Effect of *Salix alba* barks on experimentally induced obesity in rats

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Abstract

Obesity is a multifactorial cradle that grows from the interaction of metabolic, cellular, molecular, psychological, behavioral and social factors. This condition characterized by increasing in content and size of adipose tissue, and fat accumulation, leading to an increment in the weight of the body. The objective of the present study is to investigate the effects of Salix alba barks as herbal medicine on body weight parameters, lipid profiles, and metabolic inflammation in rats' experimental models of obesity. In the current study, we used forty apparently healthy Wister male rats were involved in the present study, divided into four groups. Obesity was induced by the administration of high-fat diets for 8 weeks to stimulate adiposity. The first group received a normal diet with a daily dose of distilled water intraperitoneal and left without treatment and considered as a control group. The remaining three groups that were induced to be obese, received (Orlistat 35 mg/kg and Salix alba 150mg/kg) after the induction period for 28 days, except one group left without treatment. The blood was collected from all animal groups, and then serum obtained for the biochemical analysis. Our results showed that in obese animals, body weight and body mass index were significantly reduced by Salix alba after 4 weeks of treatment. Fasting cholesterol, TG, LDL, VLDL, TNFα, and visfatin and leptin were significantly decreased, while HDL, IL10, and adiponectin significantly elevated by Salix alba compared with HFD induced obese animal group. To conclude, Salix alba barks improve lipid profile as well as reducing the elevated body weight. Salix alba barks inhibit metabolic inflammatory response associated with obesity. The adipose tissue-derived adipokines were got better with this herb.

Key words: Salix alba,Leptin, adiponetin ,visfatin , obesity.


Introduction

The World Health Organization (WHO) defines obesity as "a condition of abnormal or excessive fat accumulation in adipose tissue, to the extent that health may be impaired"(1). The WHO reported that about 13% of the world’s adult population was obese in 2016 and the prevalence of obesity in Iraq was...
30.4%. Overall, the worldwide prevalence of obesity nearly tripled between 1975 and 2016\textsuperscript{(2)}. The expansion of excess adipose tissue, characteristic of the obese phenotype is chiefly determined by the balance between lipogenesis and lipolysis/fatty acid oxidation \textsuperscript{(3)}. Visfatin also named pre-β-cell colony-enhancing factor, is produced mainly in visceral adipose tissue. The increased concentration of visfatin in obesity could be a compensatory response to maintain blood glucose levels \textsuperscript{(4)}. By reducing the glucose release from adipocytes, visfatin stimulates differentiation of adipocytes, foster the aggregation of TG from glucose and influence expression of genes encoding for diacylglycerolacyltransferase and adiponectin\textsuperscript{(5)}. Leptin is one of the most important adipose-derived hormones produced by white adipose tissue (WAT) \textsuperscript{(6)}. Leptin is a key appetite-regulating hormone, with effects on energy expenditure. Circulating levels of leptin and adipose tissue leptin mRNA expression are increased proportional to body fat mass, in obesity However in obese people; receptors of leptin are insensitive to the effects of leptin leading to leptin resistance \textsuperscript{(7)}. Tumor necrosis factor-alpha (TNF-α) is a multifunctional cytokine involved as a significant factor in the progression of insulin resistance (IR). TNF-α mRNA is over-expressed in adipose tissue in rodent models of obesity \textsuperscript{(8)}. TNF-α mRNA is over-expressed in adipose tissue in rodent models of obesity. Weight loss in fatter people is associated with a significant reduction in TNF-α mRNA expression in adipose tissue and improved insulin sensitivity. In addition, TNF-α controls IL-6 synthesis and both are pro-inflamatory factors associated with obesity and inflammation with diabetes \textsuperscript{(9)}. Interleukin-10 is an anti-inflammatory cytokine, which is a major inhibitor of pro-inflammatory cytokine and chemokine production. In addition, a group of researchers conducted the first study which showed a significant relationship between lower levels of IL-10 and metabolic syndrome. In this regard, plasma levels of IL-10 are strongly associated with insulin sensitivity in healthy subjects and a decrease in obese patients \textsuperscript{(10)}. IL-10 can restore normal insulin signaling through two ways, firstly by inhibiting NADPH oxidase-induced oxidative stress and this has been associated with aberrant insulin receptor substrate activation, secondly by antagonizing the actions of IL-6 and TNF-α \textsuperscript{(11)}. Adiponectin is expressed in adipose tissues with higher expression in subcutaneous adipose tissue (SAT) than in visceral adipose tissue (VAT) \textsuperscript{(12, 34)}. The level of adiponectin decreased with increased body fat and increased with weight loss \textsuperscript{(13)}. Adiponectin acts as an insulin sensitizer, stimulating fatty acid oxidation in an AMP-activated protein kinase (AMPK), and peroxisome proliferator-activated receptor-α (PPAR-α) dependent manner \textsuperscript{(14)}. In animal studies, the injection of adiponectin for the long term, causing a decrease in triglyceride storage in liver and muscle, so there is a decline in triglyceride and free fatty acid levels and a rise in HDL concentration \textsuperscript{(15)}. The WHO reported that 75\% of the world population still depends on plant-based traditional medications for primary health care \textsuperscript{(16)}. In the last few years, there has been continuous growth in the field of herbal medicine and these drugs are gaining much attention from developing as well as developed countries because of their natural origin and relatively fewer side effects \textsuperscript{(17, 35)}. A large number of natural plants with the traditional claim of antidiabetic, antiobesity, antioxidative and anti-inflammatory activities have been studied worldwide and their efficacy has been validated \textsuperscript{(18)}. However, there are still a number of medicinal plants, which are traditionally used but their scientific efficacy has not been studied exclusively. On the basis of this background, we have
selected Salix alba barks for our study. White willow (Salix alba L.), is a willow belongs to the genus Salix and family Salicaceae. Willow bark has several different components, including flavonoids, tannins, in addition to salicin. Salicin is considered the main active ingredient. Willow bark contains up to 20% flavonoids and condensed tannins (19). Of interest is the fact that the salicin and the salicin related content of willow bark extract cannot fully explain its clinical efficacy. In addition to the salicin-related constituents, various polyphenolicsand flavonoids are also present (20). The effects of willow bark include analgesic, anti-inflammatory, antipyretic, and antiplatelet activity. These components of willow bark are thought to have lipoxygenase-inhibiting and antioxidant effects as well as prevention prostaglandin and cytokine release (21).

**Materials & Methods**

**Chemicals and Reagents**

Salix alba bark extract was purchased from Bulk Supplements / USA, while Orlistat was purchased from Wuhan Shu Ou Technology /China. High Fat Diet (HFD) was purchased from Research Diets, Inc. (New Brunswick, USA). Body weight was measured in the morning of the first and the last day of treatment administration by Balance: Sartorius TE64 (Germany). Serum levels of triglycerides (TG), total cholesterol, and high-density lipoprotein cholesterol (HDL-c) were measured enzymatically using commercial kits (Bio Merieux / France) with the aid of a spectrophotometer (Apel, Japan). Low-density lipoprotein cholesterol (LDL-c) was calculated by Friedewald formula: LDL-c = Total cholesterol – [HDL-c + (TG/5)] (22). The serum concentration of Adiponectin and visfatin were measured by ELISA kits from Cusabio Technology/USA, while serum concentrations of Leptin, TNF α and IL10 were estimated via ELISA kits from Abcam/England. All ELISA tests were performed with the aid of an ELISA plate reader (Elx800TM, Bio-Tek, and Winooski, VT, USA).

**Study animals**

Forty Male Wistar rats weighting 200–250 grams at age of 8–10 weeks were purchased from the National Center for Drug Control and Research (NCDCR) (Baghdad, Iraq), and were maintained in an air-conditioned room with the mean temperature of 22-25°C and hu-midity of 55% ± 5% with a 12-hour light/12-hour dark cycle. All the rats were provided with commercially available rat normal pellet diet, which contained carbohydrate 60% (w/w), fat 2% (w/w), protein 17.5% (w/w), and fiber 8% (w/w), and water ad libitum. The rats were allowed one week to acclimate to the animal house environment before the commencement of our experiment. Institutional Review Board of College of Medicine / Al-Nahrain University, Baghdad, Iraq approved the study protocols.

**Induction of obesity**

According to the diet-induced obesity model in the study of Aranaz et al., 2017 (23), Thirty Wistar male rats were fed a high-fat diet (HFD) with a total kcal value of 4.73 kcal/ g (45 kcal% energy as fat, 20 kcal% as protein, and 35 kcal% as carbohydrate ) for a period of 8 weeks. The tested rats with BMI greater than 0.68 g/cm2 were selected for the experimental work (24). The control group rats have
received a regular diet which is a standard pellet containing required mineral and vitamins while other groups of rats were continued to receive a high-fat diet during the course of the experimental period for additional 4 weeks. Animals had ad libitum access to their specific diet and tap water.

**Experimental Design**

In this experimental study, 40 male Wistar rats were randomly allocated (simple randomization) to four groups (ten rats in each group). One group was randomly selected and assigned as the control group (group 1) and obesity was induced in three other groups by the administration of HFD. Salix Alba barks were dissolved in distilled water (DW) and Orlistat was suspended in 0.1% DMSO and administrated orally once a day in the morning for 28 days. The studied groups and attributed treatments were as follow:

- **Group 1**: control (DW)
- **Group 2**: Obese control (DW)
- **Group 3**: Obese + Orlistat (35 mg/kg/day)
- **Group 4**: Obese + Salix Alba barks (150 mg/kg/day)

The initial body weight of all animals was measured before they are administered any drug, and the bodyweight of rats was individually recorded every week. At the end of the intervention trial, the weight gain (%) was calculated to indicate the incidence of obesity as follow:

\[
\text{Weight gain (\%)} = \frac{\text{Final body weight (g) - Initial body weight (g)}}{\text{Initial body weight (g)}} \times 100\%
\]

In addition, the body length was measured before they were administered any drug and at the end of each week. The Body mass index (BMI) was calculated according to the formula:

\[
\text{Body mass index (BMI)} = \frac{\text{body weight (g)}}{\text{body length (cm)}}^2
\]

The BMI for male adult Wistar rats ranged between 0.45 and 0.68 g/cm2, and any value above these limits considered as an indicator of obesity. At the end of the intervention trial, the body mass index change (BMI Δ) between BMI at zero-day and BMI at 28 days, was calculated to determine the obesity index in rats. Serum adiponec tin, leptin, visfatin, TNFα, and IL10 were documented after 28 days in a fasting condition. The animals were anesthetized using inhalation of diethyl ether. A blood sample was collected by cardiac puncture and serum was separated immediately. The animals were anesthetized using inhalation of diethyl ether. A blood sample was collected by cardiac puncture and serum was separated immediately.

**Statistical analysis**

Data were summarized, analyzed and presented using two software programs: SPSS (statistical package for social sciences) version 23 and Microsoft Office Excel 2013. Quantitative (numeric) variables were expressed in the form of mean and standard deviation. One way ANOVA was used to study the difference in mean of numeric variables among more than two groups; then followed by post hoc least significant difference (LSD) test to evaluate the mean difference between any two groups. The level of significance was considered at \( P \leq 0.05 \) (25).
Results & Discussion

Effect of Orlistat and *Salix alba* Barks on body weight

In comparison between HFD induced obese group and control group, we found a highly significant increase (P<0.01) in means for body weight gain % and body mass index change of the HFD group. When compared the means of weight parameters of Orlistat and Salix Alba treated groups with HFD induced obese group, we noticed that there is a significant decrease (P<0.05) in both weight parameters means in both treatment groups. In comparison between the two treatment groups, we found that metformin showed a non-statistically significant reduction in body weight gain % and body mass index change compared to Salix Alba animals, as shown in table (1).

Table (1): Mean body weight gain percentage and body mass index change in the control, obese control and study treatment groups.

<table>
<thead>
<tr>
<th>Type</th>
<th>Mean ±SD Control Group</th>
<th>Mean ± SD High Fat Diet group</th>
<th>Mean ± SD Orlistat Group</th>
<th>Mean ± SD <em>Salix Alba</em> Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight gain%</td>
<td>26.51±3.38 C</td>
<td>30.73±4.78 A</td>
<td>16.0 ±3.36 B</td>
<td>16.47 ±4.68 B</td>
</tr>
<tr>
<td>Body mass index Δ</td>
<td>0.14 ±0.01 C</td>
<td>0.23±0.02 A</td>
<td>0.11 ±0.02 D</td>
<td>0.12 ±0.02 D</td>
</tr>
</tbody>
</table>

Capital letters for comparison among groups; similar letters for no difference; different letters for significant differences; SD: Standard deviation.

The only study that investigated the effect of *Salix alba* barks on body weight conducted by Armstrong et al. (26), and stated the significant weight loss effect but this study has several limitation, most important them was administration of thermogenic supplement containing seven herbal constituents one of them is *Salix alba* barks and this supplement contains ephedrine which is potent approved antiobesity drug. Also, this study implemented on small sample size (only 14 subjects). The antiobesity effect of this herbal medicine may be contributed to its different phytochemical constituents from which, Salicortin, a salicylate glycoside, abundant the Salicaceae family, having the most potential to inhibit adipogenesis in the 3T3-L1 cell line (27). Also, chlorogenic acid improve body weight, lipid metabolism, and obesity-related hormones levels in high-fat-fed mice by its ability to significantly inhibit fatty acid synthase, 3-hydroxy-3-methylglutaryl CoA reductase, and acyl-CoA: cholesterol acyltransferase activities, while they increased fatty acid β-oxidation activity and peroxisome proliferator-activated receptors α expression in the liver compared to the high-fat group (28).
Epicatechin, one of *Salix alba* components has anti-obesity effects through diverse mechanisms include increased fat oxidation, stimulation of sympathetic nervous system activity, upregulation of mRNA level of fat β-oxidation genes, downregulating the expression of enzymes involved in fat synthesis, and increased expression of adipose tissue uncoupling proteins. Many of these effects are exerted through the induction of genes or inhibition of transcription factors. By correction of colonic microbiota, catechins improve the production of small absorbable metabolites in the colon, which can display anti-obesity effects after absorption (29). Epicatechin showed the potent inhibitory effect of pancreatic lipase enzyme so decrease fat absorption (30). Rutin, a natural compound of *Salix alba* regulated whole-body energy metabolism by enhancing brown adipose tissue activity. Rutin treatment significantly reduced adiposity, increased energy expenditure, and improved glucose homeostasis in both genetically obese (Db/Db) and diet-induced obesity mice (31).

**Effect of Orlistat and *Salix alba* Barks on lipid profile**

In comparison between HFD induced obese group and control group, we found highly significant increase (P<0.01) in means for serum total cholesterol, triglyceride, low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) of HFD group, except high-density lipoprotein (HDL) that shows significant decrease (P<0.05) in its mean. When compared the means of lipid profile parameters of Orlistat and Salix Alba treated groups with obese group, we noticed that there is significant decrease (P<0.05) in cholesterol, triglycerides, LDL and VLDL means in both treatment groups, while the results revealed significant increase (P<0.05) in HDL mean for all treated animals. In comparison between the two treatment groups, we found that Orlistat showed statistically significant improvement (P<0.05) in triglycerides VLDL, LDL and HDL compared to Salix Alba, while we revealed non-statistically significant improvement with respect to Salix Alba treated rats, as shown in table (2).

**Table (2): Mean serum lipids in the control, obese control and study treatment groups**

<table>
<thead>
<tr>
<th>Type</th>
<th>Mean ± SD Control Group</th>
<th>Mean ± SD High Fat Diet group</th>
<th>Mean ± SD Orlistat Group</th>
<th>Mean ± SD Salix Alba Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>65.40 ±5.20 C</td>
<td>134.21 ±17.7 A</td>
<td>101.70 ±6.30 B</td>
<td>103.15 ±9.71 B</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>85.81 ±7.80 C</td>
<td>120.97 ±11.4 A</td>
<td>105.90 ±9.37 B</td>
<td>113.98 ±7.90 D</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>91.91 ±11.60</td>
<td>56.72 ±5.40</td>
<td>60.17 ±5.20</td>
<td></td>
</tr>
</tbody>
</table>
18.79 ±2.40 
C 
A B E 

VLDL (mg/dl) 
17.16 ±3.40 
C 
24.19 ±2.40 
A 
21.18 ±1.90 
B 
22.79 ±1.68 
D 

HDL (mg/dl) 
29.45 ±3.16 
C 
18.11 ±1.82 
A 
23.80 ±2.33 
B 
20.19 ±3.77 
E 

Capital letters for comparison among groups; similar letters for no difference; different letters for significant differences; SD: Standard deviation.

The suggested explanations for these effects are the presence of chlorogenic acid and epicatechin in our herb that could be sharing the responsibility for the hypolipidemic effect found here. Reinforcing this notion, some studies performed by Li et al. (32) and Wan et al. (33) reported the modulation of lipid metabolism by chlorogenic acid decreasing TC, TG, and LDL but not increasing HDL levels. Although, Nishi and Kumar (34) showed increment in HDL level, besides the improvement on the lipid profile. The effects may be due to up-regulating the expression of hepatic erxosome proliferator-activated receptor (PPAR-α). The results of Lin CH et al. (35) study on mice treated with epicatechin stated the increased expression of fatty acid oxidation enzymes, including peroxisome proliferator-activated receptor α (PPARα) and mRNA levels of carnitinepalmitoyltransferase1a. These mice also expressed lower levels of lipogenic genes such as fatty acid synthase (FAS), as well as lower mRNA levels of sterol regulatory element-binding protein 1c and liver adipocyte fatty acid-binding protein 2, leading to a reduction in plasma triglyceride levels. On the other side, the hypolipidemic activity of Salix Alba extract could be attributed to an increase in insulin concentration. Insulin has many important functions including activating lipoprotein lipase, hydrolyzing triglycerides, increasing the uptake of fatty acids into adipose tissue, increasing triglyceride biosynthesis and inhibiting lipolysis (36).

Effect of Orlistat and Salix alba Barks on Adipokines

In comparison between HFD induced obese group and control group, we found a highly significant increase (P<0.01) in means for serum total visfatin and leptin of HFD group, except adiponectin that shows a significant decrease (P<0.05) in its mean. When compared the means of adipokines parameters of Orlistat and Salix Alba treated groups with the obese group, we noticed that there are significant decrease adipokines parameters in visfatin and leptin means in both treatment groups, while the results showed a significant increase (P<0.05) in adiponectin mean for all treated animals. In comparison between the two treatment groups, we found that Orlistat showed statistically significant improvement.
(P<0.05) in leptin compared to Salix alba, while we discovered statistically significant improvement (P<0.05) in adiponectin with respect to Salix Alba, whereas we revealed non-statistically significant improvement in visfatin with respect to Salix Alba, as shown in table (3).

**Table (3): Mean serum adiponectin, leptin and visfatin in the control, obese control and study treatment groups**

<table>
<thead>
<tr>
<th>Type</th>
<th>Mean ± SD Control group</th>
<th>Mean ± SD High Fat Diet group</th>
<th>Mean ± SD Orlistat Group</th>
<th>Mean ± SD Salix Alba Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adiponectin (ug/ml)</td>
<td>3.87 ±0.24 A</td>
<td>3.47 ±0.70 D</td>
<td>4.71 ±0.56 B</td>
<td>3.95 ±0.71 A</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>2.61 ±0.23 C</td>
<td>5.17 ±1.17 A</td>
<td>3.90 ±1.30 D</td>
<td>4.38 ±1.90 E</td>
</tr>
<tr>
<td>Visfatin (ng/ml)</td>
<td>20.34 ±6.23 C</td>
<td>47.45 ±7.35 A</td>
<td>36.58 ±8.73 B</td>
<td>38.14 ±8.59 B</td>
</tr>
</tbody>
</table>

Capital letters for comparison among groups; similar letters for no difference; different letters for significant differences; SD: Standard deviation.

The level of visfatin decreased upon treatment with Salix alba barks product. This influence due to Salix alba enhances insulin sensitivity and insulin upregulated visfatin protein expression, which was subsequently attenuated by it. The action of insulin on visfatin expression may occur indirectly, in part, through the up-regulation of IL-6 in abdominal adipose tissue. These studies also established that visfatin appears to be regulated via both NF-κB and c-Jun Kinase \(^{(37)}\). Our findings also showed Salix alba down-regulate circulating visfatin concentrations, paralleled with a significant reduction in insulin levels, in vivo. So, depending on the following facts, the reducing effect of both agents on visfatin concentration relies on their ability to decrease circulating insulin level as cleared in our study and to down-regulate IL6 as shown in Drummond et al study \(^{(38)}\).

The findings of our current experimental work cleared the lowered level of adiponectin after Salix Alba treatment, these actions may be due to the collective impact of different phytochemical constituents of our extract product. The mechanisms responsible for these actions may occur through an adiponectin receptor-mediated signaling pathway. Chlorogenic acid elevates the adiponectin level in visceral fat and the adiponectin receptors in liver and muscle in db/db mice \(^{(39)}\). Also, there were showed a decrease in adipose tissue NF-κB and an increase in adiponectin in the salsalate treated group in another
In another study by Cho et al. (2007), catechin increased expression and secretion of adiponectin in murine adipocytes 3T3-L1 (41). Also, Salix alba bark extract increase and normalize leptin concentrations compare to the FSTZ group. Leptin secretion by adipocytes is stimulated by insulin, and plasma leptin significantly correlates with plasma insulin (42). Thus the improving effect of Salix alba on plasma insulin level may play a role in leptin normalization. While the leptin reduction effect of Salix alba barks in HFD induced obese rats may be due to the effect of salicin as its main active constituent. Salicin is AMPK activator (43), mTORC1 is already suppressed as a result of activated AMPK and suppressed mTORC1, reduce the translation of leptin mRNA and down-regulates promoter activity for leptin genes (44).

### Effect of Orlistat and Salix alba Barks on inflammatory cytokines

In comparison between HFD induced obese group and control group, we found a highly significant increase (P<0.01) in mean for serum TNFα of HFD group, and a significant decrease (P<0.05) in serum IL10 mean. When compared the means of inflammatory cytokines parameters of Orlistat and Salix alba treated groups with the obese group, we noted that there is significant decrease (P<0.05) in TNFα means in both treatment groups, while the results demonstrated significant increase (P<0.05) in IL10 means for Salix alba treated animals only. In comparison between the two treatment groups, we found that Orlistat showed statistically significant improvement (P<0.05) in TNFα compared to Salix alba, while we noticed a non-significant improvement in IL10 when compared with Salix Alba, as shown in table (4).

**Table (4): Mean serum TNF and IL10 in the control, obese control and study treatment groups**

<table>
<thead>
<tr>
<th>Type</th>
<th>Mean ±SD Control group</th>
<th>Mean ± SD High Fat Diet group</th>
<th>Mean ± SD Orlistat group</th>
<th>Mean ± SD Salix Alba Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF α (pg/ml)</td>
<td>20.15±6.38 C</td>
<td>47.67±7.78 A</td>
<td>25.70 ±10.36 B</td>
<td>22.25 ±8.68 B</td>
</tr>
<tr>
<td>IL 10 (pg/ml)</td>
<td>48.02±10.2 C</td>
<td>26.87 ±7.39 A</td>
<td>27.23 ±8.24 A</td>
<td>53.68 ±8.69 B</td>
</tr>
</tbody>
</table>

*Capital letters for comparison among groups; similar letters for no difference; different letters for significant differences; SD: Standard deviation.*

In the present study, the treatment with Salix alba barks resulted in a significant reduction and elevation in serum TNF α and IL10 levels respectively. These findings may be contributed to different phytochemical constituents of this product. Firstly, Salicin markedly decreased TNF-α, IL-1β and IL-6 concentrations and increased IL-10 concentration. In addition, western blot analysis indicated that
D(-)-Salicin suppressed the activation of MAPKs and NF-κB signaling pathways stimulated by LPS \(^{(45)}\). NF-κB is a key transcription factor involved in the regulation of pro-inflammatory cytokines and chemokines, such as TNF-α. There are many reports on the inhibition of the NF-κB signaling pathway by various flavonoids through inhibition of NF-κB translocation, NF-κB-dependent transcriptional activity, and iNOS expression by the inhibition of IκB degradation \(^{(46)}\). Recent studies reported that the protective role of quercetin or catechin against inflammatory reactions was related to MAPKs pathways \(^{(47)}\). Catechin alone significantly inhibited the phosphorylation of three MAPK family proteins (ERK, p38, and c-JUN) \(^{(48)}\). Also, catechin up-regulates the number and anti-inflammatory activity of Tregs through chromatin remodeling by alteration of histone acetylation – deacetylation and suppression of NF-kB, leading to the induction of IL10 release \(^{(49)}\).

**Conclusions**

*Salix alba* barks have a positive role in body weight reduction in obese rats. *Salix alba* barks have some advantageous effect on lipid parameters especially by elevating HDL and reducing total cholesterol, TG and LDL. *Salix alba* barks inhibit metabolic inflammatory response associated with obesity which might further contribute to its effect in the management of such cases. *Salix alba* barks have a profound improving effect on adipokines released from adipose tissue during obesity, explaining their roles in the management of these metabolic abnormalities.

**References**


