Pharmaco-toxicological study of *Opuntia ficus indica* L. aqueous extract in experimental animals

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Article History: Received 3rd August 2013, Revised 3rd September 2013, Accepted 5th September 2013.

Abstract: *Opuntia ficus indica* is used in traditional medicine for the treatment of hyperlipidemia, hypercholesterolemia, diabetes and dermal burns. The aim of present study was to analyze and compare the effects caused by the *Opuntia ficus indica* aqueous extract on serum and lipid parameters in white male rabbits (initial mean weight 1.95 kg). Rabbits were divided into two groups (n=6), the first group represented the control group, fed with standard diet; the second group was fed with the control diet supplemented orally with OAE (2ml/kg), once a day, 7 days per week, for 3 months. Food and water were provided *ad-libitum*. The Rabbits body weights were measured every week. Organ weights were determined at the end of treatment. Blood samples were subject to the determination of fasting blood glucose, serum lipid profile, serum protein and albumin, creatinine and urea. The results showed that there was a significant difference in the body weight of the two groups. The relative weights in the OAE group of pancreas and kidneys were similar to those of the control, while, weights of liver were lower than those in the control group. Biochemical analysis showed that cholesterol (CHOL) and triglycerides (TG) were significantly decreased in blood plasma respectively in OAE group. Glucose level (GLU) was significantly lower in OAE group; the rest of the parameters (Albumine, Total proteins, Creatinine, Urea) were not significantly affected. However, these variations do not show any biological toxicity.

Keywords: *Opuntia ficus indica*; Liver; Serum; Cholesterol; Triglycerides; glucose; rabbits.

Introduction

Cactus (*Opuntia ficus-indica*), commonly known as prickly pear, belongs to the family Cactaceae. Family Cactaceae is reported to contain about 130 genera and nearly 1500 species. This plant is native of Mexico and it is widely distributed in Mexico and in all American hemispheres as well as in Africa and in the Mediterranean basin (Manpreet et al. 2012)

Previous studies demonstrated that species of Opuntia are rich in flavonoids (kaempferol, quercetin, narcissin, taxifolin and other phenolics); lactones known as alpha-pyrones (opuntiosides) (Qiu et al. 2007); terpenoids (lupenone, freideline, and others) and alkaloids (mescaline, hordenine, tyramine, and others) (Lee et al. 2003, Jiang et al. 2003). Betalain pigments (betanin, indicaxanthin) are at least found in the fruits (Butera et al. 2002) and act as anti-oxidants.

It has been used in traditional folk medicine because of its role in treating a number of diseases and conditions, including anti-inflammatory effects hypoglycemic effects inhibition of stomach ulceration, neuroprotective effects Through antioxidant actions and also used for treating diabetes, burns, bronchial, asthma and indigestion in many countries over the world. It is also used in Pharma industry as a pharmaceutical agent. The fruit, as well as cactus stem are used to prepare value-added products, such as jam, squash, wine, pickle, body lotions, shampoo, creams, etc. It also has several medicinal and industrial uses. Its seeds can be used as flavouring agents. Due to the remarkable biological activity of Opuntia and its constituents, it will be appropriate to develop them as a medicine (Manpreet et al. 2012).

Therefore, the aim of the current study was to evaluate the effect of diet supplemented with cladodes aqueous extract (OAE) comparatively
to a control diet, given to adult rabbits, on some organ weights and serum lipid profile parameters.

Material and methods

Vegetable Material

*Opuntia ficus indica* cladodes or (prickly pear), thorny varieties, come from Constantine region, (Algeria). The annual average temperatures are in the order of 15.15°C. The maximum of temperatures reaches 33.68°C in July, whereas the minimum reaches 2.73°C in January. The pluviometry average is of 600 mm. The cladodes picking had been realized during February 2011.

Animal and husbandry

Healthy rabbits (New Zealand, white, male, 4 months old, and initial mean weight 2.316 kg) were purchased from a local supplier (Hamma Bouziane, Constantine, Algeria) and used for this study. The animals were kept in individual standard cages. A temperature of 22 ± 2°C, 50 – 75 %, relative humidity and a 12h light-dark cycle were maintained in all the times of experiment. Food and water were provided *ad libitum*. The animals were acclimated to laboratory conditions for a period of 7 days prior to the experiment initiation.

*Opuntia ficus indica* extraction

Picked cladodes had been washed, thorns took away, and crushed with a grinder (Moulinex), the solution, thus, obtained had been filtered. It is this solution that will be administrated per-os only to rabbits.

Experimental protocol and drugs administration

Animals Tests

The study was carried out on 12 New Zealand (male, white, initial mean weight 2.316 kg, age 16 weeks) rabbits. After an acclimatization of 7 days in laboratory conditions, the rabbits were divided randomly into two groups, each of six. Animals of first group were not treated and served as control (CRL group), the others served as tested group (OAE group). To all the animals of this group, the OAE was applied, once a day, 7/7 days, in a dose of 2ml/kg body weight, per-os for 3 months successively. Body weights were measured every 7 days during 12 weeks.

Experimental Procedure

After 90 days of feeding, to avoid the rabbits stress, blood samples extracted from rabbits’ marginal ear vein were performed in heparin tubes. Serum samples were drawn from blood after centrifugation at 3000 x rpm for 10 min. They were kept at -20°C prior to the analysis of blood parameters.

The selected blood parameters were performed in the biochemical laboratory of Constantine, and included Cholesterol (CHOL), Tri-glyceride (TG), blood Creatinine (CREA), glucose (GLU), total proteins (TP), albumin (ALB), and Urea.

Liver, pancreas and kidneys were taken and weighed for the determination of relative organ weight.

Statistical analysis

Data were analyzed statistically by student’s t-test. Mean values were obtained from the average of independent measurements. Differences between groups were considered significantly at least at P ≤0.05.

Results and discussion

During the experimentation period, no mortality was reported in the animals. All rabbits remained healthy and they were available for assessment.

Food intake effects on weight gain and some organ weights

Rabbits Body weight

The table number 1 represents the obtained results of the body weight variation of normal rabbits groups and the experimented rabbits after a daily treatment of 90 days by *Opuntia ficus indica* cladodes aqueous extract in a dose of 2ml/kg.
The obtained results in our study have shown that the OAE administration induced a slight gain in the body weight at the treated rabbits group. This gain is in the order of 2.961%, 4.01%, 5.011%, 5.922%, and 6.833% and of 8.2% in relation to the initial body weight after each week of treatment. Otherwise, the sampling healthy group underwent during the same period a regular gain of 9.146%, 12.715%, 16.694%, 17.760%, and 18.744% and of 20.795%. The body weight average statistical results analysis changing between the two sampling groups is significant (Figure 1).

### Table 1: Body weight and body weight gain in control and OAE group during 12 weeks of treatment

<table>
<thead>
<tr>
<th>Groups</th>
<th>Parameters</th>
<th>J1</th>
<th>J15</th>
<th>J30</th>
<th>J45</th>
<th>J60</th>
<th>J75</th>
<th>J90</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRL</td>
<td>body weight</td>
<td>2.438 ± 0.156</td>
<td>2.661 ± 0.092</td>
<td>2.748 ± 0.057</td>
<td>2.845 ± 0.028</td>
<td>2.871 ± 0.051</td>
<td>2.895 ± 0.010</td>
<td>2.945 ± 0.04</td>
</tr>
<tr>
<td></td>
<td>% gain of body</td>
<td>0</td>
<td>9.146</td>
<td>12.715</td>
<td>16.694</td>
<td>17.760</td>
<td>18.744</td>
<td>20.795</td>
</tr>
<tr>
<td>OAE</td>
<td>body weight</td>
<td>2.195 ± 0.101</td>
<td>2.26 ± 0.106</td>
<td>2.285 ± 0.141</td>
<td>2.305 ± 0.146</td>
<td>2.325 ± 0.104</td>
<td>2.345 ± 0.006</td>
<td>2.375 ± 0.06</td>
</tr>
<tr>
<td></td>
<td>% gain of body</td>
<td>0</td>
<td>2.961</td>
<td>4.1</td>
<td>5.011</td>
<td>5.922</td>
<td>6.833</td>
<td>8.2</td>
</tr>
</tbody>
</table>

### Clinical chemistry

Statistical analysis of clinical chemistry data was registered in table 3.

The results of the *opuntia ficus indica* aqueous extract influence upon the lipidic profile in healthy rabbits and treated rabbits are gathered in the figures 2-A and 2-B. In the two rabbit groups (sampling and treated), we have noticed that the OAE administration during 3 months in a dose of 2 ml/kg has caused a significant decrease of the total cholesterol serum concentration (0.207± 0.06 g/l respectively in related to control group 0.525 ± 0.253 g/l) and the triglycerides (1.142 ± 0.255 g/l respectively in related to the control group 1.16 ± 0.338 g/l).

Glucose level (median ± errors, n=6) was significantly lower in the OAE group compared to the control group (fig2-C). In the other hand, Creatinine, Urea, Total proteins and Albumin were found to be slightly lower, but none significantly in OAE group, than those detected in control (fig 2-D, 2-E, 2-F and 2-G).

### Table 3: Plasma chemistry values in treated rabbits for 12 weeks by OFIJ and control group

<table>
<thead>
<tr>
<th>Blood parameters</th>
<th>Pa-Control (n=6)</th>
<th>OFIJ (n=6)</th>
<th>% of difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHOL</td>
<td>0.525 ± 0.253</td>
<td>0.207 ± 0.06</td>
<td>60.571 (↓)</td>
</tr>
<tr>
<td>TG</td>
<td>1.16 ± 0.338</td>
<td>1.142 ± 0.255</td>
<td>1.551 (↓)</td>
</tr>
<tr>
<td>GLU (g/L)</td>
<td>1.18 ± 0.08</td>
<td>0.93 ± 0.07</td>
<td>21.186 (↓)</td>
</tr>
<tr>
<td>CREA mg/L</td>
<td>7.6 ± 1.14</td>
<td>7 ± 0.816</td>
<td>7.894 (↓)</td>
</tr>
<tr>
<td>UREE</td>
<td>0.258 ± 0.08</td>
<td>0.222 ± 0.03</td>
<td>13.953 (↓)</td>
</tr>
<tr>
<td>TP</td>
<td>58.83 ± 4.167</td>
<td>48.75 ± 2.872</td>
<td>17.134 (↓)</td>
</tr>
<tr>
<td>ALB</td>
<td>16.5 ± 1.378</td>
<td>14.25 ± 2.06</td>
<td>13.636 (↓)</td>
</tr>
</tbody>
</table>

In a previous study, we have found a hypoglycaemic effect after enrichment of diet with OAE (Halmi et al. 2012; Ennouri and al.2007) in treated rabbits. So we have chosen some organs having an impact on the glycaemia, such as pancreas, liver and kidneys. Relative weights, in the OAE group, of pancreas and kidneys were similar to those of control, while, weights of liver were lower than those in the control group (Table 2).

### Table 2: Relative weights of some organs in control and OAE group during 12 weeks of treatment

<table>
<thead>
<tr>
<th>Organs</th>
<th>Relative weight</th>
<th>CRL</th>
<th>OAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>103.345 ± 0.2</td>
<td>86.48 ± 0.054</td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.197 ± 0.03</td>
<td>1.233± 0.165</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>8.176 ± 0.391</td>
<td>8.084± 0.547</td>
<td></td>
</tr>
</tbody>
</table>

### Figure 1: Comparison of some weight organs in control and OAE group during 12 weeks of treatment.
Int. J. Med. Arom. Plants

Toxicological and pharmacological investigations of Opuntia ficus indica

Halmi et al.

Recent studies suggest that the Opuntia ficus indica is beneficial in the weight loss by helping to regulate the sugar levels in blood as well as the cholesterol rates, to eliminate the gastric troubles, digestion problems, and give to those who consume it a quick satiety sensation. The body weights results are in accordance with those published by Brahim kamel Louacini and al, (2012) who have noticed that a treatment of 30 days by Opuntia ficus indica causes a body weights decrease in the ewes.

The Opuntia ficus indica aqueous extract can play a crucial role in the glucose serum concentration decreasing, either by the insulin secretion stimulation, or by an extra-pancreatic action and so by the influence of the glucose absorption and its use by the different tissues. The Opuntia ficus indica aqueous extract administration in rabbits has decreased the glucose serum concentration of 21.186% after the third month of treatment.

These results come so to confirm the first conclusions of Frati-Munari AC (1989), Frati-Munari AC (1990), and Godard MP (2010) who have noticed that the opuntia ficus indica extract administration causes a glycaemia significant decrease.

The Opuntia ficus indica extract can act as the same manner of certain oral antidiabetics as the glibenclamide by the closing of the canals K+/ATP, the membranous depolarization and the rush stimulation Ca2+, the first key step for the insulin secretion (Pari & Latha , 2005).

The hypoglycemic effect of the Opuntia ficus indica aqueous extract can be assimilated in the organic constituents as well as in the inorganic constituents. Among others, it is important to note that the organic constituents that the medicinal plants contain play sometimes a primordial role in the amelioration of their medicinal properties including the hypoglycemic activity. Indeed, Bhaskar and al., (2008), who have studied the aqueous extract hypoglycemic effect of Mucuna prurien « 200 mg/kg » in the rats becoming diabetics by the STZ, indicate that a certain number of essential minerals such as Na, K, Ca, Zn, Mg, Fe, Cu and Mn can be associated to an insulin liberation mechanism and its activity.

Discussion

In our study, we have noticed that the Opuntia ficus indica aqueous extract oral administration in a daily dose of 2ml/kg during three months has also decreased the gain average of the rabbits body weight in relation to the one observed in the sampling healthy group.

Figure 2: The comparison of some biochemical parameters in the rabbits’ plasma from control group (CRL) and the treated rabbits with Opuntia ficus indica extract for 12 weeks.
Some flavonoids, that have been isolated from plants, inhibit the glucose carriers in the intestines, decrease the gene expression which control the gluconeogenesis, increase the glucose storage in the liver and reduce the glycogen degradation (Waltner-Law and al., 2002; Shimitzu and al., 2000; Li and al., 2004; Sarkhail and al., 2007).

A great number of research works have shown that the hypoglycemic effect of several plants containing the polysaccharides, terpenes, flavonoids as well as other several compounds (Sarkhail et al., 2007) according to various mechanisms. The literary studies have shown that *Opuntia ficus indica* is rich of these compounds, thus it is possible that the plant hypoglycemic action must be linked to the presence of these compounds.

In our study, we have registered a significant decrease of the total cholesterol serum concentration and triglycerides. Several authors report that the decreasing of the serum lipids concentration by a diet or therapeutic drugs lowers strongly the risks of the coronary heart diseases (Eddouks and., 2007). New drugs research -able to reduce and/or to regulate total cholesterol serum concentration and triglycerides- has gained momentum in recent years. The plants extract constitute a potential candidate, they contain frequently a very complex mixture of different molecules, separate polarity, capable to reduce the lipids serum concentration by different mechanisms (Eddouks and al., 2004).

We have noticed that in the experimented rabbits, a three months treatment by an *Opuntia ficus indica* aqueous extract (a dose of 2ml/kg) has allowed the reducing of the total cholesterol serum concentration with a significant decrease of 60.571% in related to the sampling rabbits.

The obtained results are in accordance with those published by Anthony Oguogho and al., (2009) and Monia Ennouri and al., (2007); they have noticed that with rats the *Opuntia ficus indica* aqueous extract treatment has caused a significant decreasing of the total cholesterol plasmic concentration in relation to those observed in the healthy sampling.

The underlying mechanism by which the *Opuntia ficus indica* aqueous extract has exercised its cholesterol-lowering agent effect is shown by a decreasing of cholesterol intestinal absorption, by the linking with biliary acids in the intestine and by the biliary excretion increasing (Kritchevsky, 1978; Kelly).

The *Opuntia ficus indica* aqueous extract could also react by reducing the cholesterol biosynthesis specifically by the reducing of the HMG-CoA reductase activity (Kedar & Chakrabarti, 1982; Sharma and al., 2003). Besides, the *Opuntia ficus indica* aqueous extract has decreased the serum cholesterol by modifying the lipoprotein metabolism: the LDL absorption reinforcement by the LDL receptors increasing (Slater and al., 1980) and/or by increasing the activity of the Lecithin- Cholesterol Acyl Transferase (LCAT) (Khanna and al., 2002). Moreover, we have also noticed that the *Opuntia ficus indica* aqueous extract daily administration during three months caused a non-significant decrease of triglycerides serum concentration in the treated rabbits group (1.551 %) in relation to control.

The *Opuntia ficus indica* could reduce the triglycerides serum rates by the decreasing of the fatty acid synthesis (Bopanna and al., 1997), the LDL catabolism increasing, the LCAT and the tissue lipase (Khanna and al., 2002) and/or the acetyl-CoA carboxylase inhibition (McCarty, 2001) and by the triglycerides precursor production as the acetyl-CoA and the glycerol phosphate.

A great number of research works have shown the hypolipidemic effect of several flavonoids, terpenes and other phenolic compounds (Sarkhail and al, 2007). Therefore, the *Opuntia ficus indica* hypolipidemic effect can be linked to the presence of some of these molecules.

**Conclusion**

The present study has demonstrated that the enrichment of diet with OFIJ had hypolipidemic, hypoglycemic and anti-obesity effects as compared to the control diet.

It could significantly decrease the levels of Cholesterol, triglycerides and glucose in serum. More studies are needed of to explain the poten-
tial hypocholesterolemic, hypolipidemic and hypoglycemic effects of *Opuntia ficus indica* cladodes extracts on hypercholesterolemic and other pathologies on rabbits.

**References**


