Free-fatty-acid-regulating effects of fermented red ginseng are mediated by hormones and by the autonomic nervous system

Kwang Jo Lee 1, Geun Eog Ji 1,2,*

1 Department of Food and Nutrition, Research Institute of Human Ecology, Seoul National University, Seoul, Korea
2 Research Center, BIFIDO Co. Ltd, Kangwon, Korea

1. Introduction

Of the primary energy sources in the human body (carbohydrates, proteins, and lipids), lipids are the most efficient type of energy storage (9 kcal/g) and are hence much more prevalent than carbohydrates or proteins as a form of storage [1]. This makes the process of lipid release a crucial component in understanding human energy metabolism and pathology. Several studies have reported that the incidence of metabolic syndrome in postmenopausal women is higher than in premenopausal women and that the causes are related not only to estrogen levels but also to the levels of other hormones related to lipid metabolism [2].

The chronic override of free fatty acids (FFA) in the blood may be a risk factor in human energy metabolism. A high level of FFA often correlates with type 2 diabetes, hypertension, dyslipidemia, insulin resistance, hyper uric acid, and abnormal fibrinolysis [3]. Obese individuals commonly show insulin resistance; correspondingly, their levels of fatty acids are also elevated. The most common cause of the positive correlations between FFA and several diseases is the competition between override FFA and carbohydrates in the energy oxidation process [4]. Boden et al [5] reported that after lipids were administered to test volunteers, lipid oxidation increased and carbohydrate oxidation decreased simultaneously. Compared to healthy volunteers, diabetic patients showed a 40–55% decrease in their insulin-stimulated glucose absorption rates [6].

Energy metabolism differs between the postprandial and fasting states. In the postprandial state, carbohydrates are used as a major energy source and insulin is released. In the fasting state, adipocytes release triglycerides, which are broken down into FFA and glycerol, which then enter the circulatory system. During the overnight fasting period, the burst size of FFA during the daily cycle is maximized [7].

In a fasting state, over the long term, basal metabolic lipolysis occurs when insulin levels and catecholamine levels decrease.

* Corresponding author. Department of Food and Nutrition, Research Institute of Human Ecology, Seoul National University, Seoul 151-742, Korea.
E-mail address: geji@snu.ac.kr (G.E. Ji).

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.
In the short term, acute lipolysis occurs in “fight or flight” (emergency) states. In this state, catecholamines are triggered by the sympathetic nerve system [8]. In cell membranes, those catecholamine signals stimulate β-adrenergoreceptors, which activate adenyl cyclase via simultaneous G-protein coupled receptors. Adenyl cyclase then transforms adenosine triphosphate into cyclic adenosine monophosphate (cAMP). The cAMP then binds to the regulatory module of the protein kinase A, activating it, which then phosphates hormone-sensitive lipase (HSL) [9].

Both long- and short-term lipolyses are affected by several hormones. Glucocorticoid [10], adrenocorticotropic hormone (ACTH) [11], thyroid hormone, dehydroepiandrosterone [12], inhibition of adenylyl cyclase, the activities of G-proteins, or phosphates hormone-sensitive lipase (HSL) [9].

In the short term, acute lipolysis occurs in estrogen receptor (ER) [20], which implies a possible effect of hormones, including insulin and the branchial pulse rate (the autonomic nervous system activity) affected the flux of FFA in the blood. For this analysis, a path model was established and estimates of the model fit and the hypothesis were then tested. The second aim of this study was to test whether FRG consumption affects the relationship between the independent variables of several hormones and the autonomic nervous system and the dependent variable of FFA.

The study hypotheses were: (1) ACTH, growth hormone (GH), E2, glucocorticoid, tri-iodothyronine (T3), thyroid-stimulating hormone, and/or insulin influence the release of FFA; (2) the branchial pulse rate, which represents the activity of the autonomic nervous system and affects the release of FFA from adipocytes; and (3) the consumption of FRG changes the rate of FFA release, and this release is mediated by FRG on ER or GR.

2. Materials and methods

2.1. Participants and study design

This study was approved by the Institutional Review Board of Sahmyook University (Seoul, Korea). The study participants were 117 postmenopausal women (age 50–73 yr) who were recruited from four Catholic churches. Participants with any disease, including diabetes, cardiovascular disease, dyslipidemia, and kidney disease, were excluded. None of the study participants took any supplements for 2 wk prior to or during the experiment.

 Anthropometric parameters were used to evaluate and categorize the 117 participants, who then had their branchial and ankle blood pressure and brachial and ankle blood pulse measured twice, once in the supine position and again after a 10-min rest period. Although the branchial and ankle pressures and pulse rate vary according to the spectrum of life activity, the pressure and the pulse in the supine position can be considered as the pressure and the pulse of a participant in a resting state.

After overnight fasting, blood and urine samples from the 117 participants were collected from 8:00 AM to 10:00 AM. The study participants were then divided into two groups according to the double-blind method of drawing lots. One group was supplied with capsules containing FRG powder (Bifido Inc., Gangwon-do, Korea), and the other group was supplied with placebo capsules containing edible starch for 2 wk. Because a hypothesis of this study was that ginsenosides are ligands of nuclear receptors and that the effects of a nuclear receptor can begin within 2 h, we considered that 2 wk of FRG consumption was significant.

The ingredients of the FRG capsules were as follows: crude saponin, 258.6 mg/g; compound K, 57.05 mg/g; Rg3, 53.85 mg/g; Rh2, 11.97 mg/g; Rg2, 5.72 mg/g; Rh1, 2.99 mg/g; and Rb1, 0.023 mg/g. The total weight of the FRG capsule powder was 2.1 g. After 2 wk, 24 women dropped out of the study; therefore, 93 women (49 in the FRG group and 45 in the placebo group) participated in the second blood sample collection. The reported cause of departure for 23 of the women was individual personal reasons not related to FRG consumption. One woman left the experiment after reporting insomnia associated with her consumption of FRG (Fig. 1).

Blood samples were measured at the Green Cross Reference Laboratory (Gyeonggi-do, Korea). The methods of sample analysis are listed in Appendix I.

As well as the reported effects of ginseng on FFA, red ginseng has also been shown to have a beneficial effect on insulin and glucose regulation. Vulkan et al [23] reported that red ginseng consumption improved insulin and glucose regulation in type 2 diabetes patients. Lee et al [24] showed that red ginseng has a beneficial effect on insulin sensitivity. We also reported that fermented red ginseng (FRG) showed a serial causal effect on the level of hormones, insulin resistance, and insulin levels. In an analysis of the effects of hormones on glucose blood levels, the difference between the FRG group and the placebo group was due to the level of aldosterone [25].

According to an experiment with mice, ginsenosides stimulated an acetylcholine release in the terminal of cholinergic neurons [26]. In a human study with 120 adult men, wild ginseng increased the activity of the autonomic nerves and increased the heart rate [27].
Blood samples from 20 women/group were further collected and matched according to age, height, weight, and body mass index.

2.2. Statistical analyses

The arithmetic means of the variables from both groups were analyzed by SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). The outliers of insulin and E2 were excluded and considered as missing values. Unmeasured variables were considered as random missing values and 10 datasets were generated by a multiple imputation method [28].

Path analysis has several advantages in that several variables and multiple groups can be analyzed simultaneously; moreover, the effects of decomposition and model fitness can be assessed. We used path analysis as well as traditional statistics including mean comparisons in this study. The path model was analyzed with Mplus 6.11 (Muthén & Muthén, Los Angeles, CA, USA). The data in this report are part of an FRG study that was conducted in Seoul, Korea in 2010. Only the data relevant to this analysis are presented in this report.

3. Results

3.1. Anthropometric data

There were no significant differences in age, weight, height, and body mass index between the FRG group and the placebo group (Table 1).

3.2. Arithmetic mean comparisons

Hormones showed circadian variation and seasonal variation. Despite the fact that a double-blind random sampling method was utilized in this study, there was sampling error. Therefore, the analyses of the hormones and other variables required crosstalk validation and a comprehensive assessment. We analyzed the mean comparisons of samples between the FRG group and the placebo group with three statistical methods: an analysis of covariance (ANCOVA) in the second samples (ANOVA comparison), independent t tests of the second samples (second sample t test), and independent t tests of the differences between the second and first samples (difference t test; Table 2).

In the ANCOVA comparison, the mean values of ACTH, cortisol, T3, and FFA did not show a significant difference between the two groups, whereas the level of insulin was lower in the FRG group than it was in the placebo group (p = 0.04). In the difference t test, the level of insulin was found to be lower in the FRG group than in the placebo group (p = 0.01). In the ANCOVA comparison, the level of dehydroepiandrosterone was higher in the FRG group than it was in the placebo group (p = 0.05), and the same result was shown in the difference t test (p = 0.03). In the ANCOVA comparison, the levels of E2 (p = 0.06) and GH (p = 0.06) were higher in the FRG group than in the placebo group, but the differences were not statistically significant (Table 2).

3.3. Path model

The baseline model was established based on reports in the literature. The Wald test was conducted to test the hypothesis of

Table 1

| Anthropometric Data of Participants | Mean ± SD (FRG) | Mean ± SD (Placebo) | p       |
|------------------------------------|----------------|---------------------|---------|
| Age (yr)                           | 58.5 ± 5.5     | 58.6 ± 5.8          | 0.944   |
| Weight (kg)                        | 56.9 ± 6.7     | 57.7 ± 6.9          | 0.559   |
| Height (cm)                        | 157.7 ± 5.3    | 156.6 ± 5.4         | 0.311   |
| BMI (kg/m²)                        | 22.88 ± 2.39   | 23.55 ± 2.51        | 0.189   |
| Waist circumference (cm)           | 32.7 ± 2.3     | 33.1 ± 2.4          | 0.397   |
| Hip circumference (cm)             | 36.5 ± 2.0     | 37.3 ± 2.1          | 0.284   |
| Waist/hip                          | 0.89 ± 0.03    | 0.89 ± 0.04         | 0.965   |

BMI, body mass index; FRG, fermented red ginseng; SD, standard deviation.
whether or not there was a significant difference between groups for each path. The path of cortisol on FFA and the path of the brachial pulse rate on FFA both showed a significant difference between the two groups (Table 2).

The final model was then established (Fig. 2 and Table 4). The path of cortisol on FFA and the path of the brachial pulse rate on FFA were measured freely, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients of the path of cortisol on FFA and the values of the unstandardized coefficients of the path of the brachial pulse rate on FFA were two in both cases, and the values of the other unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.

When the effects of several independent variables on the FFA levels were compared with standardized coefficients, the path coefficients of E2 on FFA were highest at 0.678 in the FRG group, whereas the other paths were analyzed with equality constraints (Fig. 2). Therefore, the values of the unstandardized coefficients were one (Fig. 2). The final model’s goodness of fit was good, as the root mean square error of approximation was 0.000 and the comparative fit index was 1.000.
In the present study, the positive relationship between the concentrations of E2 and FFA may have been due to the fasting times and the lowered E2 levels of the postmenopausal women in the present study design. Because blood samples were collected after 8 h of overnight fasting, the migration effect of FFA from the circulatory system to the adipocytes can be ignored. However, it was possible to infer that genome independent lipolysis by E2 could stimulate HSL and inositol triphosphate receptor-mediated lipolysis by E2 are important for a proper understanding of the lipid metabolic process.

The effects of E2 on lipolysis are different between subcutaneous adipocytes and abdominal adipocytes. For example, E2 treatment decreased the level of lipolysis in the adipocytes, which mediated an increased number of α2A-adrenergic receptors, whereas E2 treatment did not show any effect on the lipolysis of the abdominal adipocytes [32]. In addition, abdominal adipocytes showed a low level of α-adrenergic receptors and a high level of β-adrenergic receptors when compared to the level of β-adrenergic receptors in subcutaneous adipocytes [33]. These differences in the ratio with regard to the adrenergoreceptor type may help to explain differences in gender-dependent spatial fat accumulation.

In the present study, the accumulation pattern for postmenopausal women is different from that for men [29]. In females, the major locations of fat accumulation are in the lower body and in subcutaneous tissue, whereas in males fat accumulates in the upper body and in the organs of the abdominal cavity (visceral fat). The fat accumulation area is important in relation to the onset of MtS [30] because released FFA from abdominal adipocytes are directly transported to the liver via the hepatic portal vein, resulting in a decrease in insulin clearance and an increase in the synthesis of triglycerides and very low density lipoprotein [31]. Therefore, the movement and accumulation effect of lipids by E2 are important for a proper understanding of the lipid metabolic process.
4.2. Cortisol and FFA

Djurhuus et al [34] reported that when a physiologically high level of cortisol was injected into the adipose tissue, the level of blood FFA increased by 60%, as mediated by lipolysis stimulation. In the final model here, the path coefficient value of cortisol on FFA was positive ($p = 0.002$) in the placebo group, whereas the path coefficient value was negative ($p = 0.082$) in the FRG group. Therefore, it may be presumed that CK consumption acts as a competitive inhibitor with cortisol of the GR in this study.

In a postprandial state, insulin is released and suppresses the functions of HSL and lipolysis in adipocytes. In a fasting state, however, the level of insulin decreases, and the levels of cortisol and growth hormone increase, which in turn stimulates the expression of HSL [35]. The proper expression of HSL is important in the regulation of blood glucose. HSL-deficient mice cannot release a proper level of FFA and thus enter an insulin-resistant state [36]. However, in the present study, the growth hormone and FFA showed a significant negative relationship. These results may be due to the decreased level of GH of the postmenopausal women owing to the natural process of aging. In fact, the explanation ability levels (SMC) of GH on the FFA concentration results were only 1% in the placebo group and 2% in the FRG group.

4.3. Brachial pulse rate and FFA

Although several studies have reported that the activity of the sympathetic nervous system is related to MTS [17,37], the exact mechanism of this has yet to be elucidated. Jeon et al [38] reported that when crude saponin, including ginsenoside, was intravenously injected into rats, their heart rates increased. Because GR and ER are present in the brain stem area, it may be presumed that CK and Rg3, ligands of GR and ER, regulate the autonomic nervous system via the central nervous system. Therefore, consecutively, brain stems that have GR and ER influenced by CK and Rg3 could have an effect on how FFA is released in adipocytes. If so, it would be of interest to assess whether CK or Rg3 has the strongest effect on the brachial pulse rate in this study. ER-$\alpha$ is present in the autonomic nerve center of the brain stem, which regulates the cardiovascular system [38]. When estrogen was administered into this area, autonomic nerve regulation of the heart improved and the level of sympathetic activity decreased [39]. Furthermore, when estrogen was injected into the brain of an ovariectomized rat, its heart rate decreased [40].

GR is highly expressed in the dorsal hindbrain area and is especially prominent in the nucleus of the solitary tract [41]. These areas are centers of cardiovascular regulation. When cortisol was injected into the dorsal hindbrain of a rat, its heart rate increased within 3 days [42]. Therefore, because the autonomic effect on FFA was increased in the FRG group, CK was shown to have a stronger effect in the FRG group as compared to the placebo group.

4.4. Counteraction between cortisol and the brachial pulse

In the final path model (Fig. 2 and Table 4), two paths showed significant differences between two groups, and the significance levels were changed between the two paths and two groups. In this case, the significance levels of the path coefficients of cortisol to FFA were significant in the placebo group ($p = 0.002$) but were not significant in the FRG group ($p = 0.082$). However, the significant level of the brachial pulse on the FFA path was not significant in the
placebo group ($p = 0.428$), although it was significant in the FRG group ($p < 0.001$). These results may help researchers establish the homeostasis levels of essential components such as the major energy source, FFA, in human physiology.

In the change of significance levels, one possible cause of the "rise and fall" phenomenon between the two groups is the nature of the glucocorticoid receptors (GR). GRs can be influenced by genetic variations, redundancies, synergy, crosstalk with other nuclear receptors, and by other types of cell signaling. Therefore, in the path of cortisol to FFA, some test participants showed a significant effect of FRG consumption, whereas others did not show a strong effect. However, for the complementary path of cortisol to FFA, the path of the brachial pulse rate to the FFA level showed that the "rise and fall" phenomenon or the "seesaw" phenomenon between the cortisol level and the brachial pulse rate was related to the homeostasis of FFA.

Regarding the methodology, these results are good examples that show that path analysis may be a useful tool for the simultaneous analysis and comparison of the effects of several independent variables on dependent variables with multiple groups.

5. Conclusions

Among the several variables in this study, estrogen best explained FFA fluctuations. The brachial pulse provided a better explanation of FFA variance in the FRG group than in the placebo group. Cortisol had a strong effect on FFA release in the placebo group, but it did not have this effect in the FRG group. These "seesaw" effects between the brachial pulse rate and cortisol imply multiple routes of human physiology as regards the homeostasis of FFA. In conclusion, FRG consumption changed the effect of cortisol on FFA levels from peripheral tissues to the autonomic nervous system, whereas the level of FFA and the effects of other variables on FFA remained unchanged.

The effect of ginsenosides on human physiology depends on the ratio, dose, and treatment period of the ginsenosides. A study with a single type of ginsenoside in different environments would improve our understanding of the effects of hormones on FFA levels.

Conflicts of interest

The contributing authors declare no conflicts of interest.

Acknowledgments

This work was supported by the Next-Generation BioGreen 21 Program (No. PJ009543), by the Rural Development Administration, and by the Small and Medium Business Administration (SA114187), all of the Republic of Korea. We thank Mr John Mensing, who assisted with the proofreading of the manuscript.
### Appendix I

#### Reagents and Instruments

| Test name | Glucose($) | Insulin | Cholesterol total | LDL Cholesterol | FFA |
|-----------|------------|---------|------------------|-----------------|-----|
| Test method | enzymatic method | ECLIA | Enzymatic, colorimetry | Enzymatic, colorimetry | ACS-ACOD (colorimetry method) |
| Reagent | Kit name | Company, nationality | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA |
| Analytical instrument | Model name | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA |
| Test name | Test method | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA |
| Reagent | Kit name | Company, nationality | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA |
| Analytical instrument | Model name | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA | Siemens, NY, USA |

**Reagents and Instruments**

**Test name** Cortisol, ACTH, DHEA-S, Estrogen (E2), HGH, FI: Neafra II, Luteinizing hormone, HCG, Human growth hormone, DHEAS, Dehydroepiandrosterone, FFA, Free fatty acid, FSH, Follicle stimulating hormone, LH, Luteinizing hormone, TSH, Thyroid-stimulating hormone.
Su CF, Cheng JT, Liu IM. Increase of acetylcholine release by Panax ginseng root enhances insulin secretion in Wistar rats. Neurosci Lett 2007;412:101–4.

Yook T, Yu J, Lee H, Song B, Kim I, Roh J, Shin J, Lim S. Comparing the effects of distilled Rehmannia glutinosa, Wild Ginseng and Astragali Radix pharmacopuncture with heart rate variability (HRV): a randomized, sham-controlled and double-blind clinical trial. J Acupunct Meridian Stud 2009;2:

Rubin DB. Multiple imputation for nonresponse in surveys. New York: John Wiley & Sons; 1987.

Mattiasson I, Rendell M, Torququist C, Jeppsson S, Hulthen UL. Effects of estrogen replacement therapy on abdominal fat compartments as related to glucose and lipid metabolism in early postmenopausal women. Horm Metab Res 2002;34:583–8.

Kiesselbach AH, Vydelingum N, Murray R, Evans DJ, Hartz AJ, Kalkhoff RK, Adams PW. Relation of body fat distribution to metabolic complications of obesity. J Clin Endocrinol Metab 1982;54:254–60.

Arner P. Differences in lipolysis between human subcutaneous and omental adipose tissues. Ann Med 1995;27:435–8.

Lindberg UB, Crona N, Silvestrolpe C, Bjorntorp P, Rebuffe-Srivrce M. Regional adipose tissue metabolism in postmenopausal women after treatment with exogenous sex steroids. Horm Metab Res 1990;22:345–51.

Lafontan M, Berlan M. Fat cell alpha 2-adrenoceptors: the regulation of fat cell function and lipolysis. Endocr Rev 1995;16:716–38.

Djurhuus CB, Grahnolht CH, Nielsen S, Mengel A, Christiansen JS, Schmitz OE, Moller N. Effects of cortisol on lipolysis and regional interstitial glycerol levels in humans. Am J Physiol Endocrinol Metab 2002;283:E172–7.