Effects of *Aralia mandshurica* and *Engelhardtia chrysolepis* Extracts on Some Parameters of Lipid Metabolism in Women with Nondiabetic Obesity

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The effects of oral treatment with Aralox phytopreparation containing *Aralia mandshurica* (*Araliaceae*) and *Engelhardtia chrysolepis* (*Juglandaceae*) extracts on some parameters of lipid metabolism was studied in women with nondiabetic obesity receiving low-caloric diet. Our randomized placebo-controlled study comprising 32 volunteers showed that aralox treatment led to a decrease in total body weight and fat weight, reduced perilipin content in adipocytes and plasma triglyceride content, and stimulated activity of hormone-sensitive lipase.

Key Words: *Aralia mandshurica; Engelhardtia chrysolepis; hormone-sensitive lipase; perilipins; triglycerides*

Combined use of aralosides from *Aralia mandshurica* and dehydroquercetin-3-rhamnoside from *Engelhardtia chrysolepis* leaves stimulates hormone-sensitive lipase (HSL) and destroys the perilipin defense of lipid drops in adipocytes. Aralosides and dehydroquercetins are used individually and are safe for long-term use in pharmacologically effective doses [1-3].

We evaluated combined effects of aralosides and dehydroquercetin-3-rhamnoside as components of aralox on fat deposition, HSL activity, perilipin content in adipocytes, and plasma concentrations triglycerides and fatty acids (FA) in women with nondiabetic obesity receiving low-caloric diet.

MATERIALS AND METHODS

Randomized placebo-controlled study was carried out over 15 weeks and comprized 32 women with nondiabetic obesity (body weight 94.4±5.0 kg, body weight index (BWI) 25.2-33.4 kg/m^2, age 42±12 years). The criteria for selection into the study group were the absence of clinically diagnosed signs of diabetes, renal and thyroid diseases. The patients received no drugs modulating lipid metabolism and had no regular exercises. The patients received aralox (main group, n=16) or placebo (control group, n=16) 3 times daily 30-45 min before meals. A single dose of aralox included 150 mg *Aralia mandshurica* extract containing at least 20% triterpene saponines (aralosides) and 150 mg extract from *Engelhardtia chrysolepis* leaves containing at least 20% flavonoid (dehydroquercetin-3-rhamnoside). Daily diet was limited to 1700±100 kcal (50% carbohydrates, 25% proteins, and 25% fat). The caloricity of food was controlled by measuring urinary osmolar index [12] using a microosmometer (Needham, MA). Analysis of adipose tissues, food, and blood, measurements of body weight and fat content were carried out before and after aralox/placebo treatment. The concentrations of dehydroquercetins and aralosides in dry extracts were mea-

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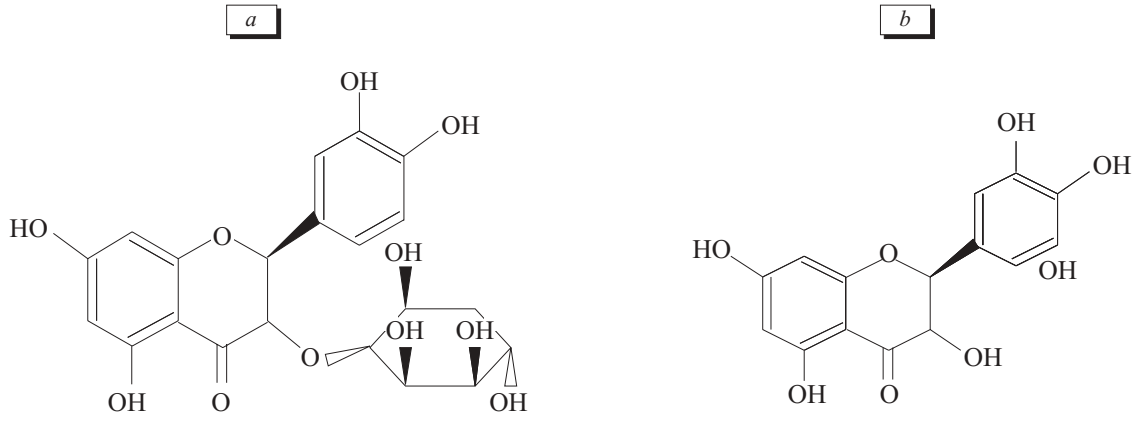

Fig. 1. Chemical structure of dehydroquercetin-3-rhamnoside (*a*) and dehydroquercetin (*b*) isolated from *Engelhardtia chrysolepis*.

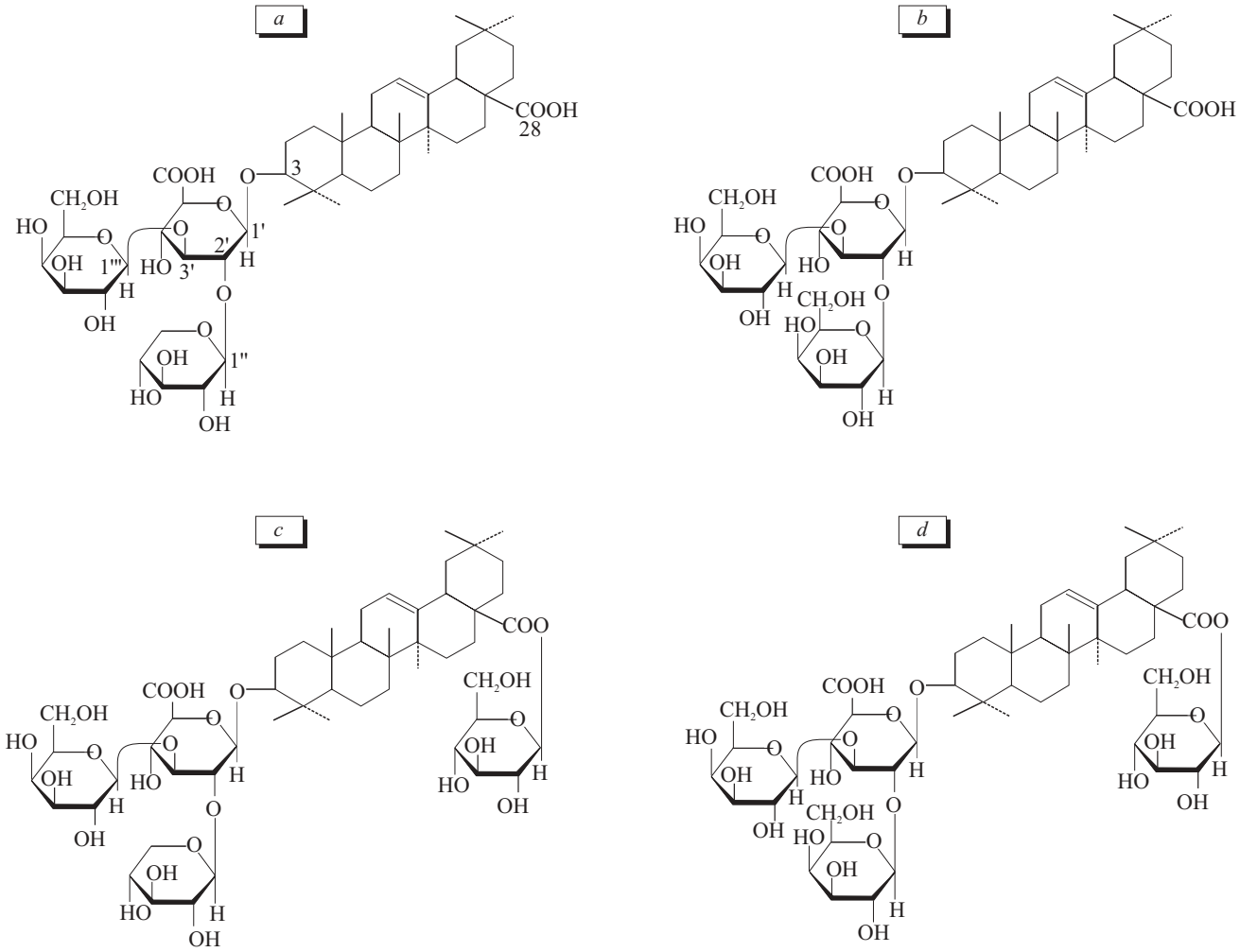

Fig. 2. Chemical structure of aralosides isolated from *Aralia mandshurica*. *a*) araloside A; *b*) araloside B; *c*) araloside C; *d*) araloside D.

sured by HPLC on a C18 reverse phase column (3.9×150.0 mm; Axis HPLC Column, MicroSolv Technology Corp.). Reference samples of dehydroquercetin-3-rhamnoside and dehydroquercetin for quantitative evaluation were gracious gifts from Institute of Biochemistry, Academy of Sciences of Georgia (Fig. 1). Araloside A reference sample was isolated in the Polinat SL (Fig. 2).

The weight of fat deposition was estimated [13] and plasma concentrations of triglycerides and FA

were evaluated as described previously [7]. Adipocyte HSL activity was evaluated using subcutaneous fat specimens (0.4-0.5 g) collected 1 day before aralox treatment and after 15-week course as described previously [6,11]. Perilipin content was measured in the fraction of lipid drops isolated from the same adipose tissue specimens by PAAG immunoelectrophoresis [9] with antibodies to perilipin (gift from Technological Institute of Canary Islands). The relative concentration of perilipin was measured using a Hoefer GS-300 scanning densitometer.

RESULTS

Thirteen women from the main group and 14 controls completed the 15-week study. No appreciable differences in physical characteristics and nutrition of examined patients in the two groups were detected before aralox/placebo treatment (Table 1).

Patients receiving aralox 3 times daily lost 4.3±0.7 kg ($p<0.001$) over 15 weeks *vs.* 0.7±0.2 kg in the placebo group (Table 2). Body weight loss under the effect of aralox was by 95% due to fat loss.

Immunoelectrophoresis of lipid drop fraction isolated from adipose tissue specimens showed 62-65 kDa proteins corresponding to perilipins. Perilipin content in adipocytes of patients treated with aralox decreased by 27.01±2.70% ($p<0.05$). No appreciable shifts in perilipin content were observed in the control group (Table 2). A course of aralox treatment promoted an increase in adipocyte HSL activity from 5.2±1.1 to 8.1±1.4 U/mg protein ($p<0.001$), while controls had virtually no changes in this parameter. Plasma FA level increased from 730±40 to 870±50 μmol/liter in the main group and remained unchanged in the placebo group. Aralox reduced the content of plasma triglycerides from 3.6±0.2 to 1.8±0.7 mmol/liter; in the controls triglyceride level did not change.

Adipocyte HSL and perilipin proteins play an important role in the regulation of lipolytic processes. HSL are responsible for triglyceride cleavage into glycerol and free FA in adipocyte lipid drops [8,10]. Lipolytic hormones activate HSL by stimulating its enzymatic activity and/or promoting its translocation from the cytoplasm to the periphery of the lipid drops [15]. Perilipin protein is located at the periphery of the lipid drop [5] and

TABLE 1. Main Physical Parameters of Examined Women and Nutrition Characteristics

Parameter	Placebo group (n=14)	Aralox group (n=13)
Physical characteristics		
age, years	43±12	42±10
heigth, cm	172±17	170±15
Daily food consumption		
total caloricity, kcal	1700±150	1700±160
carbohydrates*	50.0±5	50.0±5
fats*	25±2	25±2
protein*	25±2	25±2

Note. *Percentage of total food consumption.

TABLE 2. Aralox Effect on Some Parameters of Lipid Metabolism in Women with Nondiabetic Obesity

Parameter	Initial value		After 15 weeks	
	aralox	placebo	aralox	placebo
Body weight, kg	94.4±5.0	94.2±5.8	90.1±2.2^{+} (-4.6±1.3%)	93.7±3.0 (-0.5±0.2%)
Fat deposition weight, kg	33.3±2.2	33.6±2.1	29.2±1.2^{*+} (-12.3±3.3%)	32.9±1.4 (-2.1±0.6%)
Body weight without fat, kg	61.1±2.1	60.6±1.8	60.9±1.3 (-0.3±0.2%)	60.4±0.6 (-0.3±0.2%)
Adipocyte perilipins, arb. units	60.7±10.6	60.2±12.5	44.3±14.5^{*+} (-27.0±2.7%)	58.1±11.2 (-3±1%)
Plasma triglycerides, mmol/liter	3.6±0.2	3.5±0.5	1.8±0.7^{*+} (-49.2±5.5%)	3.4±0.8 (-2.8±5.2%)
FA, μmol/liter	730±40	740±30	870±50^{*+} (+16.1±2.1%)	755±45 (+2.0±0.2%)
HSL, U/mg protein	5.2±1.1	5.1±0.9	8.1±1.4^{*+} (+35.8±4.6%)	5.2±1.2 (+1.9±0.3%)

Note. $p<0.05$ compared to: *initial value, $^{+}$placebo.

acts as a barrier preventing HSL access to triglycerides [4,14]. Hence, HSL and perilipin proteins are targets for effective treatment or prevention of obesity. It seems that destruction of the perilipin barrier around lipid drops and activation of HSL are responsible for the decrease in the content of adipose tissues in patients receiving the test phytopreparation. Aralox in parallel with not very stringent diets can be recommended for reduction of body fat weight and plasma triglyceride level in women suffering from nondiabetic obesity.

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