetic modification to produce the desired level. The inadequacies of the conventional medicines and their unusual side effects have urged the search for alternative therapeutic agents from natural sources. There are many plants having hepato–protective properties; however only a small proportion of them is used currently in traditional medicine.

Dragon fruit, belongs to the vine cactus group from the sub–family of Cactoideae in the family Cactaceae. Once native to tropical and sub–tropical regions such as southern Mexico and Central and South America, it has been cultivated in Vietnam for the past 100 years and is now found abundantly all over the world. This fruit possess excellent cardiovascular and hepato–protective properties. A serving of 3.5 ounces or each 100 grams contains the following: Energy value–60 calories/ 251 J, Water–87 grams, Protein–1.18 grams, Fat–0.4 grams, Carbohydrates–12.94 grams, Dietary fiber–2.9 grams, Sugars (total)–7.65 grams, Vitamin A–58 international units, Vitamin C (ascorbic acid)–3% of the RDI/2.5 mg, Vitamin B1 (thiamin)–0.04 mg, Vitamin B2 (riboflavin)–0.05 mg, Vitamin B3 (niacin)–0.16 mg, Sodium–60 mg, Iron–4% of the RDI/ 1.9 mg, Magnesium–10% of the RDI/39 mg, Phosphorus–22.5 mg and Calcium–8.5 mg [26-28]. *Hylocereus undatus* is known to possess anti–oxidant, anti–inflammatory, anti–aging, anti–tumour and anti–mutagenic and anti–carcinogenic activities. It is very rich in essential anti–oxidant compounds like carotenoids, flavonoids, phenolic acids, important water–soluble colour–imparting betalain pigments consisting of red–violet betacyanins and yellow betaxanthins. These natural substances phenolic acid (e.g gallic acid) and polyphenols (e.g. flavonoids) act as bio–active scavengers, they protect human body cells from unstable free radical (ROS) molceules that are linked to chronic diseases and aging.

β–carotene molecule, precursor of vitamin A (retinol), is one powerful scavenger of singlet oxygen [29-31]. The modern medicaments that are currently available in the commercial market are quite expensive, often imposing a huge financial burden on the general population, particularly for the lower income group. The aim of our present study is to investigate the potential hepato–protective and anti–oxidant effects of *Hylocereus undatus* in CCl_4–induced experimental rat model in a dose independent manner as well as their possible side effects on the liver in search of a newer, safer, affordable and more effective medicine.

Methods and Materials

Plant Collection and Extract Preparation

Hylocereus undatus fruits were collected from a nursery located in Road 15, Dhanmondi in Dhaka. The specimen was identified by the Department of Pharmacy, University of Dhaka. The wet *Hylocereus undatus* fruit was air–dried and roughly pulverized. The powdered fruit was then extracted using 50% ethanol for several

days. In every three days interval, the extract was filtered. The obtained extract was dried at a low temperature and pressure in the rotary evaporator. Finally, the crude residue was used to carry out the necessary pharmacological tests.

Botanical Authentication

We submitted a sample of each part of our plant species under experiment in accordance with the requirements of our National Herbarium, and the herbarium authorities have conducted the appropriate measures. However, because of the pandemic's sudden and devastating wave, the authorities forced the institute to limit outsiders for a long period. We could not receive the botanical authentication (accession number) yet for the aforementioned reasons.

Drugs and Chemicals

Commonly known hepatotoxicity generating agent carbon tetrachloride, CCl4 was bought from the sigma company, USA. The standard anti–oxidant drug silymarin is used, was bought from Incepta Pharmaceuticals Ltd as Livasil 140 mg.

Experimental Animal Procurement, Nursing, and Grouping

A total of 140 male rats each weighing between (120–150 grams) were purchased from Jahangirnagar University, Savar, Dhaka. Each of them was housed in a climate–controlled environment (temperature 25±3°C, relative humidity 55±5%, and a 12–hour light/dark cycle) at the Institute of Nutrition & Food Science (INFS), University of Dhaka. They have been treated with a standard diet regimen and allowed to drink cleaned water. All of the animals were kept in this habitat for adaptation, at least a duration of one week prior conducting the study. All experimental protocols were performed according to the guidelines of Institutional Animals Ethics Committee (IEAC).

Animal Model Sample Size Detection

A total of 140 rats were randomly distributed into 14 groups, each consisting of 10 rats each. In all of the investigations, the rats were randomly picked for each group. For enhancing the validity of the investigation, we took 10 rats in each group. Some arbitrary issues regarding the pandemic situation may influence the elevation of sample size. Because our rats were kept in the animal house at the time of pandemic lockdown where the lab curator was the only person responsible for their care, and we, the researchers, visited the lab twice a week. We, on the other hand, kept a close check on the rat every day during the breeding season. In our research we included both positive and negative control groups.

Dose Selection and Route of Administration for Respective Study

Carbon tetrachloride (CCL_4) is a typical chemical agent used in the laboratory to research a variety of liver problems in both acute and chronic forms [1]. Trichloromethyl free radical (CCL_3), a CCL_4 metabolite produced by CYP2E1 isozymes, reacts with cellular lipids and proteins to form trichloromethyl peroxy radical, which attacks lipids on the endoplasmic reticulum membrane faster than the trichloromethyl free radical, causing lipid peroxidation and lobular necrosis. Hepatic damage was caused in all animal groups except the standard control group by a single oral administration of CCl_4 combined with olive oil as a vehicle in a 1:1 ratio (3 ml/kg of rat body weight). Animals with hepatic damage were given *Selenicereus undatus* extracts as a post-treatment. The extract was given orally at different doses.

Evaluation of Hepato–Protective Activity

For this experiment, 140 rats were randomly picked and equally divided into fourteen groups (Table 1).

Table 1.

Group Number	Group Specification	Treatment species	Dose Treatment species (mg/kg)	Abbreviation of Groups
1	Negative Control	Physiological Saline	10ml/kg	N
2	CCl_4 Control	N/A	N/A	A
3	CCl_4 + Silymarin	Silymarin	80	$A+S_{80}$
4	CCl_4 + Silymarin	Silymarin	120	$A+S_{120}$
5	CCl_4 + Silymarin	Silymarin	150	$A+S_{150}$
6	CCl_4 + *Hylocereus undatus*	*Hylocereus undatus*	400	$A+HU_{400}$
7	CCl_4 + *Hylocereus undatus*	*Hylocereus undatus*	700	$A+HU_{700}$
8	CCl_4 + *Hylocereus undatus*	*Hylocereus undatus*	1000	$A+HU_{1000}$
9	Silymarin	Silymarin	80	S_{80}
10	Silymarin	Silymarin	120	S_{120}
11	Silymarin	Silymarin	150	S_{150}
12	*Hylocereus undatus*	*Hylocereus undatus*	400	HU_{400}
13	*Hylocereus undatus*	*Hylocereus undatus*	700	HU_{700}
14	*Hylocereus undatus*	*Hylocereus undatus*	1000	HU_{1000}

Statistical Analysis

All our findings (raw data) belong to several groups regarding numerus parameters recorded and analysed on a broadsheet using MS Excel program. The data obtained were subject to descriptive statistics, and the results were represented as mean ± SD. We employed the "One–way Anova test" of SPSS 16 software for interpreting the inter–group heterogenicity in terms of diverse biological parameters to determine the statistical significance. The events are considered to be statistically significant while the 'p' value was detected as less than 0.05 ($p<0.5$).

Results and Findings

From the graph above, we found the evidence of weight gain in the negative control group and *H. undatus* treated groups after treatment i.e in groups 1, 12, 13 and 14 respectively. Apart from the gain of weight in these groups, the rats in group 2 to 11 showed a decrease in body weight following CCl_4 and silymarin treatment in groups 3–6, CCl_4 and H undatus treatment in 6–8, and silymarin treatment in groups 9–11. The level of Serum Glutamic–Oxaloacetic Transaminase (SGOT), a hepatic marker was reduced significantly after Silymarin. As shown by the figure above, six of the groups demonstrated statistically significant changes ($p\leq0.01$) while the other six did not. The CCL_4 and silymarin treated groups 3, 4, 5 showed a gradual decrease in SGOT levels in a dose–dependent manner and a similar pattern was observed in groups 6–8 treated with CCL_4 and plant extract. The SGOT levels in other non–CCL_4 treated groups did not fluctuate in a significant level compared with negative control group. As we can see in the figure above, six of the groups demonstrated statistically significant changes ($p\leq0.05$) group 3 and 6 and ($p\leq0.01$) in groups 4, 5, 6, 7. while the other six did not. The CCL_4 and silymarin treated groups 3, 4, 5 showed a gradual decrease in SGPT levels in a dose–dependent manner and the groups 6–8 treated with CCL_4 and plant extract also followed the similar trend. The SGPT levels in other non–CCL_4 treated groups did not fluctuate in a significant level compared with negative control group.

As we can see from the figure above, a gradual decline in the levels of ALP was observed upon administration of low, medium, high doses of *H. undatus* starting from group 3. Groups 3–5 and 6–8 demonstrated dose dependent decrease; the changes were statistically significant ($p\leq0.01$). The SGOT levels in 6 other non–CCL_4 treated groups (9–14) did not fluctuate in a significant level compared with negative control. As interpreted from the graph, statistically significant ($p\leq0.01$) changes in creatinine level was observed, higher doses of *H. undatus* progressively declined the creatinine level in CCL_4 and drug–treated groups and CCL_4 and plant extract–treated groups. Slight fluctuations were observed after administration of only the drug or plant extract in non–CCL4 treated groups (9 to 14) but they were found to be statistically non–significant. The level of total cholesterol level accelerated upon CCL_4 treatment in group 2, that level immediately lowered down significantly when drug (groups 3–4) and plant extracts (group 6–8) were administered in the rats. The change in plasma cholesterol levels was found to be statistically significant in 6 groups, ($p\leq0.05$) in group 3 and 6, and ($p\leq0.05$) while the changes were non–significant in the other 6 groups.

The administration of silymarin in groups 9, 10, 11 and *H. undatus* in groups 12, 13, 14 also lowered cholesterol to that level similar to group 1, their level remaining almost at the same level and statistically non–significant. As we can observe from the graph above, there was a sharp reduction in HDL level after administration with CCL_4 in group 2, treatment with higher doses of the plant extract reversed the results although the lowering effect was more potent in case of Silymarin than the plant extract. The rise in HDL resulted in a dose dependent manner upon administration of silymarin and *H undatus* in groups 3 to 8 respectively and the data were statistically significant ($p\leq0.05$) in group 3 and 6 and ($p\leq0.01$) in groups 4, 5, 6 and 7. No observable severe effects were found upon the drug or plant extract administration to the non–CCL_4 treated groups pointing to the safety of the plant extract. As we the graph represents, the plant extracts and drugs were gradually increased in dose, the level of LDL gradually decreased in a dose–dependent manner. However, the administration of plant extract in 4–6 showed a more pronounced change than the administration of silymarin in groups 3–5. Groups 3 and 6 showed statistically significant data ($p\leq0.05$) and 4, 5, 7, and 8 ($p\leq0.01$).

The rest of the groups (9–14) without CCL_4 administration were fed with plant extract and drug; there were almost no fluctuations in the LDL levels when compared to the negative control group and the data was not statistically significant. From the graph above, the plant extracts and drugs were gradually increased in dose, the level of triglyceride gradually decreased. Groups 3–6 which had been treated with silymarin showed more pronounced decline when compared to groups 6–8 which were treated with H undatus extracts. Groups 3 and 6 showed statistically significant data ($p\leq0.05$) and 4, 5, 7, and 8 ($p\leq0.01$). No significant deviation was spotted of the groups (9–14) when compared to the negative control group. From the graph above, the plant extracts and drugs were gradually increased in dose, the percentage of DNA fragmentation gradually decreased. Groups 3 and 6 showed statistically significant data ($p\leq0.05$) and 4, 5, 7, and 8 ($p\leq0.01$). The rest of the groups (9–14) without CCL4 administration were fed with the drug and plant extract respectively; their percentage lied within 5–10% and showed no significant deviations when compared to the negative control group. Serum Gamma–Glutamyl Transferase (GGT) is an enzyme which occurs in the liver; it may leak into the bloodstream

due to hepatocellular damage. It has been widely used as an essential index of liver dysfunction. From the graph above, we can observe that the level of GGT gradually decreases along with increasing drug dose of silymarin (group 3–5) and H undatus extracts (group 6–8).

The level of GGT declines in a dose–dependent manner from groups 3 to 8 following a gradual declining trend. Groups 3 and 6 showed statistically significant data ($p \leq 0.05$) and 4, 5, 7, and 8 ($p \leq 0.01$). The rest of the groups (9–14) without CCL_4 administration were fed with plant extract and drug; no significant deviations were found. SOD is the only anti–oxidant enzyme that scavenges the superoxide anion by converting this free radical to oxygen and hydrogen peroxide. We can observe the variation in SOD levels along with silymarin or plant extract from the graph above. As the drug dose was increased gradually, the level of SOD continued to rise in a dose–dependent form. Groups 3 and 6 showed statistically significant data ($p \leq 0.05$) and 4, 5, 7, and 8 ($p \leq 0.01$). Slight fluctuations were seen in the SOD level of rats among groups 9–14, however the change was not statistically significant when compared to the negative control. Malondialdehyde (MDA) is one of the final products of polyunsaturated fatty acids peroxidation in the cells. It is commonly known as a marker of oxidative stress and the antioxidant status in cancerous patients. MDA levels were considerably lower in CCl_4–treated groups 3–8 following the administration of silymarin and H undatus extracts respectively. The changes occurred in a dose–dependent manner; they were found to be statistically significant ($p \leq 0.05/0.01$). The six other groups without CCl_4 treatment demonstrated lower MDA values not much different from the negative control group. The changes in groups 9–14 were not statistically significant. Catalase often abbreviated as CAT is one of the enzymes with the highest turnover rates, is the main enzyme involved in reduction of H_2O_2 to water via the Fenton reaction. Following drug and H undatus administration, the enzyme levels are observed to rise significantly ($p \leq 0.05/0.01$) in a dose–dependent manner in groups 3–8 respectively. Groups 9–14 showed statistically non–significant changes where the CAT levels declined in groups 12, 13 and rose in groups 11 and 14 compared to the negative control.

Discussion

Hepato–protective activity of *Hylocereus undatus* (dragon fruit): Dragon fruit is rich in nutrients such as flavonoid, vitamin B1, B2, C, gallic acid, phenol, tannins, saponins, steroids etc [1,2]. Apart from its' nutritional point it is well known for medicinal purposes like in hepatic protection [3]. Our *in–vivo* study in rats has provided valuable information of hepatoprotective effect of dragon fruits. In Figure 1, we found the evidence of weight gain in *H. undatus* and Silymarin treated groups after CCL_4 induced liver injury. In Figure2, CCL_4 induced increased Serum Glutamic–Oxaloacetic Transaminase (SGOT) level, which is a hepatic marker were reduced significantly after Silymarin use. Consecutive increased use of dose of Silymarin reduced SGOT level in a significant amount. *H. undatus* administration in CCL_4 treated rats did not lower SGOT level as much as Silymarin did. The SGOT levels in other non-CCL_4 treated groups did not fluctuate in a significant level compared with negative control groups. This signifies the fact that no possible harm upon administration of Silymarin or *H. undatus*. Some previous studies have come to an agreement with our results using following plant extracts- *Hyssopus officinalis*, *Cichorium inthybus*, *Hemidesmus indicus*, *Rhododendron arboretum* [4-6].

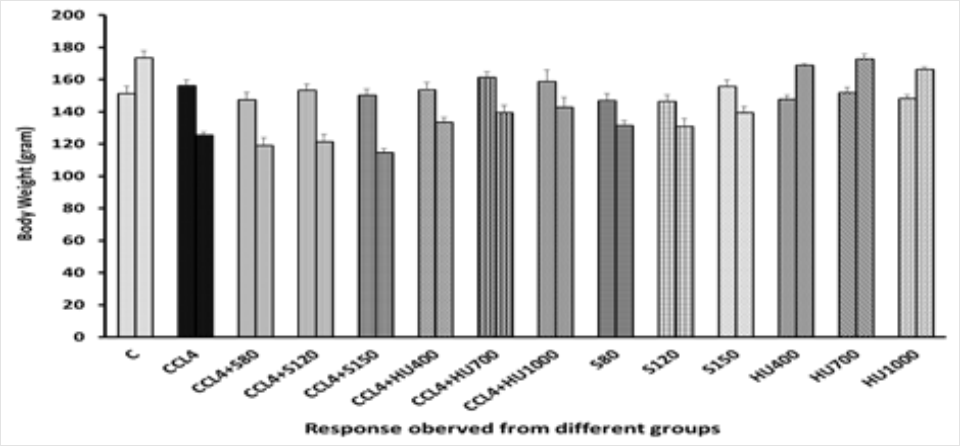

Figure 1: The body weight of rats (in grams) of 14 groups represented before and after completing the experiment.

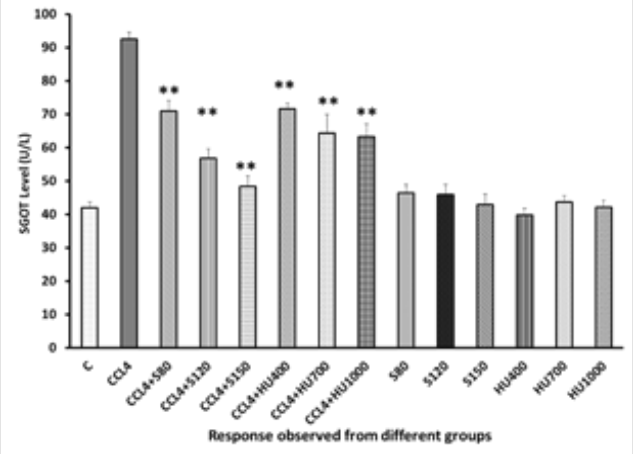

Figure 2: The SGOT (U/L) level of rats from 14 groups. The data were expressed as a mean ± standard deviation.
Note: (**indicates statistically significant change).

From Figure 3, we can observe the significant reduction in SGPT level upon administration of both Silymarin and *H. undatus* in CCL_4 treated group, although Silymarin reduced the SGPT level slightly more than *H. undatus*. Like SGOT level, SGPT level was not deviated much after Silymarin or plant extract administration in non-CCL_4 treated groups. Some previous studies on the following plant extracts support our data- *Chrysanthemum balsamita*, *Echinacea pallida*, *Calendula officinalis*, *Oenothera biennis*, *Hyssopus officinalis*, *Hemidesmus indicus*, *Rhododendron arboreum* [5,6]. Gradual decline in ALP level was observed upon administration of low, medium, high dose of *H. undatus* as we can see from Figure 4. The result is almost similar as Silymarin in CCL_4 treated groups. *H. undatus* and Silymarin administration in no-CCL_4 treated groups were unlikely to cause harmful effect in rats as we found no significant fluctuation in result compared with negative control. The increase level of enzyme by the extract may be due to the prevention of the leakage of intracellular enzymes by its membrane stabilizing activity [7]. Same kinds of results have found in some studies for *Pisonia aculeate*, *Solanum xanthocarpum*, *Beta vulgaris*, *Clerodendrum inerme*, *Rhododendron arboretum*, *Clutia abyssinica* [5-11].

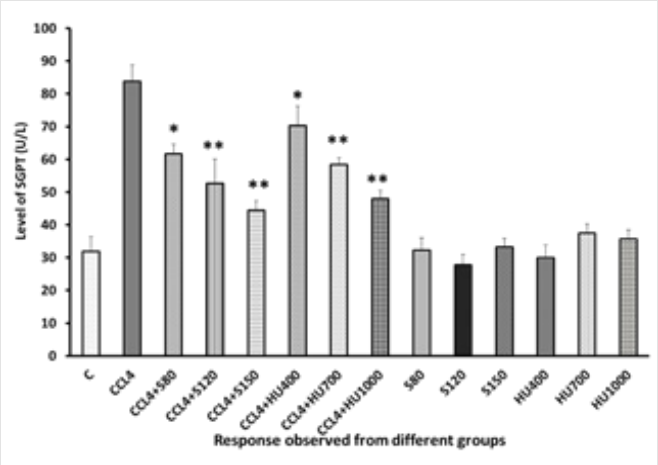

Figure 3: SGPT (U/L) level of rats from 14 groups. The data were expressed as mean ± standard deviation.
Note: (*indicates statistically significant change).

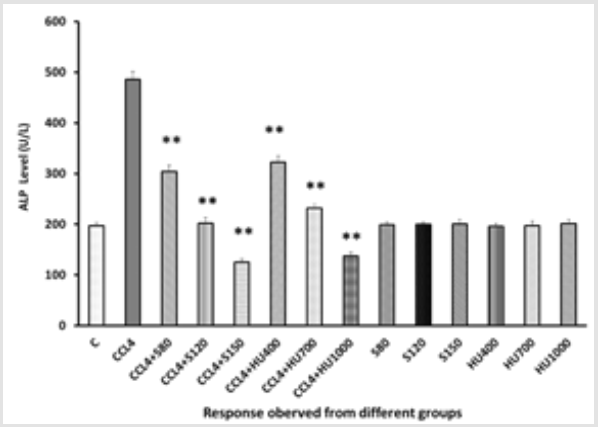

Figure 4: ALP (U/L) level of rats from 14 groups. The data were expressed as mean standard deviation.
Note: (*indicates statistically significant change).

In Figure 5, higher doses of *H. undatus* progressively declined the creatinine level in CCL_4 treated groups. Still, reduction level done by Silymarin administration was slightly more. There were some fluctuations observed after administration of the drug and plant extract in non- CCL_4 treated groups but they were not significant. In Figure 6, as Total cholesterol level heightened upon CCL_4 treatment, that level immediately lowered down significantly when plant extracts were administered to those groups. Silymarin administration also lowered cholesterol to that level. There are some studies found to be coincided with our results, using *Beta vulgaris*, *Clerodendrum inerme*, *Rhododendron arboreum* plant extracts [5,9,10]. As we can observe the significant reduction in HDL after administration with CCL_4 from Figure 7, treatment with higher doses of the plant extract reversed the result. Although the lowering effect was more potent in case of Silymarin than the plant extract. No observable severe effects were found upon the drug or plant extract administration to the non- CCL_4 treated groups pointing to the safety of the plant extract.

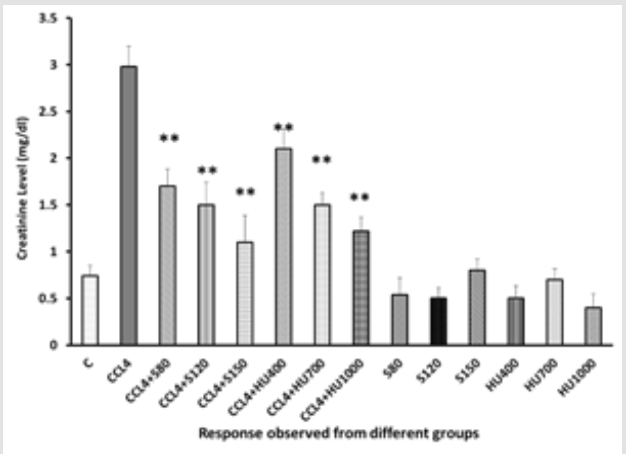

Figure 5: Creatinine (mg/dl) level of rats from 14 groups. The data were expressed as a mean standard deviation.
Note: (*indicates statistically significant change).

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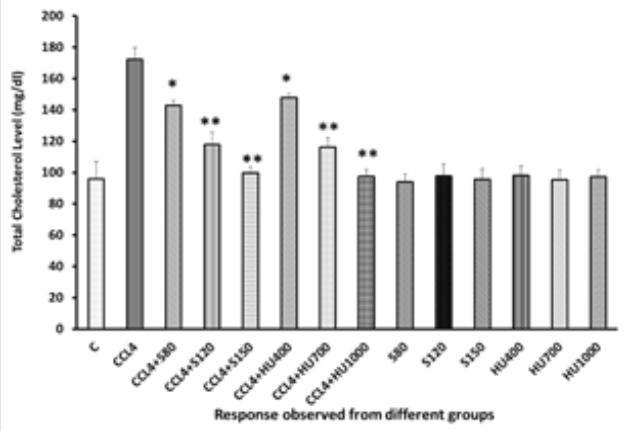

Figure 6: Total cholesterol (mg/dl) level of rats from 14 groups. The data were expressed as mean ± standard deviation.
Note: (*indicates statistically significant change).

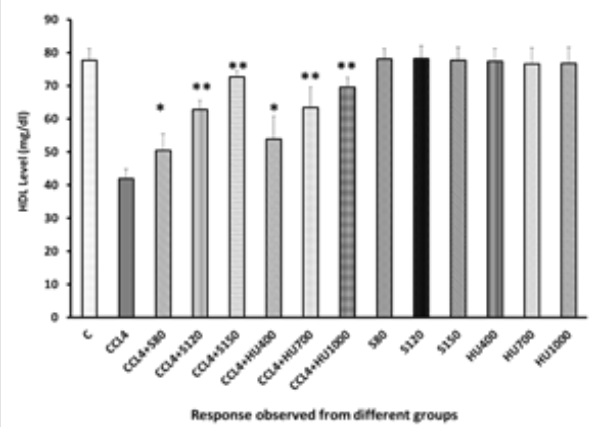

Figure 7: HDL (mg/dl) level of rats from 14 groups. The data were expressed as a mean ± standard deviation.
Note: (*indicates statistically significant change).

As the doses of plant extracts and drugs were increased gradually, the level of LDL also gradually decreased as we found from the Figure 8. The lowering effect of Silymarin was slightly more pronounced than *H. undatus*. The rest of the groups without CCL_4 which were fed with plant extract and drug; showed no significant deviations compared to negative control group. Same kinds of effects have found in some studies on *Solanum xanthocarpum*, *Beta vulgaris* [10,11]. In Figure 9, the triglyceride level decreased with gradual increase of plant extract and drug. The trend of lowering was almost same for both drug and the extract. Same result have obtained for - *Clerodendrum inerme*, *Rhododendron arboreum* plant extracts [5,9]. Although the reverse results were spotted on in case of Beta vulgaris [10]. DNA fragmentation rate was increased due to CCL4 induced hepatic injury as we acknowledged from Figure 10. The introduction of plant extract and the drug gradually reduced the percentage of DNA fragmentation rate. In Figures 11 & 12, when CCL_4 increased the γ GT level, plant extracts and Silymarin were given to lower the level. High dose of *H. undatus* (1000mg) lowered the level significantly.

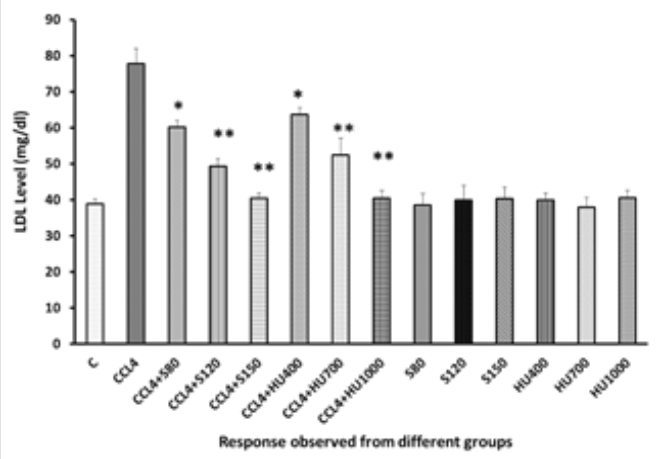

Figure 8: LDL (mg/dl) of rats from 14 groups. The data were expressed as a mean ± standard deviation.

Note: (*indicates statistically significant change).

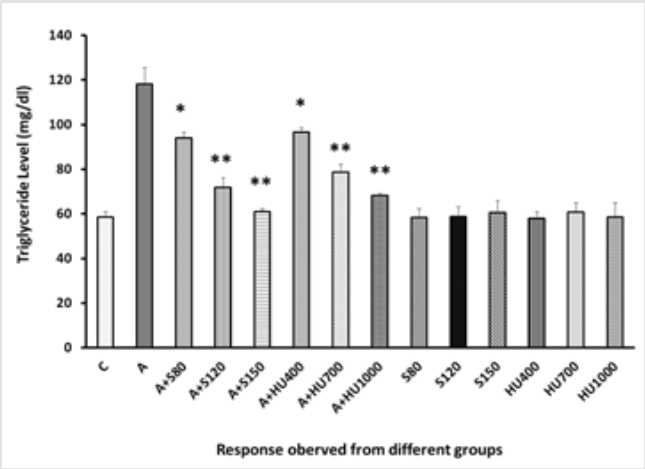

Figure 9: Triglyceride level of rats from 14 groups after administering the drug or *H undatus* plant extract. The data were expressed as mean ± standard deviation.

Note: (*indicates statistically significant change).

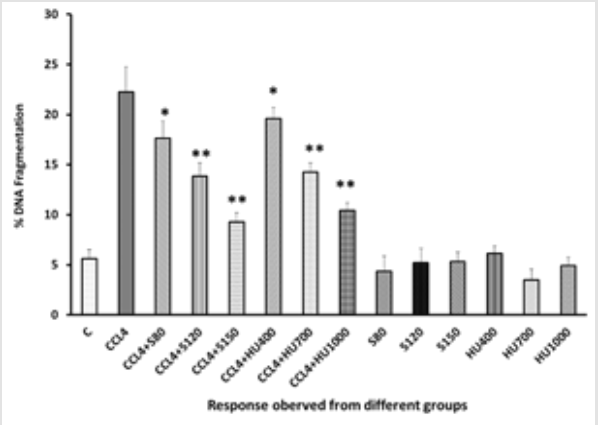

Figure 10: Comparison of percentage DNA fragmentation in 14 groups of rats after administering the drug or *H undatus* extract. The data were expressed as mean ± standard deviation..

Note: (*indicates statistically significant change).

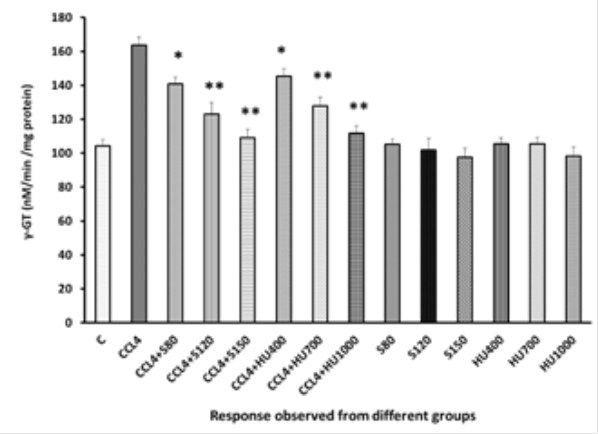

Figure 11: γ–GT (nM/min/mg protein) of rats from 14 groups after administering the drug or *H undatus* plant extract. The data were expressed as mean ± standard deviation.

Note: (*indicates statistically significant change).

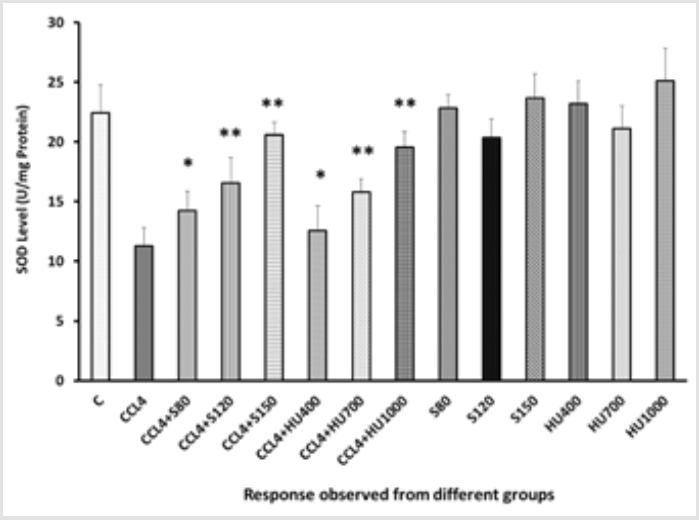

Figure 12: SOD (U/mg Protein) of rats from 14 groups after administering the drug or *H undatus* plant extract. The data were expressed as mean ± standard deviation.

Note: (*indicates statistically significant change).

As from Figure 13, CCL_4 reduced the SOD level a bit much. Administration of high doses of plant extracts and the Silymarin reversed the result towards normal. No lethal evidence of the plant extracts were found as no significant variation in non- CCL_4 groups was noted. Same types of results were observed from Figure 14, where treatment of drug and the plant extracts increased the CAT level. High level of CAT & SOD established the reduction in oxidative damage from superoxide and peroxide radicals [7]. Some of the previous studies complied with the result in case of *Pisonia aculeate*, *Zanthoxylum armatum*, *Carya illinoinensis*, *Solanum xanthocarpum* [7,11,12,13]. Punarnavashtak kwath, an ayurvedic preparation containing several plant extracts- *Boerhaavia diffusa*, *Picrorhiza kurroa*, *Tinospora cordifolia*, *Zingiber officinalis*, *Berberis aristata*, *Terminalia chebula*, *Azadirachta indica* and *Tricosanthes dioica* gave almost similar effects upon administration into groups which had CCL_4 induced hepatotoxicity [14]. In Figure 14, CCL_4 induced high level of MDA was attenuated at a significant rate when administered with high doses of drugs and plant extracts. Studies on *Zanthoxylum armatum*, *Carya illinoinensis*, *Solanum xanthocarpum*, *Aspalathus linearis*, *Borago officinalis* have showed same type of effects [12-16].

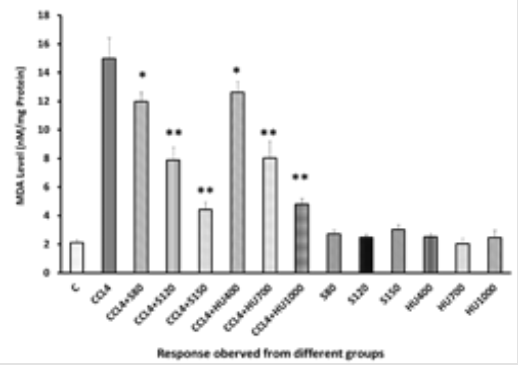

Figure 13: MDA (nM/mg protein) of rats from 14 groups after administering the drug or *H undatus* plant extract. The data were expressed as mean ± standard deviation.

Note: (*indicates statistically significant change).

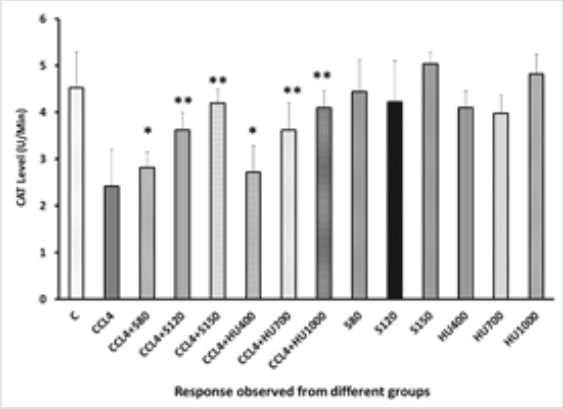

Figure 14: CAT (U/Min) of rats from 14 groups after administering the drug or *H undatus* plant extract. The data were expressed as mean ± standard deviation.

Note: (*indicates statistically significant change).

As a hepatotoxic chemical, CCL_4 induces hepatic membrane damage through oxidation processes [15,17]. Elevated serum enzyme levels (SGOT, SGPT, ALP, Creatinine, LDH, MDA, γ-GT) which are hepatic markers for liver damage are lowered to a significant level upon administration of our test extract in this study. Along with those markers, hepato-protective SOD, CAT, HDL levels have increased to a level justifying the hepato-protection ability of our test extract. Comparing with Silymarin, *Hylocereus undatus* has showed hepatoprotective activity no less than an established hepatoprotective drug. Also, possibility of serious side effects have been nullified as the graphs have showed no fluctuations of result upon administration of the test extract compared to the negative control groups. Our findings match with some previous studies. Although the safety assessment needs to be done in a larger scale before using it as hepato-protective drug source.

Conclusion

Ethanolic extracts of the *Hylocereus undatus* have been shown to have the capacity to reverse several abnormal pathophysiological states in rodent models, as shown by our results. Also, our study suggested that the extract may boost the therapeutic activity to a moderate degree in a dose-dependent manner. So, new roads for disease management may be unwrapped. If the pharmacological response of *Hylocereus undatus*, is carefully analyzed in the future.

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