Effects of *Aloe woodii* gel methanolic extract on the liver function changes induced by high sugar intake in female albino rats

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Abstract

Consuming sugar-added foods and sweetened beverages is being a familiar habit associated with many diseases. Folk information in Yemen indicates the therapeutic effects of *Aloe woodii* on some diseases. So, the aim of this study is to evaluate the ameliorated effect of *Aloe woodii* gel extract on liver lesions in female rats induced by high table sugar intake. This study lasted 11 weeks and was divided into two periods. The first period was for high table sugar supplement, whereas the second was for the treatment by the methanolic extract of *Aloe woodii* gel. At the end of the experiment, body weights were recorded, blood samples were taken, and liver samples were also taken for the histopathological examination supported by quantitative measurement. Results: There was no remarked change in the body weights between groups, but there was an accumulation of the visceral fat and an elevated of alanine aminotransferase (ALT) level in the sugar group. Histopathological examination of liver tissues in the sugar group revealed many degenerated manners such as vacuolation and/or ballooning of hepatocytes and inflammation. However, the treatment by *Aloe woodii* gel led to an ameliorate of the histopathological changes, but had no effect on ALT level. Conclusion: High sugar supplement induced high visceral fat accumulation and many lesions in liver tissue, whereas *Aloe woodii* treatment ameliorated these effects.

Keywords: Table sugar, *Aloe woodii*, liver, quantitative analysis, ballooned hepatocyte.

Introduction

Table sugar, sucrose C\(_{12}\)H\(_{22}\)O\(_{11}\), is a disaccharide molecule formed by 50% fructose and 50% glucose that are bonded via glycosidic linkage (73). Table sugar is produced in plants then it is refined (18). After absorption, the metabolism of glucose and fructose follows different pathways in which glucose can be used directly by the cells to produce energy in a variety of organs, while the excess of it is converted to glycogen in the liver. However, fructose is primarily metabolized in the liver, which takes up at least 50% of the initial fructose flux, and is processed by the liver into citrates, aldehydes, and for the most part, into lipid droplets (65).

In the last decades, the consumption of added and free sugars is increased, so there is attention to this spot as an environmental driver for obesity (41). When large amounts of refined food that contains high percentages of sucrose are consumed, beneficial nutrients may be deported from the diet that can contribute to an increase of chronic diseases risk and the development of metabolic syndrome (23). Sugar added to foods and drinks adds extensive calories without any benefits, but it may aggravate the metabolic complications in different tissues (4). There are some obtained results from the experimental models confirming that the consumption of sugar-added foods is associated with increased risk for obesity (66), cardiovascular diseases (41, 78), metabolic disorders (44), non-alcoholic fatty liver disease (NAFLD) (2, 42), cognitive decline (69) and kidney disease (67).

Meanwhile, the use of diets with high amounts of simple carbohydrates results in a reduction of the antioxidants reserves (8, 34). In addition, it has been found that cancer cells readily utilize fructose to support proliferation, especially fructose which is use for nucleic acid synthesis (37). Also, because of the preferred entry of fructose into lipogenesis, an increased intake of sucrose has...
Effects of Aloe woodii gel methanolic extract on the liver function…… Bushra Y. H. Al-Khatib

been shown to induce hyperlipidemia in humans and rodents (16, 52, 62). Additionally, when the amount of ingested carbohydrate exceeds the total calorie needs, the rate of de novo hepatic lipogenesis increases by 10 times (1, 72). Further, fructose has a main role in the development of abnormalities changes in obese patients with NAFLD because it can induce adipose tissue creation that is related to insulin resistance (38). In addition, there are many pathohistological changes of the liver which associated fat and sugar enriched diet such as steatosis, lobular inflammation, hepatocyte ballooning, and portal inflammation (20).

Aloes belong to Aloaceae family and there are at least 600 known species of aloes all over world. In Yemen, the total number of aloes species is 26, half of them is endemic (13 species) (50). Many of aloes species have been used as botanical medicines in many countries since centuries (24, 26, 61). Although the genus Aloe has many species, few, such as A. vera and Aloe ferox, are globally used for commercial purposes (54). A. vera, especially, is the most popular and commercial aloe, so it has a high interest in the research field (29).

All Aloes species are leaf-succulent xerophytes (49) that developed water storage tissue (76), so most aloes have thick and fleshy leaves (48) with an inner parenchyma called aloe gel (7). Recently, aloe gel is highly widespread in commercial therapeutic and beautifying preparations (58, 61). There are many components of gel that have been described, but the main ones being polysaccharides and glycoproteins which have many biological activities (35, 60). There are many valuable and useful uses of aloe gel such as its uses as a topical material for burns, cuts, herpes simplex, eczema, psoriasis and as oral material for hyperlipidemia, diabetes, gastric ulcer, mouth ulcer as an edit by Reynolds (60) and Hossain et al. (26).

One of Yemeni aloes species is Aloe woodii which is distributed from west of Saudi Arabia to Yemen as reported by the World Checklist of Selected Plant Families in 2016 (28). The researches and information of this species are very little, so this study was interested to show some of its therapeutic effects. Aim of study: Based on folk medicine in Yemen, this study aimed at evaluating the therapeutic effect of the methanolic extract of Aloe woodii gel on the body weight and on the liver tissue lesions which is induced by high table sugar intake, that resembles the current human dietary pattern.

Materials and methods
A: Collection of Plant Material
Aloe woodii leaves were collected from Qaryat Allsharqi (longitude:43.58.333 & Latitude: 15.58.333), Kuhlan Afar District, Hajjah Governorate, Yemen. Identification of this plant was done by Dr. Hassan Ibrahim, a botanist at the Biology Department, Faculty of Science, Sana'a University.

B: Plant gel preparation and extraction
Healthy and fully grown leaves of Aloe woodii were selected and washed with distilled water. The outer layer of the leaves was removed, then the gel was scraped by sterilized knife and collected in a suitable pot. The gel was dried in the oven then it was powdered. For the extraction, 50 grams of the powdered gel was soaked in 500 ml of absolute methanol at room temperature, then the solution was filtered using Whatmann No.1 paper. The extract was evaporated to dryness to obtain the crude extract. At the time of rats treatment, the extract was dissolved in a known volume of distilled water (53, 64).

C: Animals
The present study was applied on albino female rats that were purchased from the Animal House in the Science Faculty, Sana’ University where the experiment was done. Animal experiments were carried out according to the "Guide for the Care and Use of Laboratory Animal (1996)" (12) prepared by the National Academy of Science and published by the National Institutes of Health. The protocol was approved by the Committee of Experimental Animals Care and Use, Sana’a University. During the experimental period, animals were kept in suitable cages with the
Effects of *Aloe woodii* gel methanolic extract on the liver function ……Bushra Y. H. Al-Khatib

observance of adequate experimental conditions at room temperature (25±5°C) as well as they had *ad libitum* standard diet and excess of water.

**D: Experimental design**

This experiment lasted 11 weeks (from the first week of February 2016 to the third week of April 2016) and was carried out on 18 rats with an average weight of 122± 10 g at the beginning of the experiment (W1). The experiment was divided into two periods, the first (7 weeks) was for a high supplement of table sugar, while the second (4 weeks) was for the treatment by *Aloe woodii* gel extract. In the first period, the animals initially were randomly divided into two groups: a control group (CG) included 6 rats and an experimental group (EG) included 12 rats. Control group was fed *ad libitum* of standard diet and had excess of tap water throughout the experiment time (11 weeks), whereas the EG group received daily water supplemented with table sugar, ordinary table sugar obtained from the market (200g sugar / L of water), besides the same standard diet, for 7 weeks. At the last day of the 7th week (49th day of the experiment), the body weight of rats in both groups was recorded (W2) to obtain the percentage of body weight changes. The treatment with *Aloe woodii* was in the second period of the experiment that started in the eighth week in which rats in EG group were divided randomly into three groups and the body weight of rats in each group was recorded (W3). The dividing experimental group’s design in the second period was as follow:

a. Sugar group (SG) of 4 rats that were continued to receive water supplement with table sugar (200 g/L water).

b. Aloe group (AG) of 4 rats that received water without table sugar, but they were daily and orally received the methanolic extract of *Aloe woodii* gel (0.5 mg/kg BW) for 4 weeks .

c. Recovery group (RG) of 4 rats that were also received water without sugar or anything else. This group was left for 4 weeks for auto-recovery.

At the end of the experiment (complete 11 weeks) and 12 hrs of the last treatment, the body weight of rats was recorded (W4). Rats were anesthetized by an appropriate amount of anesthetic, ethyl ether, under anesthetic conditions and sacrificed, and the samples for the experimental tests were taken.

**E: Alanine aminotransferase (ALT) test:**

Blood samples from the ophthalmic venous plexus (orbital sinus) of rats were with drawn in clean sterile tubes containing EDTA. Plasma samples were obtained after centrifugation at 3000rpm for 15 minutes, then they were kept at -80°C until used to determent the level of ALT as an indicator for the harmful in the liver.

**F: Histopathological studies:**

All the experimented rats were dissected and the livers of rats were disconnected, immediately, washed in saline solution and cut in small pieces; then fixed in 10% neutral buffer formalin solution for the histological study. Paraffin sections (5microns) were prepared and stained with hematoxylin and eosin stains for microscopic examination (5).

**G: Histopathological quantitative analysis**

Quantitative analysis of the histopathological changes in livers was based on the mean± SD obtained from the measurements and was applied on liver sections using an ocular micrometer calibrated with a stage micrometer. The frequency of the histopathological changes was based on the measurements mean obtained from the measurement in 10 microscope fields (21) within an area 0.36 mm² at 40X as well as within an area 0.012mm² at 400X.
Effects of Aloe woodii gel methanolic extract on the liver function……..Bushra Y. H. Al-Khatib

H: Statistical analysis:
Results were expressed as the mean ± standard deviation (SD). Statistical significance was determined by one-way analysis of variance (ANOVA) (Graph Pad Prism version 6 software). P values less than 0.05 for data were considered significant.

Results
1- Body weight:
Concerning rats body weight, there was none remarked changes between all groups in this study, whether in the first period or in the second period of the experiment, as shown in Table (1). However, there was an increase in the amount of visceral (abdominal) adipose tissue in sugar treated rats (SG) (Fig. 1, B), especially around some organs, like the kidney (Fig. 1, C), when compared with the control rats (CG) (Fig. 1, A). In comparing with SG, the visceral fat was less in the aloe group (AG) and recovery group (RG), especially in AG.

Table (1): Mean ± SD and percentage of changes of rats body weight under the effect of table sugar intake and Aloe woodii treatment

<table>
<thead>
<tr>
<th>Groups in the first period</th>
<th>CG (6 rats)</th>
<th>EG (12 rats)</th>
</tr>
</thead>
<tbody>
<tr>
<td>W1, mean± SD</td>
<td>122.4± 10.10</td>
<td>122.6± 10.81</td>
</tr>
<tr>
<td>W2, mean± SD</td>
<td>193.5± 9.00</td>
<td>189.8± 18.50</td>
</tr>
<tr>
<td>% change between W1 and W2</td>
<td>58.088</td>
<td>54.812</td>
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</table>

<table>
<thead>
<tr>
<th>Groups in the second period</th>
<th>CG (6 rats)</th>
<th>SG (4 rats)</th>
<th>AG (4 rats)</th>
<th>RG (4 rats)</th>
</tr>
</thead>
<tbody>
<tr>
<td>W3, mean± SD</td>
<td>196.5± 7.689</td>
<td>188.3± 16.47</td>
<td>170.2± 6.458</td>
<td>191.2± 32.67</td>
</tr>
<tr>
<td>W4, mean± SD</td>
<td>202±7.65</td>
<td>200.30±19.86</td>
<td>180.00 ±9.00</td>
<td>200.30±12.74</td>
</tr>
<tr>
<td>% change between W3 and W4</td>
<td>2.798</td>
<td>6.372</td>
<td>5.757</td>
<td>4.759</td>
</tr>
</tbody>
</table>

CG: Control group, EG: Experiment group, SG: Sugar group, AG: Aloe group, RG: Recovery group. W1: Body weight at 1st day, W2: Body weight at 49th day, W3: Body weight at 50th day, W4: Body weight at 78th day. % change= mean of the terminal body weight- mean of the initiated body weight/ mean of the initiated body weight.

Fig. (1): Visceral fats of rats in control group (A) and in sugar group (B& C) in this experiment.

2- ALT plasma level :
When comparing between the groups in the present study regarding ALT plasma level, there was a statistically significant increase between all the experimental groups and the control group as represented in Fig (2). Furthermore, in comparison with the control group, the significance of the increase of ALT level was higher in the sugar group (SG) and recovery group (RG) (p >0.001)
Effects of *Aloe woodii* gel methanolic extract on the liver function……..Bushra Y. H. Al-Khatib

more than in aloe group (AG) (p >0.01). In addition, there was a statistically significant increase in ALT level in RG (p >0.01), compared to other treated groups (SG and AG).

3- Histopathological examination:

Liver sections of rats in the control groups (CG) showed almost a healthy architecture that had a well-preserved cytoplasm and a prominent nucleus of hepatocytes as well as normal central veins as shown in Fig. (3, A). However, liver sections of the sugar groups (SG) (Fig. 3, B & C) revealed many degenerated characteristics in which the vacuolating, swelling and ballooning of hepatocytes represented the main changes in all sections in this group. Swelling and ballooning hepatocytes (cloudy swelling) were characterized by a generalized volumetric increase and a pale cytoplasm with many vacuoles and clear spaces, whereas the nuclei appeared normal in size and position. Moreover, inflammatory condition with infiltration of mononuclear cells was observed. Necrosis and fatty changes of hepatocytes repeatedly appeared in sections. Also, there was vasodilation in some veins with partial congestion. On the other hand, *Aloe woodii* treatment in the aloe group (AG) caused a partial improvement in the structure of liver, compared to SG, whereas some degenerated changes were still found like vacuolar degenerated of hepatocytes (Fig. 3, C). In contrast to AG, the ameliorate of liver sections of recovery group (RG) (Fig. 3, E & F) was slight with many degenerated changes which were highly resembling these in the sugar group, such as vacuolar and swelling of hepatocytes, necrosis, inflammation, fatty change, and congestion.

4- The quantitative assessment of liver lesions

As shown in Table (2), all scores of histopathological lesions in the liver of the sugar group were significantly higher than that of the control group. The significance of lesions in SG was as follow: swelling/ballooning of hepatocytes and fatty change (P< 0.001), necrosis, inflammation, vasodilation (P < 0.01) and congestion ((P < 0.05). *Aloe woodii* treatment in AG significantly caused a decrease in the lesions scores of necrosis, inflammation, vasodilation (p< 0.01) and congestion ((P< 0.05) when compared with SG group, while the greatest decrease of lesions was detected with fatty and swelling/ballooning changes (P<0.001). On the other hands, as noticed in Table 2, scores of some lesions (swelling/ballooning changes, necrosis, inflammation, congestion) were higher in RG, compared to AG. Furthermore, vacuolating and/or swelling of hepatocytes were significantly higher in RG, compare with both CG and AG (P< 0.001) and close to SG. Also, necrosis and inflammation scores in RG were significantly decreased, compared to SG, but were higher than in AG.
Fig. 3: Photomicrographs of the liver sections showing in: A, control group (CG), normal hepatocytes architecture (H) with normal central vein (CV); B & C, sugar group (SG), many degenerated features like inflammatory regions (In) with infiltration of mononuclear cells, vacuolation/ballooning of hepatocyte (arrows), necrotic cells (arrowheads), fatty changes (asterisks), congestion (Co) with vasodilation as in picture C; D, aloe group (AG), look like more or less control group with some degenerated changes like vacuolar changes (arrows) and necrosis (arrowheads); E & F, recovery group (RG), have degenerated changes almost resemble that in sugar group like inflammation region (In), vacuolation/swelling changes (arrows), necrosis (arrowheads), fatty changes (asterisks), congestion (Co) (H&E, 400X).
Effects of Aloe woodii gel methanolic extract on the liver function……..Bushra Y. H. Al-Khatib

Tab. (2): Quantitative analysis for histopathological lesions of liver under the effect of high sugar intake and Aloe woodii treatment in the experiment rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>CG</th>
<th>SG</th>
<th>AG</th>
<th>RG</th>
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<tr>
<td>Histopathological status</td>
<td></td>
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<tr>
<td>Vaculation/ balloonining of hepatocyte (#)</td>
<td>3.55± 1.25</td>
<td>16.40± 2.10</td>
<td>6.20± 0.50</td>
<td>14.7± 0.20</td>
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<td>a: ***</td>
<td>a: <em>, b</em>*:</td>
<td>a: ***, c: ***</td>
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<tr>
<td>Necrosis (#)</td>
<td>5.85±0.91</td>
<td>13.10± 2.69</td>
<td>7.26± 0.72</td>
<td>8.05± 0.15</td>
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<td>a: **</td>
<td>b: **</td>
<td>b: *</td>
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<tr>
<td>Fatty changes (#)</td>
<td>0.633±0.23</td>
<td>7.007± 1.73</td>
<td>0.65± 0.15</td>
<td>1.15± 0.35</td>
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<td>+</td>
<td>a: ***</td>
<td>b: ***</td>
<td>b: ***</td>
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<tr>
<td>Inflammation (# #)</td>
<td>0.25±0.05</td>
<td>1.87±0.56</td>
<td>0.45±0.05</td>
<td>0.90±0.60</td>
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<tr>
<td>Congestion (# #)</td>
<td>0.1</td>
<td>1.56±0.66</td>
<td>0.75±0.05</td>
<td>1.3±0.30</td>
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<tr>
<td>Vasodilation (# #)</td>
<td>0.15±0.05</td>
<td>1.46±0.47</td>
<td>0.70±0.40</td>
<td>0.20±0.10</td>
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CG: Control group, SG: Sucrose group, AG: Aloe group, RG: Recovery Results expressed as mean ± SD of the numbers of lesions in 10 field for three rats per group.
a: significant compared with the control group (CG), b: significant compared with the sugar group (SG), c: significant compared with aloe group (AG), NS: no significant.*P<.05; **P<.01; ***P<.001.

Discussion
The present study found that there was none remarkable changes of the body weights between all groups under the impact of sugar or aloe treatment, but there accumulation of visceral fats in the sugar group decreased in the aloe group. This outcome is in agreement with some studies which found that feeding with high sucrose diets, with or without high-fat diets, did not increase the animal body weight over the long term (3, 11, 55). This may be explained by the incidence of metabolically obese, but normal-weight individuals who have obviously larger amounts of visceral adipose tissue was associated with some metabolic disorders (13). Stanhope and Havel (71) and Ludwig et al. (39) suggested that the fructose moiety of sucrose was accountable for the increase in abdominal fats and lipid dysregulation. Moreover, studies in humans declared that high doses of fructose can result in insulin resistance, intra-abdominal fat accumulation and fatty liver (72). Also, Morsy et al. (46) suggested that the increase in the percentage of daily dietary sucrose level could worsen the hepatic metabolic disturbance that is reflecting on its function.

It has been found that intake of fructose-sweetened beverages encouraging visceral adiposity (16) which has a greater threat for the development of insulin resistance and the metabolic syndrome more than subcutaneous fat stores (71). This syndrome is related with the lower expression and activity of hormone-sensitive lipase and reduced tyrosine phosphorylation of the insulin receptor that results in a reduction of the responsiveness of visceral fat to the anti-lipolytic effects of insulin (59). Furthermore, it has been found that diets with higher carbohydrate content
than fat induces the de novo hepatic lipogenesis that plays an important role in glucose homeostasis and development of hypertriglyceridemia and hyperinsulinemia (68, 70). The hyperinsulinemia led to the increased hepatic synthesis of fatty acids, triglyceride accumulation in the hepatocytes, with subsequent steatosis. Furthermore, the principal role of fructose as an inducer of fatty liver by both stimulating de novo lipogenesis and blocking β-fatty acid oxidation is related with the unique metabolism of fructose by fructokinase which leads to a drop in ATP with nucleotide turnover and uric acid generation. Consequently, the proinflammatory and prooxidative effects of uric acid lead to surges in gut permeability and endotoxemia that exacerbates the lipogenic process in the liver and coupled with mitochondrial dysfunction that results in NAFLD (31).

Sugar group in the present study exhibited a significant increase in the plasma level of ALT compared with the control group. This result is in harmony with degenerated aspects revealed by the microscopic examination of the liver which supported through the quantitative study of the histopathological changes that included swelling, vacuolation and/ or ballooning of hepatocytes, necrosis, fatty changes, and inflammation. Morsy et al. (46) also found a gradual increase in ALT level in liver tissue homogenate in an accordant manner with the increase of the consumed sucrose. Additionally, the previous study found a gradual increase in the level of serum cholesterol and triglyceride that might explain the accumulation of visceral adipose in our study. Also, as found by Ishimoto et al. (29), wild-type mice that received high fat high sucrose diet showed an increase in serum ALT and AST levels as well as an elevated of intrahepatic expression of TNF-α as proinflammatory cytokine, MCP-1(a chemotactic factor), and the monocyte-macrophage marker that might explain the inflammatory developing in our experiment. Further, the previous study documented the mitochondrial oxidative stress of hepatocyte through an increase of superoxide generation, an increase of mitochondrial NOX4 and a decreased manganese superoxide dismutase expression. Moreover, the nucleotide turnover associated fructose metabolism that resulted in the production of uric acid can also induce mitochondrial oxidative stress and the accumulation of lipids in the liver (10, 33). Besides that, Lima et al. (36) demonstrated the role of the diet enriched with sucrose in oxidative stress generation, the antioxidants reserves reduction, and hepatic steatosis as well as the hepatocellular ballooning which was observed clearly in our study. All these evidences of oxidative stress associated with high sucrose diet may give the reason for cells degeneration that was noticed in our study.

On the other hand, the histopathological changes that occur in the present study in the sugar group may be referred to Advanced Glycation Endproducts (AGES) generation. As previously documented, AGEs can be endogenously formed as a consequence of high dietary sugar intake and interfere with many cell functions such as lipid synthesis, inflammation, antioxidant defenses, and mitochondrial metabolism. Moreover, dietary AGEs has an adverse effect on different signaling pathways that can contribute to the onset of liver damage and other organs like the brain (4).

The most degenerated manner of hepatocyte by high table sugar intake in our study was the vacillation of hepatocytes that developed to swelling and ballooning. As documented previously by Lackner (32), hepatocellular ballooning is regarded as a key feature for nonalcoholic steatohepatitis (NASH) diagnosis in which ballooned hepatocyte is characterized by edema and cytoplasmic rarefaction resulting in enlarged cells with clear appearances (51). Furthermore, cellular ballooning in NASH is associated with considerable accumulation of fat droplets along with dilation of the endoplasmic reticulum and injury of the cytoskeleton (9, 32). Further, our notes in the present study about the histopathological features related to high table sugar intake are in accordance with observations obtained through the transmission electron microscopy of liver tissue of rats treated with high diet sucrose in a study carried out by Morsy et al. (46) in which they demonstrated many swollen degenerating hepatocytes associated with severe disruption of the cell membrane, fat droplets included inside the cytoplasm, edema of the intercellular spaces and infiltration with inflammatory cells. Some mitochondria, rough endoplasmic reticulum, and nuclei were abnormally and/ or destroyed. Also, there was damage to the endothelial lining of blood sinusoids with excessive bleeding.

ALT plasma level in the aloe group, in this study, was close to the level in the sugar group, revealing non-effect of Aloe woodii on this indicator. However, the significance of ALT increase...
Effects of Aloe woodii gel methanolic extract on the liver function …..Bushra Y. H. Al-Khatib

was higher in the sugar group than that in the aloe group, compared to the control group. It is surprising that the level of this indicator was very high in the auto-recovery group, compared to all other groups in this experiment, especially to the control group. So, there was a need for further studies with more liver functions tests. In contrast, liver lesions induced by high sugar supplement were significantly ameliorated under the effect of aloe treatment as demonstrated by the histopathological examination of liver sections which was supported by the quantitative analysis. The ameliorated effect of Aloe woodii on the liver histological construction was clear when compared with the liver structure in the recovery group.

There was a continual search, during the period of this study, for any previous studies on the therapeutic effects of the Aloe woodii or about its chemical composition, but unfortunately, there was no any result, so the present research may represent one of the earliest researches about the therapeutic effect of this aloe species. However, Aloe vera has the highest number of studies of aloe species, therefore, this study could illustrate some results related to the therapeutic effects of Aloe vera that may be related to our results because there are some common ingredients found among species in aloe genus, like polysaccharides, acetylated glucomannan, arabino galactans, rhamnogalacturonans, glucomannan, , acetylated mannan and some other phenolic component (14).

It has been found that Aloe vera gel complex reduced body weight, body fat mass, and insulin resistance in obese prediabetes and early nontreated diabetic Patients (15). Also, isolated phytosterols from Aloe vera induces the reduction of fatty acid synthesis as well as increases the fatty acid oxidation in the liver that helps the reduction of intra-abdominal fat and improvement hyperlipidemia (45). Further, A. vera gel extract prevents ethanol-induced fatty liver by suppressing mRNA expression of lipogenic genes in the liver (63).

Moreover, when the levels of lipid peroxidation and hydroperoxides increase in the liver and kidney tissues of diabetic rats, the treatment with Aloe vera gel extract adjusts these levels to near normal levels as well as it induces a significant increase of the levels of reduced glutathione, superoxide dismutase, catalase, glutathione peroxidase and glutathione-S-transferase (57). In addition, Aloe vera gel exhibited significant hepatoprotection against oxidative stress induced by carbon tetrachloride in which stopped and repaired the increase of liver lipopolysaccharide, alkaline phosphatase, serum transaminases, and total bilirubin (47). Werawatganon et al. (77) also reported that Aloe vera gel attenuated liver injury in mice with aceterminophen-induced hepatitis, in which it repaired the lesions of liver architecture, provided anti-oxidative effects against oxidative damage through its work to minimize the level of hepatic lipid peroxidation and increased the level of glutathione as well as it decreased the raising in IL-12 and IL-18 cytokines in which passing these cytokines from Kupffer cells and macrophages of the liver into the bloodstream leads to the inflammation developed. Besides lipid peroxidation of cell membrane results in a decrease of membrane fluidity, inability to restore ionic gradients that finally cause cellular swelling or tissue inflammation, that were clearly apparent in our study related with high sugar intake.

Furthermore, Aloe vera comprises considerable amounts of antioxidants, like α-tocopherol and flavonoids, as documented by Lee et al. (35) and Hamman (25). The ameliorated of the degenerated cells and the decrease of necrosis with Aloe woodii gel treatment in our study may be related to the improvement of the antioxidant level in which the antioxidant effect generally prevents cells damage and aids the regeneration and replaces the degenerated cells.

The ameliorated effect of Aloe vera gel may be attributed to its polysaccharide active contents and other agents (6). Further, A. vera gel contains more than 70 biologically active compounds that show anti-inflammatory, antioxidant and anti-carcinogenic activities as well as they are also effective in improving the immune system (24). The major active polysaccharide of Aloe vera gel is acemannan (75) that is reported to have many therapeutic effects. In addition, the active glycoproteins such as lectins, proteases, anti-bradykinins, and anti-prostaglandins agents, which was found in Aloe vera gel might play some role in the therapeutic activity and might explain the anti-inflammatory effects of A. vera extract (30, 61). Further, C-glucosyl chromone that was isolated from A. vera gel extracts is regarded as a novel anti-inflammatory compound (27).

Moreover, Aloe vera inhibits the cyclooxygenase pathway and reduces prostaglandin E2 production from arachidonic acid (43) as well as it reduces leukocyte adhesion and the
Effects of *Aloe woodii* gel methanolic extract on the liver function……Bushra Y. H. Al-Khatib

proinflammatory cytokines (17). Also, Aloe formulas suppress obesity-induced inflammatory responses by reducing transcription factor 1/peroxisome proliferator-activated receptor and 11β-hydroxysteroid dehydrogenase 1 as well as it enhances anti-inflammatory cytokines in white adipose tissue and liver (56). All the previous studies clarify the anti-inflammation effect of *Aloe vera* gel extract which may be related to the same effect that occurred in our study by *Aloe woodii* gel extract.

**Conclusion:** High intake of table sugar causes some adverse effect in females albino such as an accumulation of visceral fats, without any significant increase in the body weight, an increase in plasma level of ALT and many histopathological lesions in liver tissue including vacuolation, swelling, ballooning, fatty changes and necrosis of hepatocytes and inflammation. *Aloe woodii* treatment ameliorated the accumulation of visceral fats and the lesions of the liver, but not the ALT level.

**Declarations:** This manuscript is an original investigation as well as it is not submitted elsewhere for publication.

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Effects of Aloe woodii gel methanolic extract on the liver function …..Bushra Y. H. Al-Khatib


Effects of Aloe woodii gel methanolic extract on the liver function ……Bushra Y. H. Al-Khatib

Effects of *Aloe woodii* gel methanolic extract on the liver function …..Bushra Y. H. Al-Khatib

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Effects of Aloe woodii gel methanolic extract on the liver function. Bushra Y. H. Al-Khatib


تأثيرات المستخلص الميثانولي لهلام الصبار Aloe woodii في تغيير وظيفة الكبد في إناث الجرذان البيضاء المسببة بتناول مستوى عالي للسكر

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الملخص

أصبح استهلاك الأطعمة والمشروبات المحللة والغنية بالسكر عادةً مألوفاً ولكنها ترافق بظهور العديد من الأمراض. من ناحية أخرى تشير معلومات الطب الشعبي في اليمن إلى تأثيرات علاجية لنوع الصبار Aloe woodii ضد بعض الأمراض، ولذا هدفت هذه الدراسة لتقييم التأثير المحسن لمستخلص هلام Aloe woodii في الأضرار الكبدية في إناث الجرذان واستدلاله باستهلاك كميات كبيرة من السكر المكرر. استمرت هذه الدراسة لمدة 12 أسبوعاً قسمت على فترتين، الفترة الأولى كانت للتزويد بكميات عالية من السكر بينما الفترة الثانية كانت للمعالجة بالمستخلص الميثانولي لهلام Aloe woodii. في نهاية مدة التجربة تم تسجيل أوزان الجرذان واتخاذ عينات من الدم وكذلك عينات من الكبد وُصَحَا المريض. النتائج: لم تكن هناك أي تغيرات وزنية مميزة بين مجموعات الدراسة، ولكن كان هناك تجمع واضح للدهون الحشوية، وكذلك ارتفاع في مستوى ALT. الفحص النسيجي المرضي الذي دُرس في مجموعتي الدراسة، لم يظهر فجوات في خلايا الكبد ومناطق ظهور كميات كبيرة من السكر المكرر. ومعالجة جرذان السكر المكرر Aloe woodii أدت إلى تحسن في التغيرات النسيجية وانخفاض في مستويات ALT. النتالي المستخلص الميثانولي لهلام Aloe woodii أظهر تحسن في التغيرات النسيجية في الكبد بناء على نتائج الفحص النسيجية. الكلمات المفتاحية: السكر المكرر، الصبار Aloe woodii، الكبد، الخلايا الكبدية البالونية.