COMPARATIVE STUDY OF THE PROTECTIVE EFFECT OF SILYMARIN AND COLCHICINE IN INDUCED LIVER FIBROSIS

BY
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Abstract
The comparative protective effect of SM (200 mg/kg P.O daily), COL (0.1 mg/kg P.O daily) and mixture of SM and COL (200 mg/kg and 0.1 mg/kg P.O daily respectively) each given for 28 days on the CCl₄ liver fibrosis were studied. Collagen content in livers of animals treated with CCl₄ was increased compared to control and histopathological examination of liver samples by Masson's Trichome stain (MTC) showed that collagen accumulated in the portal area resulting in the formation of fibrotic tissues. SM has shown a significant recovered enzyme activities in all the changes observed in LF induced by CCl₄ rats, except for serum total cholesterol and serum alkaline phosphatase which were reduced only 35% and 80% respectively as compared with CCl₄ treated rats. The mixture of SM & COL was more potent in the hepatoprotective drugs than COL only, but SM was the best hepatoprotective drug.

Key words: Carbon tetrachloride (CCl₄); Liver Fibrosis (LF); Silymarin (SM) and Colchicine (COL).

Introduction
The main causes of liver diseases are viral, autoimmune, drug/toxin, alcohol and nonalcoholic fatty liver disease (Pinzani and Rombouts, 2004). Liver damage goes through several stages which are fatty liver, liver fibrosis and liver cirrhosis. LF defined as the reversible wound-healing process that occurs as a result of a repeated injury and wide range of inflammatory reactions in the liver (Mera et al., 2014). LF results from chronic damage to the liver in conjunction with the excessive accumulation of extracellular matrix proteins including collagen (Seki et al., 2009). Early stages of fibrosis are reversible either by removal of the specific stimulus or by treatment with antifibrotic medications, whereas late stages, progressing to cirrhosis are less reversible (Ellis and Mann, 2012). CCl₄ induced hepatic injury as it used as experimental model for anti-inflammatory and hepatoprotective drug screening, promoting hepatic pathology similar to that observed in humans (Li et al., 2013). Acute administration of a large dose of CCl₄ causes severe necrosis, while chronic administration of lower doses...
of CCl₄ frequently used to induce LF (Risal et al., 2012). SM used to regenerate liver cells damaged by alcohol or drugs, protect against industrial poisons, such as CCl₄ (Catalina et al., 2003). Also, SM has an activity against lipid peroxidation as a result of free radical scavenging and the ability to increase the cellular content of GSH. In addition to its ability to regulate membrane permeability and to increase membrane stability in the presence of xenobiotic damage. SM inhibits the transformation of stellate hepatocytes into myofibroblasts, which are responsible for the deposition of collagen fibers leading to cirrhosis. COL effectively inhibits collagen synthesis and fibrosis in experimental animal models; COL is used in the following cases: primary biliary cirrhosis and alcoholic cirrhosis (Rodriguez et al., 1998). COL protects the liver of experimental animals against several hepatotoxins and inhibits polymerization of microtubules, a process that is believed to be required for collagen secretion. Thus, it is believed to work as an antifibrotic compound by two ways; the first is inhibition of the cellular secretion of procollagen leading to its intracellular accumulation (Mosnier et al., 1991), the second a stimulation of collagenase activity (Hellstrom and Bivalacqua, 2000).

Materials and Methods

Animals

Female albino rats obtained from the animal house of the Institute of Ophthalmology (Giza, Egypt). The animals acclimatized for period of two weeks to adapt themselves with the new location at the animal house. They housed under appropriate conditions of controlled humidity, temperature and light with free access to water and standard pellet rat diet. All animals received human care in compliance with the state authorities following the Egyptian rules of animal protection.

Chemicals

All chemicals from analytical and purified grade provided from Sigma-Aldrich Company. (St. Louis USA), El-Gomhoreya Chemical Co. (Cairo, Egypt), Merck (Darmstadt, Germany) and MUP “Medical Union Pharmaceuticals” (Ismailia, Egypt).

Design of the work

A total of fifty five female albino rats (140-180 g) randomly divided into the five groups. Duration of the experiment was twenty eight days. The groups distributed as follows: **Control group**: rat injected with 2 ml/kg corn oil I.P twice weekly for four weeks and given 2 ml D.W daily P.O. **Rats injected with CCL₄**: rats injected with 2 ml/kg CCl₄ I.P, dissolved in corn oil (1:1, v/v), twice weekly for four weeks (Yachi et al., 2010). **Rats injected with both SM & CCL₄**: rats received 200 mg/kg SM suspension P.O daily (Li et al., 2012) and they also injected with 2 ml/kg CCl₄. **Rats injected with both COL & CCL₄**: rats received 0.1 mg/kg COL P.O dissolved in distilled water daily (Huang et al., 2015) and they also injected with 2 ml/kg CCl₄ I.P. **Rats injected with SM, COL & CCL₄**: rats received both 200 mg/kg SM plus 0.1 mg/kg COL P.O daily, for four weeks. Rats injected with 2 ml/kg CCl₄ I.P after 2 hr from the ingestion of SM and COL drugs.
Measuring parameters

Physical parameters

Organ index (liver & spleen) calculated as follows: Organ index = (organ weight/ rat body weight) X 100 (Yang et al., 2005).

Biochemical serum analysis

At the end of experiment, fasted rats anesthetized by diethyl ether. Blood samples obtained from the retro-orbital junction. All photometric measurements carried out using Shimadzu spectrometer UV-1201 (Japan). Serum Tests: Total cholesterol (Watson, 1960), the activity of alanine aminotransaminase (ALT) activity & aspartate aminotransaminase (AST) activity (Reitman and Frankel 1957), alkaline phosphatase (ALP) activity (Belfield and Goldberg, 1971), direct bilirubin (DB) and total bilirubin (TB) (Doumas et al., 1985).

Biochemical assay of liver homogenate

The liver was dissected, weighted. Tissue homogenates (20% w/v) made by homogenization with saline for one minute using TRI-R, homogenizer. Tubes centrifuged at 3000 rpm for 15 minutes. Assessment of fibrosis markers in Hydroxyproline (HP) content (Reddy and Enwemeka 1996). Assessment of oxidative stress markers as determination of catalase (CAT) activity ((Claiborne, 1985), determination of superoxide dismutase (SOD) (Minami and Yoshikawa 1979), determination of glutathione-s-transferases (GST) (Habig et al., 1974), determination of reduced glutathione (GSH) (Beutler, 1963) and determination of malondialdehyde (MDA) content (Uchiyama and Mihara, 1978).

Histopathological examination

Hematoxylin and Eosin (H&E) for routine histological examination, Masson’s Trichome stain (MTC) for fibrosis markers (Bancroft and Gamble, 2008).

Statistical analysis

All data expressed as mean ± standard error of mean (χ ±SEM). Descriptive statistics were performed using Microsoft Excel 2010. All analysis & graphics were performed using Graph pad prism (windows version 5; Graph pad software 2007). Difference between means was assessed by ANOVA test. Differences were considered statistically significant at P < 0.05.

Results

The clinical characteristics as difference of body weight (BW), liver & spleen index as well as the serum levels of (ALT, AST, TC, ALP, DB & TB), hepatic homogenate (HP, MDA, SOD, GSH, GST & CAT) of the studied subjects will be showed in Tables (1, 2).

Concerning, the TC as shown in figure (1) was significantly higher in CCl4, SM+CCl4 and SM+COL+CCl4 groups as compared to normal group. Also, it was significantly lower in SM+ CCl4, COL+CCl4 & SM+COL+CCl4 groups as compared to CCl4 alone treated group. Also it was lower in COL+CCl4 & SM+COL+CCl4 groups as compared to SM+CCl4 group.

Additionally, AST, ALT & ALP as shown in table (2) were significantly higher in CCl4, SM+CCl4 COL+CCl4 & SM+COL+CCl4 groups as compared to normal group. Also, it was significantly lower in SM+CCl4, COL+CCl4 & SM+COL+CCl4 groups as compared to CCl4 alone treated group.
Concerning the serum level of DB and TB as shown in figure (3), they were significantly higher in CCl₄, COL+CCl₄ & SM+COL+CCl₄ groups as compared to normal group. Also, they were significantly lower in SM+CCl₄, COL+CCl₄ & SM+COL+CCl₄ groups as compared to CCl₄ alone treated group. Also, they were significantly higher in COL+CCl₄ as compared to SM+CCl₄ group.

Concerning the hepatic hydroxylproline, as shown in figure (4) it was significantly higher in CCl₄, COL+CCl₄ & SM+COL+CCl₄ groups as compared to normal group. Also, they were significantly lower in SM+CCl₄, COL+CCl₄ & SM+COL+CCl₄ groups as compared to CCl₄ alone treated group. Also, they were significantly higher in COL+CCl₄ & SM+COL+CCl₄ as compared to SM+CCl₄ group.

Additionally, the hepatic MDA as shown in figure (5) was significantly higher in CCl₄, SM+CCl₄, COL+CCl₄ & SM+COL+CCl₄ groups as compared to normal group. Also it was significantly lower in SM+CCl₄, COL+CCl₄ & SM+COL+CCl₄ comparing to CCl₄ alone treated group. While it was significantly higher in COL+CCl₄ & SM+COL+CCl₄ groups comparing to SM+CCl₄. Concerning the hepatic SOD, GST, GSH & CAT as shown in figure (6,7,8&9). They were significantly lower in CCl₄, SM+CCl₄, COL+CCl₄ & SM+COL+CCl₄ groups as compared to normal group. Also, they were significantly higher in SM+CCl₄, COL+CCl₄ & SM+COL+CCl₄ groups as compared to CCl₄ alone treated group. In addition, they were significantly lower in COL+CCl₄ & SM+COL+CCl₄ as compared to SM+CCl₄ group.

Additionally, the liver and spleen index as shown in figure (10) were significantly higher in all CCl₄ treated groups comparing to normal one. Also they were significantly lower in SM+CCl₄, COL+CCl₄ & SM+COL+CCl₄ groups comparing to CCl₄ alone treated group.

Table (1): physical parameters in all studied groups (x̅±SEM).

<table>
<thead>
<tr>
<th>Factor</th>
<th>Controls</th>
<th>CCl₄</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Alone</td>
</tr>
<tr>
<td>BW at beginning of experiment</td>
<td>144.60±1.93</td>
<td>162.2 ± 1.35</td>
</tr>
<tr>
<td>BW at end of experiment</td>
<td>162.20±1.94</td>
<td>154.80 ± 2.53</td>
</tr>
<tr>
<td>Liver index</td>
<td>2.68 ±0.04</td>
<td>4.01 ± 0.12</td>
</tr>
<tr>
<td>Spleen index</td>
<td>0.24 ±0.00</td>
<td>0.47 ± 0.02</td>
</tr>
</tbody>
</table>

All results are expressed as mean ± SEM
Table (2): The levels of serum (ALT, AST, TC, ALP, DB & TB), hepatic homogenate (HP, MDA, SOD, GSH, GST and CAT) of the studied subjects.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Controls</th>
<th>CCl₄</th>
<th>SM-CCl₄</th>
<th>COL-CCl₄</th>
<th>SM-COL-CCl₄</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
<th>P4</th>
<th>P5</th>
<th>P6</th>
<th>P7</th>
<th>P8</th>
<th>P9</th>
<th>P10</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC(mg/dl)</td>
<td>54.0 ± 2.85</td>
<td>113 ± 2.70</td>
<td>93.8 ± 2.70</td>
<td>58.0 ± 2.47</td>
<td>80.5 ± 2.20</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>NS</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>ALT(U/l)</td>
<td>21.60±0.96</td>
<td>70.70±1.24</td>
<td>30.40±1.86</td>
<td>50.30±3.74</td>
<td>39.00±1.23</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
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<td>&lt; 0.05</td>
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<tr>
<td>AST(U/l)</td>
<td>28.90±1.05</td>
<td>66.90±2.06</td>
<td>31.40±0.90</td>
<td>46.40±1.22</td>
<td>33.80±1.22</td>
<td>&lt; 0.05</td>
<td>NS</td>
<td>&lt; 0.05</td>
<td>NS</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>NS</td>
</tr>
<tr>
<td>ALP(U/l)</td>
<td>48.60±0.92</td>
<td>108 ±4.12</td>
<td>68.90±1.1</td>
<td>65.90±1.77</td>
<td>60.80±1.85</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
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<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>DB(mg/dl)</td>
<td>0.41±0.01</td>
<td>0.88±0.02</td>
<td>0.50±0.02</td>
<td>0.65±0.03</td>
<td>0.57±0.02</td>
<td>&lt; 0.05</td>
<td>NS</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>NS</td>
</tr>
<tr>
<td>TB(mg/dl)</td>
<td>0.65±0.02</td>
<td>1.54±0.03</td>
<td>0.77±0.02</td>
<td>0.93±0.03</td>
<td>0.84±0.02</td>
<td>&lt; 0.05</td>
<td>NS</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>NS</td>
</tr>
<tr>
<td>HP(µg/g)</td>
<td>150.2± 0.25</td>
<td>248 ± 3.15</td>
<td>159.1 ± 2.88</td>
<td>184.7 ± 3.30</td>
<td>171 ± 2.68</td>
<td>&lt; 0.05</td>
<td>NS</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
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<tr>
<td>MDA(nmol/g tissue)</td>
<td>61.24±1.86</td>
<td>132.3 ±3.87</td>
<td>73.38 ±1.45</td>
<td>97.36 ±1.86</td>
<td>85.4 ±0.95</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
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<tr>
<td>SOD(U/l)</td>
<td>8.90 ± 0.13</td>
<td>2.81 ±0.19</td>
<td>7.52 ±0.10</td>
<td>5.72 ±0.11</td>
<td>6.69 ±0.09</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
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<tr>
<td>GSH(U/l)</td>
<td>0.613±0.022</td>
<td>0.16 ±0.015</td>
<td>0.518±0.009</td>
<td>0.403±0.019</td>
<td>0.47±0.011</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
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<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>NS</td>
</tr>
<tr>
<td>CAT(U/g tissue)</td>
<td>33.29 ±0.58</td>
<td>12.74 ±0.41</td>
<td>28.22 ±1.12</td>
<td>20.39 ±0.70</td>
<td>24.69±0.82</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
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</tr>
<tr>
<td>GST (nmol/min/g)</td>
<td>145.8 ±2.02</td>
<td>73.53 ±1.44</td>
<td>130.9 ±2.71</td>
<td>88.85 ±2.04</td>
<td>111.40±1.56</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
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</tr>
</tbody>
</table>

Results are expressed as mean ± SEM. p1 for control and CCl₄, p2 for control and SM+CCl₄, p3 for control and COL+CCl₄, p4 for control and SM+COL+CCl₄, p5 for CCl₄ and SM+CCl₄, p6 for CCl₄ and COL+CCl₄, p7 for CCl₄ and SM+COL+CCl₄, p8 for SM+CCl₄ and COL+CCl₄, p9 for SM+CCl₄ and SM-COL+CCl₄, p10 for COL+CCl₄ and SM+COL+CCl₄.
Figure (1): Serum TC level

Figure (2): Serum ALT, AST & ALP enzymes.

Figure (3): Serum DB & TB.

Figure (4): Hepatic HP content.

Figure (5): Hepatic MDA content.

Figure (6): Hepatic GST enzyme.

Figure (7): Hepatic SOD enzyme activity.

Figure (8): Hepatic CAT enzyme activity.
Figure (9): Hepatic GSH.

Figure (10): liver and spleen index.

The Histopathological liver examination: Hematoxylin and Eosin (H&E) for routine histological examination will be showed in table (3).

<table>
<thead>
<tr>
<th>H&amp;E showing Fatty change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
</tr>
<tr>
<td>CCl4</td>
</tr>
<tr>
<td>SM+CCl4</td>
</tr>
<tr>
<td>COL+CCl4</td>
</tr>
<tr>
<td>SM+COL+CCl4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>H&amp;E showing necrobiosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
</tr>
<tr>
<td>CCl4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>H&amp;E showing inflammatory cells infiltration in portal area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
</tr>
<tr>
<td>CCl4</td>
</tr>
<tr>
<td>COL+CCl4</td>
</tr>
</tbody>
</table>

mean (U/l) Groups

mean (gm) liver index spleen index
Table (3): The Histopathological liver examination for fibrosis marker by H&E.

<table>
<thead>
<tr>
<th>Histopathological alteration by H&amp;E</th>
<th>Control</th>
<th>CCl4</th>
<th>SM+CCl4</th>
<th>COL+CCl4</th>
<th>SM+COL+CCl4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatty change</td>
<td>-</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Necrobiosis</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Portal infiltration reaction</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Where (+++) for severe with range 75-100%, (++) for moderate with range 50-75%, (+) for mild with range 25-50% and (-) for Nil with range 0-25%.

This study showed H&E liver staining in SM group, showed a moderate fatty change in few hepatocytes only, and so SM protect the liver from necrosis, so it is considered an anti-inflammatory drug. Also, COL group, showed a mild dilatation and congestion in central and portal veins with few inflammatory cells infiltration in the portal area, so SM protect the liver from necrosis, so it is considered an anti-inflammatory drug. Finally, the mixture of SM+COL, showed a mild fatty change in few hepatocytes.

Table (4): The Histopathological liver examination for fibrosis marker by MTC.

<table>
<thead>
<tr>
<th>Histopathological alteration by MTC</th>
<th>Control</th>
<th>CCl4</th>
<th>SM+CCl4</th>
<th>COL+CCl4</th>
<th>SM+COL+C Cl4</th>
</tr>
</thead>
</table>

This study showed MTC, in CCl4 group showed extensive accumulation of connective tissues resulting in the formation of continuous fibrotic septa, nodules of regeneration and noticeable alterations to the central veins, compared to those of the healthy controls. COL protected liver tissues, showed a reduced collagen deposition. SM only and the mixture of both COL+SM protected tissues, showed a negative collagen deposition.

2. Discussion

The liver damage produced by the administration of CCl4, was evidenced by the characteristic pattern of histological and biochemical alterations. Both COL & SM significantly prevented the serum, liver homogenates & histological alterations induced by CCl4. The presence of LF was evidenced by histological and biochemical determinations in liver tissues. COL given at the dose of 0.1mg/kg rat 'day' along with CCl4 partially inhibits collagen synthesis. COL has an antifibrogenic effect and significantly reduced the amount of collagen as compared to that found in rats receiving CCl4 only. Also, SM co-treatment partially prevents CCl4 induced LF.
Hydroxyproline levels in tissue hydrolysates are a direct measure of the amount of collagen present (Colgrave et al., 2012). The present study showed a significantly increased hepatic HP content in the (CCL₄, COL+CCl₄ & SM+COL+CCl₄) groups when compared with the control group. This study was in agreement with those of (Yang et al., 2012) whom reported that increased expression of hepatic HP is another liver index that represents the degree of LF. Also, the present study showed a significantly decreased hepatic HP content in the (SM, COL and the mixture of SM & COL) groups when compared with the CCL₄ group. This study was in agreement with (Li et al., 2011).

Our data revealed that CCl₄ treatment significantly increased levels of MDA and decreased levels of SOD, CAT, GSH & GST activities in liver tissues. These results were similar to the previous reports (Breikaa et al., 2013). Administration of COL or SM also prevented the increase in liver peroxidation caused by CCl₄. Lipid peroxidation is one of the primary events of CCl₄ induced liver damage (Hernandez-Gea and Friedman, 2011). The changes produced by CCl₄, in the plasma membrane structure and stability are associated with alterations in its lipid composition and these changes are followed by the increases in lipid peroxidations produced by its free radical metabolites. The total protection against MDA increase could be an effect of COL on plasma membrane of the hepatocytes.

The overproduction of ROS in hepatocytes may cause cell death by damaging DNA, proteins, lipids and carbohydrates (Khan and Ahmed, 2009). The imbalance between the production of ROS and antioxidant defense causes oxidative stress (OS), leading to significant physiological challenges. Hepatic damage induced by CCl₄ is associated with OS due to CCl₄ induced FR production (Wang et al., 2011). This study was in agreement with (Nagata et al., 2007) who reported that the mechanism of FR damage included ROS induced peroxidation of the polyunsaturated fatty acid, causing further oxidation of membrane, lipids and proteins. This study was in agreement with (Khan et al., 2009) who reported that result showed significant reduction in GSH contents as well as significant depletion in the activity of phase II metabolizing enzymes; GST & GSH (Gumieniczek, 2005) and have an agreement with investigation following CCl₄ intoxication (Manna et al., 2007). SOD is known to be reduced markedly in CCl₄ induced hepatic damage (Chen et al., 2007) while OS could be ameliorated via the elevation of hepatic SOD level (Tirkey et al., 2005). This study was in agreement with (Kiruthiga et al., 2010) who reported that administration of SM significantly protected SOD, CAT, GSH & GST activities by directly scavenging ROS which in turn lowering serum cholesterol and lipid peroxide. There is no doubt that SM has antioxidant like activity and this could be due to the presence of various flavonoids, as reported with (Xiao-hui et al., 1997).

This study showed H&E liver staining in a control group of rats showed a normal architecture with both central and portal veins. Also, H&E for liver examination of CCl₄ exposed rats resulted in moderate necrosis in hepatic parenchyma; severe fatty changes; mild dilatation in central and portal veins as well as inflammatory cells infiltration; fibrosis and degenerative changes in the portal area. These results are in agreement with (Turkdogan et al., 2003).

In conclusion, our findings indicate that SM & COL drugs have potent antifibrotic activities. These results were in agreement with (Kershenobich et al., 1988) who reported that COL is thought to act on collagen accumulation in two ways; the first an inhibition of the cellular secretion of procollagen leading to its intracellular
accumulation, the second a stimulation of collagenase activity. Our findings also indicate that SM and/or COL may be useful in the protection and prevention of hepatic toxicity in CCl₄ treated rats, recovered enzyme activities in the liver (decreased hepatic damage), improved cellular injuries & also have potent antioxidant activities that might protect the liver and improve the symptoms of liver injuries by scavenging the ROS to overcome the oxidative damage caused by CCl₄ in artificially induced hepatic injury.

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دراسة مقارنة التأثير الوقائي لكل من السيليمارين والكولوشينس في تليف الكبد المحدث

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محتوى

1. مقدمة
2. جمع البيانات
3. نتائج
4. استنتاج

يتناول هذا البحث دراسة التأثير الوقائي لكل من السيليمارين والكولوشينس في تليف الكبد المحدث، والدرجات المؤكدة الناجح عن حقن رابع كودريل الكربون مقارنة بالعملاء الضاربة من البكاء، وتم قياس بعض العوامل مثل العامل الفيزيائي وتعلم زمن السم، ومعاك الفيد، ومعاك السلال العامل الكيميائي (اختبارات على المصل) وتم إزاحة الآل عين أمينتيا الامب، البروتينات أمينتيا الامب، الفوسفات الفي، البلازمو الكلي، والبلازمو الغير مباشر والكولسترول الكلي، وميارات إحباط على جنس وتمبل مؤشرات الإحماء الهليت جامعون منتجات تليف الكبد المحدث.

أجريت الأبحاث على خمسة وخمسين من إناث الجرذان تتراوح أوزانهن من 140 إلى 180 جرام وفسمت إلى خمسة كما يلي: 1. المجموعة الأولى: تتكون من إناث الجرذان التي تمثل المجموعة الضاربة 2. المجموعة الثانية: تتكون من إناث الجرذان التي تم حقنها رابع كودريل الكربون في الخصائص البيروتينية مرتين أسبوعياً 3. المجموعة الثالثة: تتكون من إناث الجرذان التي تم حقنها رابع كودريل الكربون (0.00 مجم/كم بطرق الفم) مرة يوماً، ثم تم حقنها رابع كودريل الكربون في الخصائص البيروتينية مرتين أسبوعياً 4. المجموعة الرابعة: تتكون من إناث الجرذان التي تم حقنها ب الخليط من السيليمارين والكولوشينس عن طريق الفم مرة يوماً لمدة أربعة أسابيع، ثم تم حقنها رابع كودريل الكربون.

أوضحت النتائج التالية بعد مرور أربعة أسابيع:

1. رابع كودريل الكربون أحدث إفراضاً محسسًا بوصفه الكبد كليًا ذا دالة إحساسية مقارنة بالجموعة الضاربة، بينما الكولوشينس حس الكبد من التليف المحدث، بينما السيليمارين والكولوشينس أحدث إفراضاً لكنه أفضل من الكولوشينس بصرد، لكن السيليمارين أحدث إفراضاً محسّةً ذا دالة إحساسية.

2. رابع كودريل الكربون أحدث إفراضاً محسسًا بوصفه الكبد كليًا ذا دالة إحساسية، بينما الكولوشينس حس الكبد من التليف المحدث، بينما السيليمارين والكولوشينس أحدث إفراضاً لكنه أفضل من الكولوشينس بصرد، بينما السيليمارين أحدث إفراضاً محسّةً ذا دالة إحساسية.

3. رابع كودريل الكربون أحدث إفراضاً محسسًا بوصفه الكبد كليًا ذا دالة إحساسية، بينما الكولوشينس حس الكبد من التليف المحدث، بينما السيليمارين والكولوشينس أحدث إفراضاً لكنه أفضل من الكولوشينس بصرد، بينما السيليمارين أحدث إفراضاً محسّةً ذا دالة إحساسية.

4. رابع كودريل الكربون أحدث إفراضاً محسسًا بوصفه الكبد كليًا ذا دالة إحساسية، بينما السيليمارين والكولوشينس أحدث إفراضاً لكنه أفضل من الكولوشينس بصرد، بينما السيليمارين أحدث إفراضاً محسّةً ذا دالة إحساسية.

أتطلع أن تتزايد الأبحاث المستقبلية والبحثات الدقيقة في هذا المجال، والإنتاج داخل أسامة الكبد، بينما السيليمارين بصرد، وال reklas الكولوشينس كلاماً ادحاً إنفاضاً بعد الخلايا الميغية والعلاج باختيار الدواء المثلى.