Protective and therapeutic Effects of Fucoidan, brown algae extract, against Diclofenac sodium hepatonephrotoxicity in rat

By

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SUMMARY

Fifty male Sprague-Dawley rats were equally divided randomly into five groups to assess the protective and therapeutic effects of fucoidan against diclofenac sodium induced hepatonephrotoxicity. Elevated serum enzyme, increase expression of TLR4, massive hepatic necrosis, fibrosis, calcified mitochondria besides nephritis and coagulative necrosis of renal epithelium were noticed in rats intramuscularly (IM) injected with diclofenac sodium (50mg/ kg. B. wt.). Fucoidan administration prior and simultaneously with diclofenac sodium ameliorated the induced hepatonephropathy. It lowered the serum enzymes and malondialdehyde (MDA) formation besides restoring the normal histological structure. Fucoidan (therapeutic trials) slightly ameliorated the effects previously induced by diclofenac sodium when compared with the protective trial. TLR4 mRNA expression, measured by reverse transcriptase polymerase chain reaction (RT-PCR), was significantly decreased in the rat's liver of the protective and therapeutic groups when compared with the diclofenac sodium treated group. In conclusion, our finding proved that fucoidan administration prior and simultaneously or after diclofenac sodium induced a protective and therapeutic effects. Moreover, it reduced the hepatorenal damage through scavenging oxidative stressors and down regulating the pro-inflammatory cytokines and TLR4.

Key words: fucoidan, diclofenac sodium, protection and therapy, serum profile, nephrohepatopathy, TEM.

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INTRODUCTION

Brown seaweeds have been the mainstay of the Japanese diet and have been documented in traditional Chinese medicine for over 1000 years (McLellan and Jurd, 1992). Brown seaweeds produce different polysaccharides, namely alginates, laminarans and fucoidans (Lee et al., 2008 and Painter, 1983). Fucoidan is cell wall polysaccharide composed of variable amounts of L-fructose, uronic acids, galactose, xylose and sulfate esters. (Lee et al., 2004 and Quanbin et al., 2003). Fucoidans have anticoagulant (Chevolot et al., 2001), anti-thrombogenic, anti-tumor (Thompson and Dragar, 2004 and Maruyama et al., 2006), antiviral (Thompson and Dragar, 2004), anti-inflammatory (Cumashi et al., 2007), and antioxidant effect besides immunomodulating activities (Jung So et al., 2007 and Zhao et al., 2007). Few studies have reported the effect of fucoidan on pro- and anti-inflammatory cytokines (Irhimeh et al., 2007). The anti-inflammatory effect of fucoidan is attributed to preventing leukocytic migration, anti-complement effect and anti-proliferation effect on smooth muscle cells (Quanbin et al., 2003 and Yang et al., 2006). Administration of fucoidan increased the activities of antioxidant enzymes and glutathione levels, thus decreased reactive oxygen species, hydroxyl and peroxyl radicals besides mitochondrial swelling (Veena et al., 2008 and Yang et al., 2006).

Anti-inflammatory drugs are traditionally classified into steroidal and non steroidal (NSAIDs) (Lee and Katayama, 1992 and Villa et al., 2006). NSAIDs primarily inhibit prostaglandin synthesis by inhibiting COX isoenzyme-metabolism of arachidonic acid resulting in decreased inflammation and pain (Okulik and Jubert 2006). Diclofenac sodium is a lipophilic and weakly acidic compound that has analgesic, anti-inflammatory, antirheumatic and antipyretic properties (Boelsterl, 2003 and Miwa et al., 1997). Toxicity induced by diclofenac sodium resulted in mitochondrial dysfunction and depletion of ATP, GSH, lipid peroxidation and change in calcium concentration in liver and kidney cells (Galati et al., 2002 and O’connor et al., 2003). The production of active diclofenac sodium metabolites in liver induced direct cytotoxicity, generation of reactive oxygen species, mitochondrial swelling and oxidation of NADPH (O’connor et al., 2003). Mitochondrial injury, apoptosis and / or necrosis and liver damage associated with diclofenac sodium was suggested to be based on peroxidase-catalyzed production of NSAID radicals which resulted in oxidized GSH.
and NADPH (Galati et al., 2002). The aforementioned mechanisms resulted in proliferation of bile ducts, hepatocellular degeneration and non-specific hepatitis with portal and lobular activity in diclofenac toxicity (Bort et al., 1991 and Gabry et al., 1999).

Toll-like receptors (TLRs) are expressed on the surface of the dendritic cells, macrophages and intestinal epithelial cells. TLRs recognize conserved microbial structural molecules and induce innate immune response that is essential for host defense against invading microbial pathogens (Takeda and Akira, 2005; Medzhitov, 2001 and Rhee and Hwang, 2000). Broadly, TLRs can activate two branches of downstream signaling pathways: MyD88-dependent and MyD88-independent pathways (Takeda and Akira, 2005). The activation of MyD88-dependent signaling pathway leads to the induction of inflammatory gene products including cytokines and cyclooxygenase-2 (COX-2) (Rhee and Hwang, 2000). Moreover activation of the TLR4 induces specific signaling pathways that lead to the liberation of nuclear factor- kappa beta (NF-k β) and activation of pro-inflammatory cytokine transcription such as IL-1, IL-6 and TNF-α (Mc Gavin and Zachary, 2007). The present study was conducted to evaluate the efficacy of fucoidan to ameliorate the diclofenac sodium hepatonephrotoxicosis by assessing the induced lesions, using light and transmission electron microscopy, biochemical alterations and TLR4-expression.

MATERIALS AND METHODS
2.1. Experimental animals and design:
Fifty male Sprague-Dawley rats (200-250 g) were purchased from the Animal Research House of Holding Company for Biological Products & Vaccines, Agoza, Giza, Egypt. The rats were divided into 5 equal groups which were separately housed in five clear polycarbonate cages. They were provided with a standard animal diet and water ad libitum. All experiments were performed in accordance with protocols approved by the Animal Care and Use Committee of Mansoura University (Egypt). Gp. (1) was the control. Gp. (2) was orally given fucoidan (200 mg/kg. B.wt.) for 21 days. Gp. (3) was IM injected with diclofenac sodium (50mg/kg. B.wt.) twice weekly for 21 days. Gp. (4) (protective) was daily orally given fucoidan (200 mg/kg. B.wt.) for 42 days. From the beginning of the 22nd day, the rats were IM. injected with diclofenac sodium (50mg/kg. B.wt.) twice weekly for 21 days, 2 hours after fucoidan treatment. Gp. (5) (therapeutic) was IM injected with diclofenac sodium (50 mg/
kg. B. wt.) twice weekly for 21 days and then fucoidan (200 mg/kg. B.wt.) was orally given for other 21 successive days.

2.2. Chemicals:
Diclofenac sodium (dechlorphen) ampoules (75 mg/3 ml) were purchased from Pharco Pharmaceutical Co. Alexandria, Egypt. Fucoidan powder was purchased from Sigma Chemical, Co. Ltd. (St. Louis, MO, USA). The chemicals were stored under proper conditions according to Sigma instructions.

2.3. Assay of serum enzymes
Blood and sera-samples were obtained from the tail vein at the end of the experiment. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were evaluated by using commercial test kits (Randox Laboratories LTD Co., UK.) according to Reitman and Frankel (1957). Creatinine and urea were evaluated by using kits provided by Colorimetric Randox, UK. MDA (Bioxytech Oxis International, Inc) according to Satoh (1978).

2.4. RNA extraction and RT-PCR analysis for TLR4:
Total RNA was isolated from rat livers using the acid guanidinium thiocyanate-phenol-chloroform extraction methods (Chomczynski and Sacchi). Briefly, Five mg RNA from each liver sample was subjected to reverse transcription using moloney murine leukemia virus reverse transcriptase in a 50-ml reaction volume. Aliquots of the reverse transcription mix were used for PCR amplification of the fragments specific for Toll-like receptor-4 (TLR4) using the primer pairs listed in table (1) for Toll-like receptor 4 (TLR4). The primer was obtained from metabion international AG, Lend-Christ-Strasse 44\,I, Martinsried \,Deutschland. The identities of the resulting PCR products were confirmed by sequence analysis. The PCR products were run on a 2% agarose gel, recorded on a Polaroid film, and the bands were quantitated by densitometry.

Table (1): Primer sequence for RT-PCR analysis.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Primer sequence</th>
<th>Length (bp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLR4</td>
<td>Sense 5' TGC TGC CAA CATCAT CCA 3'</td>
<td>304</td>
</tr>
<tr>
<td></td>
<td>Antisense 5' TTT TCC ATC CAA CAG GGC TTT T 3'</td>
<td></td>
</tr>
</tbody>
</table>
2.5- Pathological Examinations
All animals were humanely sacrificed at the end of experiment. Liver and kidney- specimens were collected for histopathological examination. Specimens were immediately fixed in neutral buffered formalin and 5µ thick paraffin sections were prepared, stained with hematoxylin and eosin, and Masson Trichrome (Bancroff et al., 1990). The stained sections were blindly microscopically examined by two experts.

2.6- Transmission Electron Microscopy (TEM):
Two specimens (size, about 1 mm³ each) were freshly collected from the left hepatic lobe, fixed in 5% glutaraldehyde and post-fixed in 1% osmium tetroxide. The specimens were dehydrated in graded acetone and finally embedded in epon 812. Semi-thin sections, 0.5-1µ thick, were prepared from blocks, using LKB ultra microtome, The sections were stained by toluidine blue, examined by light microscope and regions for preparation of ultrathin sections were oriented. Ultrathin sections (500-800 Å) were made using Leica ultramictotome and fixed on copper grids (200µ meshes). Ultrathin sections were stained in uranyl acetate and lead citrate. Sections were transmitted in a Jeol, CX11 transmission electron microscope n EM Unit, of Assiut University and photographed.

2.7- Statistics
Statistical analyses of the biochemical data were done by the Mann–Whitney U-test. P < 0.005. It was accepted as a statistically significant value.

RESULTS
3.1- Evaluation of liver and kidney function using biochemical parameters:
The serum biochemical analyses of Gps (1 & 2) were apparently normal. Fucoidan significantly decreased the serum transaminases, urea & creatinine in Gps (4&5), when compared with Gp (3) as shown in table (1). Gp. (4) showed significantly decreased levels of serum biochemical parameters, when compared with gp. (5).

3.2. Fucoidan significantly decreased lipid peroxidation
Our results showed a significantly increased MDA in rats of gp (3) when compared with gp. (1). It was significantly decreased in gps (4&5) when compared with gp (3).

3.3. Effect of fucoidan and diclofenac sodium on TLR4 mRNA expression
Rats of gp (3) showed increased mRNA expression of TLR4 (30.2 ng) when compared with gp. 4 (23.7 ng), and gp 5 (24.4 ng) (Fig. 1).

3.4- Effect of pre-, simultaneous
and post-fucoidan administration on hepatic and renal lesions, induced by diclofenac sodium.

Macroscopically, the liver (gp 3) was enlarged and showed multiple scattered dark foci on their surfaces (Fig: 2). Microscopically, periportal necrosis with round cell infiltration besides, hyperplastic epithelial lining of the bile ducts and newly formed bile ductules were seen (Fig 3). The liver showed severe congestion of the hepatic sinusoids with hypertrophic Von kupffer cells containing dark brown pigments, The hepatocytes showed hydropic degeneration and steatosis with dysplasia and massive coagulative necrosis (Fig: 4). Moreover, the portal veins were congested. Perihepatitis, interlobular fibrosis or intralobular fibrosis were stained blue with Masson's Trichrome stain (Fig: 5). The Kidneys were small in size with scattered necrotic foci on their surfaces. Microscopically, coagulative necrosis of renal tubular epithelium was surrounded with round cells besides congested blood vessels, particularly at the corticomedullary junction (Fig 6). Moderate interstitial fibrosis and membranoproliferative glomerulonephritis were noticed.

Macroscopically, liver (gp 4) was of normal size and consistency besides being slightly darker in color. Microscopically, the liver showed mild degenerative changes and few round cells infiltration in the portal areas (Fig: 7). Hypertrophic Von kupffer cells and slightly congested central veins and hepatic sinusoids were seen. The kidneys showed few degenerative changes of the epithelial lining of some renal tubules (Fig: 8). On the other hand the livers of rats (gp.4) showed less severe lesions than those observed in gp.(3). Such lesions were focal coagulative necrosis infiltrated with round cells besides hemorrhage, degenerative changes and congested hepatic sinusoids and central veins (Fig: 9). The portal areas showed fibroblastic proliferation, hyperplastic epithelial lining of the bile ducts, brown pigments and round cell-infiltration (Fig:10). The kidneys of gp (5) showed degenerative and necrotic changes of the renal epithelial lining, interstitial round cell-infiltration and congestion besides cystic dilatation of some renal tubules (Fig: 11).

5.3. Semi thin, toluidine blue stained sections and TEM changes

Semi thin, toluidine blue stained sections of gp. (3) showed marked hepatic steatosis represented by numerous fat globules in the hepatic cells (Fig: 12), while gp. (4) showed few fat globules in some hepatic cells with active kup-
pfer cells in the hepatic sinusoids (Fig 13). Moreover, gp. (5) showed hepatic degenerative changes with active Von Kupffer cells in hepatic sinusoid (Fig: 14). TEM of gp. (3) showed electron dense mitochondria (calcified), fat globules and marked depletion of glycogen (Figs: 15-17). Gp (4) showed mild depletion of glycogen granules with presence of few fat globules (Fig: 18). Gp (5) showed marked hepatic glycogen-depletion, dilation of the bile canaliculi and blocked hepatic sinusoids with fat storing cells and active Von Kupffer. Other hepatocytes showed pyknosis with destructed cell organelles (Fig 62).

Legends

Fig (1): Semiquantitative analysis of electrophoretic pattern of TLR4 RT-PCR assay where lane +ve C (+ve control for TLR4), lane –ve C (-ve control for TLR4), lane 1 (gp.4), lane 2 (gp.3), and lane 3(gp.5) besides M: molecular weight marker = 100 bp DNA ladder.

Fig (2): Liver (gp.3) showing multifocal necrotic foci (arrows)

Fig (3): Liver (gp.3) showing hyperplastic epithelial lining of bile duct (arrowhead), newly formed ductules and periportal hepatic necrosis (arrow).

Fig (4): Liver (gp.3) showing congested sinusoids, steatosis (arrow) and necrosis of hepatocytes (arrowhead)

Fig (5): Liver-portal tract (gp.3) showing blue-stained proliferated fibrous tissue (B) with Masson Trichrome

Fig (6): kidney (gp.3) showing coagulative necrosis of renal epithelium (thin arrow) besides interstitial round cell infiltration (thick arrow)

Fig (7): Liver (gp.4) showing moderately vacuolated hepatocytes.

Fig (8): kidney (gp.4) showing cloudy swelling of renal tubular epithelium and moderate crescentic hyperplasia of the parietal layer of Bowman's capsule.

Fig (9): Liver (gp.5) showing focal hemorrhage (H).

Fig (10): portal tract (gp.5) showing hyperplasia of biliary epithelium (thick arrow), fibroblastic proliferation, brown pigments (thin arrow) and few mononuclears (arrowhead).

Fig (11): kidney (gp.5) showing degeneration (D) and necrosis (N) of renal epithelium besides round cell infiltration (R).

Fig (12) Semithin section, liver (gp.3) showing fatty change represented by numerous fat globules in the hepatic cells (yellow arrow). Toluidine blue.
Fig: (13) Semithin section, liver (gp.4) showing mild degenerative changes in hepatic cells with activation of sinusoidal kupffer's cells. Toluidine blue. 100 X.

Fig: (14) Semithin section, liver (gp.5) showing few fat globules in some hepatic cells, with active kupffer's cells in the hepatic sinusoids. Toluidine blue. 100 X.

Fig: (15) TEM of liver(gp.3) showing hepatocytes overloaded with large numerous fat globules. Mag. 11000 X.

Fig: (16) TEM of liver(gp.3) showing bundles of collagen fibers among hepatocytes. Mag. 11000 X

Fig: (17) TEM of liver(gp.3) showing marked depletion of glycogen with hydropic degeneration. Mag. 8800 X.

Fig: (18) TEM of liver(gp.4) showing apparently normal hepatic cell (N) with its characteristic nucleus and other cell organelles and mild depletion of glycogen granules with presence of kupffer's cells and fat storing cell. Mag. 6000 X.

Fig: (19) TEM of liver (gp.5) showing a bundle of collagen fibers among hepatic cells with marked depletion of glycogen granules. Mag. 8800 X.
Table (1) Some serum biochemical parameters of liver and kidney function tests and lipid peroxidation (means ± SE) in gps (1-4). Gp.5 ?

<table>
<thead>
<tr>
<th>Parameters</th>
<th>ALT U/L</th>
<th>AST U/L</th>
<th>Urea mg/dl</th>
<th>Creatinine mg/dl</th>
<th>MDA nmol/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20.4a ±1.82</td>
<td>28.24a ±2.48</td>
<td>13.9a ±1.01</td>
<td>0.82a ±0.10</td>
<td>14.1a ±0.92</td>
</tr>
<tr>
<td>2</td>
<td>22.1a ±1.98</td>
<td>26.24a ±3.45</td>
<td>12.95a±1.15</td>
<td>0.78a ±0.11</td>
<td>13.18a ±0.98</td>
</tr>
<tr>
<td>3</td>
<td>65.8d ±4.21</td>
<td>94.75d ±7.21</td>
<td>24.1c ±1.85</td>
<td>1.15b ±0.13</td>
<td>23.4b ±2.01</td>
</tr>
<tr>
<td>4</td>
<td>35.2b ±2.99</td>
<td>45.4b ±3.45</td>
<td>16.9b ±1.55</td>
<td>0.84a ±0.12</td>
<td>16.2a ±1.46</td>
</tr>
<tr>
<td>5</td>
<td>41.8c ±2.95</td>
<td>59.8c ±3.21</td>
<td>18.2b ±1.72</td>
<td>0.88a ±0.11</td>
<td>15.8a ±1.32</td>
</tr>
</tbody>
</table>
DISCUSSION

The current investigation showed that fucoidan protected and partially ameliorated the adverse effects of NSAIDs through scavenging the oxidative stress and down regulating the TLR4 and pro-inflammatory cytokines. NSAIDs cause morbidity worldwide. The most commonly used pharmaceutical products contribute to the morbidity rate, consequently, there is a need for some bioactive alternatives to subside the adverse effects of NSAIDs (Choi et al., 2010). Our results showed that IM injection of Diclofenac sodium increased the liver transaminases, MDA, serum urea and creatinine. The aforementioned results are sequelae of the hepatic and renal degenerative changes, necrosis, leukocytic infiltration and fibrosis. Our results are in accordance with Gabry et al.(1999), Aydin et al. (2003) and Taib et al.(2004). Diclofenac sodium is metabolized in liver through ring hydroxylation, catalyzed by cytochrome isoenzymes to the major oxidative metabolite, 4'-hydroxydiclofen (4'-OH) (Stierlin and Faigle, 1979). Recently, the in vitro studies showed that the mechanism of diclofenac toxicity is related to impairment of ATP synthesis by mitochondria, and production of active metabolites, particularly n,5-dihydroxydiclofenac, which resulted in direct cytotoxicity, generation of reactive oxygen species, mitochondrial swelling and oxidation of nicotinamide adenine dinucleotide phosphate (NADPH) (O’connor et al., 2003). So the toxic effect of diclofenac on hepatocytes is due to induction of mitochondrial impairment, together with a futile consumption of NADPH (Bort et al., 1999). The semi thin section and TEM examination of liver of rat, given diclofenac sodium, showed numerous fat globules, glycogen depletion and calcified mitochondria. Mitochondrial changes could be due to the effect of diclofenac metabolites on the mitochondrial inner membrane, uncoupling of respiration by proton shuttling and opening of the mitochondrial membrane permeability transition pore resulted in decreased mitochondrial transmembrane potential which led to depletion of ATP synthesis (Masubuchi et al., 1998, Moreno-Sanchez et al., 1999, Masubuchi et al., 2002 and Boelsterli 2003). The interlobular and intralobular fibrosis could be attributed to generation of reactive oxygen species. Our results are in agreement with He et al., (2006) who mentioned that oxidative stress is relevant to the formation of fibrosis in most chronic liver diseases accompanied by decline of antioxidant abilities. The decline of GSH and accumulation of lipid peroxidation have a key role.
in pathogenesis of liver diseases.

Seaweeds have been widely used as a food source and in medicine because it's well-balanced natural source of trace elements and harmless, as Fucoidan. The latter is sulfated polysaccharides of brown algae. It contains L-fucose residues as the main sugar constituent along with sulfate esters. Fucoidan has many biological activities (anti-coagulant, anti-thrombosis, anti-inflammatory, anti-liver failure, anti-viral and anti-tumor activities) (Thompson and Dragar, 2004, Maruyama et al., 2006 and Chevolot et al., 2001). However, few studies have reported the modulatory effect of fucoidan on pro- and anti-inflammatory cytokines (Irhimeh et al., 2007). The present investigation showed that the pathological and serum biochemical parameters of rats, given fucoidan, almost regained its normal levels. Our results are in harmony with Li et al., (2005) who mentioned that fucoidan didn't induce any side effects in rats, given the standard doses.

On the other hand, the lesions, TEM changes, and serum biochemical parameters of gp (4) were improved, when compared with gp (3). Our results are in agreement with Quanbin et al., (2003), Zhang et al., (2003), Jin Heo et al., (2005), Raghavendran et al., (2005) and Yang et al., (2006) who reported that the antioxidant activity of fucoidan is attributed to its efficacy in scavenging hydroxyl and peroxyl radicals as well as peroxynitrite ions and blocking the activated protein-1 (AP-1) in activated macrophages besides strong inhibition of DNA damage and lipid peroxidation. Moreover, the anti-inflammatory effect of fucoidan is attributed to prevention of leukocytic emigration, anticomplement effect and anti-proliferative effects on smooth muscle cells. Our results suggest that fucoidan has protective effects against diclofenac toxicity in rat. On the other hand, the liver and kidney function test parameters, MDA, RTPCR of TLR4, lesions and TEM changes were more increased in gp (5) than gp(4), indicating a weak therapeutic effect of fucoidan than being protective. Our results are in agreement with He et al. (2006) who mentioned that the oxidative stress accompanied by decline of the antioxidant abilities, is relevant to fibrosis in most liver diseases. Quite unexpectedly, the hepatic stellate cells appeared to be involved in the hepatic immune response, since they expressed TLRs and activation of the NF-κB (expression of mRNA of TLR4 increased in GPV) resulted in increased cytokine production (Kisseleva et al., 2009). Dilatation
of bile canaliculi in TEM of GPV is due to covalent interactions of acyl glucuronides, produced with target proteins in proximal biliary tree as a result of high local concentration of metabolite, alkaline pH of bile and abundant expression of target proteins at canalicular membrane, facing lumen. Moreover, diclofenac administration to rats decreased the activity of a number of canalicular membrane proteins (Boelsterli, 2003).

The higher expression of m RNA of TLR4 in gp. (3) more than gps. (4&5) indicates that the highest formation of pro-inflammatory cytokines was in gp. (3) and the lowest in gp. (4). Our results are in agreement with Boelsterli (2003) and Mcgavin and Zachary (2007) who mentioned that kupffer cells are activated through the TLR4, expressed on their cell-surface. Intracellular signal- transduction-pathways are activated upon activation of the TLR4 in addition to diclofenac activated NF-k β and AP-1 activation. The highly activated NF-k β is translocated into the nucleus to increase the transcriptional factor formation, as pro-inflammatory IL-1, IL-6 and TNF-α that mediate the inflammatory response. the lower expression of m RNA of TLR4 in gp. (4) than gp. (5) indicates that the protective effect of fucoidan against diclofenac toxicity is better than its therapeutic effect in rats. It could be concluded that the oral administration of fucoidan induced a protective effect against the side-effects of diclofenac sodium. Meanwhile the treatment trials showed moderate improvement of hepatic and renal function-parameters.

REFERENCE


Masubuchi, Y.; Saito, H. and Horie, T. (1998): “Structural requirements for the hepato-


791.


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التأثر الواقئ و العلاج للفيوكودان (مستخلص الطحالب البنية) ضد لئسم الكبد و الكلوى بديكلوفيناك الصوديوم في الجزائر

أحمد السيد النجار و حسین سعد حسين
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الملخص العربي
في هذه الدراسة تم استخدام خمسون فأرا (200 إلى 250 جرام) قسمت بالتساوي إلى 5 مجموعات لدراسة التأثير العلاجي و الواقئ للفيوكودان ضد لئسم الكبد والكلي والكلي الناتج عن ديكليوفيناك الصوديوم. وقد تم استخدام الخصوص البياثولوجي بالميكروسكوب الضوئي والإلكتروني وكذلك قياس إنزيمات الكبد والكلي وتفاعل البلمرة المتسلسل لقياس مدى فاعلية استخدام الفيوكودان في الوقاية والعلاج من الآثار الجانبية لاستخدام ديكليوفيناك الصوديوم. وقد لوحظ في المجموعة التي حققت ديكليوفيناك الصوديوم زيادة في إنزيمات الكبد والكلي و كذلك proinflammatory cytokine(نحثة في العوامل المحفزة للالتهاب) وزيادة في العوامل المحفزة للالتهاب وتفاقم تكثيف ونخرية في الكبد. كما أظهر الفحص بالميكروسكوب الإلكتروني للميتوكوندريا في خلايا الكبد أنها متبللة وكاسية. وكاسية الشكل هذا إلى جانب نفاد الجليقوجين، والتلف وزيادة نشاط وتضخم خلية أيتو والخلية المتميزة المناعية الساكنة للكبد والكلي وزيادة في النسيج الليفي في الكبد. ومن ناحية أخرى وجد أن استخدام الفوكودان قبل أو أثناء حقن ديكليوفيناك الصوديوم أدى إلى تحسن في أنسجة الفقاران، وظائف إنزيمات الكبد والكلي و كذلك الميلانودين ونقص في العوامل المحفزة للالتهاب في المجموعة الحامية والعلاجية. كما أوضحت الدراسة أن الدور الوقائي للملعقة المستخلصة من الأعشاب البحرية (الفوكودان) أقوى كثيراً من دورها العلاجي في تخفيف حدة الآثار الناجمة عن التسمم بديكلوفيناك الصوديوم.

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