

Additive postprandial blood glucose–attenuating and satiety-enhancing effect of cinnamon and acetic acid

Samuel Mettler^{a,*}, Isaline Schwarz^b, Paolo C. Colombani^a

^aDepartment of Agricultural and Food Sciences, ETH Zurich, 8092 Zurich, Switzerland

^bDepartment of Biology, ETH Zurich, 8093 Zurich, Switzerland

Received 27 August 2009; revised 4 October 2009; accepted 6 October 2009

Abstract

Cinnamon and vinegar or acetic acid were reported to reduce the postprandial blood glucose response. We hypothesized that the combination of these substances might result in an additive effect. Therefore, we determined the 2-hour postprandial blood glucose and satiety response to a milk rice meal supplemented with either cinnamon or acetic acid on their own or in combination. Subjects ($n = 27$) consumed the meal on 4 occasions as either pure (control trial), with 4 g cinnamon, 28 mmol acetic acid, or the combination of cinnamon + acetic acid. Blood glucose and satiety were assessed before eating and 15, 30, 45, 60, 90, and 120 minutes postprandially. At 15 minutes, the combination of cinnamon + acetic acid resulted in a significantly reduced blood glucose concentration compared with the control meal ($P = .021$). The incremental area under the blood glucose response curve over 120 minutes did, however, not differ between the trials ($P = .539$). The satiety score of the cinnamon + acetic acid trial was significantly higher than that in the control trial at 15 ($P = .024$) and 30 minutes ($P = .024$), but the incremental area under the curve of the satiety response did not differ ($P = .116$) between the trials. In conclusion, the significant effect of the combination of cinnamon and acetic acid on blood glucose and satiety immediately after meal intake indicated an additive effect of the 2 substances. Whether larger doses of cinnamon and acetic acid may result in a more substantial additive effect on blood glucose or satiety remains to be investigated.

© 2009 Elsevier Inc. All rights reserved.

Keywords: Acetic acid; Cinnamon; Glycemia; Human; Satiety response
Abbreviations: IAUC, incremental area under the curve.

1. Introduction

Currently, there is a rapid rise in the prevalence of obesity and diseases related to impaired glucose tolerance and insulin resistance, involving rising public health costs associated with these diseases [1,2]. The quality and quantity of the diet may have an influence on blood glucose regulation [3], and a parameter that classifies foods according to their blood glucose rising potential is the glycemic index [4]. There is growing

evidence that diets with a reduced glycemic index and glycemic load may be beneficial in the prevention and treatment of several diseases such as insulin resistance, diabetes, and coronary heart disease [5–8]. Next to the quality of the carbohydrate fraction per se, other macronutrients, food ingredients, or food processing [9–11] as well as lifestyle factors such as physical activity [12,13] may influence the postprandial glycemic response.

For example, it has been shown that mixing cinnamon (*Cinnamomum cassia*) into a meal significantly reduced the postprandial blood glucose response [14,15], probably by influencing insulin receptor phosphorylation [16] and by reducing gastric emptying rate [14]. Next to the acute effects

* Corresponding author. INW Nutrition Biology, LFH A2, ETH Zurich, CH-8092 Zürich, Switzerland. Tel.: +41 44 632 73 84; fax: +41 44 632 11 28.
E-mail address: samuel-mettler@ethz.ch (S. Mettler).

of cinnamon, it has also been shown that the administration of a cinnamon supplementation over 2 to 6 weeks reduced fasting blood glucose in type 2 diabetic subjects [17] and postprandial glucose tolerance and insulin sensitivity in healthy sedentary men and women [18]. A blood glucose-lowering effect has also been reported when vinegar or acetic acid was added to foods, both in animal [19] and human [20,21] experiments. This effect has been explained with a delayed gastric emptying [22].

So far, the influence of cinnamon and vinegar or acetic acid on blood glucose or satiety has only been investigated in isolation. We hypothesized that the combination of these substances might result in a combined or additive effect. Therefore, this study aimed to investigate whether the combination of cinnamon and acetic acid might result in an additive blood glucose-lowering or satiety-enhancing effect compared with the isolated substances. Insight into potential additive or combined effects on blood glucose and satiety could provide useful information for the treatment and prevention of diabetes or impaired blood glucose tolerance.

2. Methods and materials

2.1. Subjects

Nine men and 18 women participated in this study. All 27 participants were non-smokers and apparently healthy (subjects were not aware of any metabolic disorder as assessed by questionnaire). Mean age, body mass index and fasting blood glucose were 26 ± 6 and 25 ± 6 years (mean \pm SD), 23.8 ± 1.6 and 21.3 ± 2.2 kg·m⁻², 4.5 ± 0.3 and 4.5 ± 0.2 mmol·L⁻¹ for men and women, respectively. The study was approved by the ethical committee of the ETH Zurich and all subjects gave written informed consent.

2.2. Study design

Each subject completed 4 trials in a randomized order. In each trial, the subjects received 1 of the 4 test meals, which consisted either of the control meal, the control meal with 4 g cinnamon (*C cassia*; Gewürzmühle Brecht GmbH, Eggenstein, Germany), the control meal with 28 mmol (1.68 g) acetic acid (Fluka Chemie GmbH, Buchs, Switzerland), or the control meal with 4 g cinnamon + 28 mmol acetic acid. The 4 tests had to take place within 4 weeks and with a minimal gap of 2 days between the tests [23,24].

The control meal consisted of 194 g vanilla milk rice (Milchreis Vanille; Migros, Zurich, Switzerland) and 33 g glucose (C*DEX 02001; Cerestar, Castelmassa, Italy) dissolved in 300 mL water. This control meal provided 75 g carbohydrates, 5 g fat, and 7 g protein. The acetic acid was dissolved in the glucose drink, whereas the cinnamon was mixed into the milk rice. The glucose drink was divided into three 100-mL portions, which had to be drunk before, in the middle, and after consumption of the milk rice. Another 100 mL of pure water was consumed at the end of the test meal.

2.3. Blood glucose testing

The pretest standardization was done individually [23,25]. Regularly exercising subjects were allowed to exercise the day before a test, but the exercise had to be replicated before the other tests and no exercise was allowed after dinner. Subjects were asked to consume a carbohydrate-rich meal of their choice for dinner, but again, the meal had to be replicated before the other tests. The dinner had to be consumed before 10 PM, and cinnamon and vinegar or foods containing cinnamon were not allowed before and after the pretest dinner [15].

Subjects arrived in the laboratory in the morning after an overnight fast of at least 10 hours. First, the pretest standardization was checked by questionnaire. After fasting capillary blood sampling had been taken by the finger prick method, the test meal was served. After this, blood samples were taken at 15, 30, 45, 60, 90, and 120 minutes after the fasting blood sample [23]. Each blood sample was taken in duplicate and analyzed with an amperometric glucose analyzer (BIOSSEN C_line; EKF-diagnostic GmbH, Barleben, Germany). The average of the duplicate measurement was used for further calculations. The average coefficient of variation of the duplicate measurement was 1.6%. Satiety was assessed by a 20-ary satiety rating scale [26] at the same time points when blood glucose was measured. Subjects were given a blank scale at every time point without access to the ratings of the previous time point or trial.

2.4. Statistical analyses

Subject number was estimated using a SD of the variability of the blood glucose incremental area under the curve (IAUC) of approximately 20% [13,24]. Twenty-four subjects were required to achieve a statistical power of 80% ($P = .05$, 2-sided) to detect an effect size of 12%, which is slightly less than the effect size as reported by Solomon and Blannin [15]. This included also a power of greater than 80% to detect an effect size as reported for acetic acid or vinegar [22,27]. To compensate for dropouts, we increased the number of subjects slightly. Therewith our study included more subjects than any other cinnamon, acetic acid, or vinegar study [14,15,19,21,22,27,28]. The incremental area under the blood glucose and satiety curve (IAUC) was calculated geometrically, ignoring areas below the fasting value [23]. Statistical analyses was performed with SAS for windows (version 9.1; SAS Institute Inc, Cary, NC) using mixed model analysis of variance (2-factorial) for repeated measures, with Bonferroni correction, and with a random subject effect. Data are presented as mean \pm SE, unless otherwise stated. Values of $P < .05$ were considered to indicate statistical significance.

3. Results and discussion

3.1. Blood glucose

The IAUC of the blood glucose did not differ between the trials (main effect of cinnamon: $F = 2.78$, $P = .100$; main

effect of acetic acid: $F = 0.35$, $P = .554$; interaction cinnamon * acetic acid: $F < 0.01$, $P = .978$). However, there were main effects of cinnamon ($F = 11.3$, $P = .001$) and acetic acid ($F = 4.07$, $P = .047$) on the blood glucose at 15 minutes (Fig. 1). The interaction cinnamon * acetic acid was not significant ($F < 0.01$, $P = .978$). There was a significant difference (post hoc, $P = .002$) between the control trial (6.44 ± 0.17 mmol·L⁻¹) and the cinnamon + acetic acid trial (5.80 ± 0.15 mmol·L⁻¹).

One difference between our study and the ones reported in the literature is the cinnamon dose. Hlebowicz et al [14] and Solomon and Blannin [15] reported significantly reduced blood glucose IAUC by adding 6 and 5 g of cinnamon to a rice pudding and a glucose drink, respectively. We used 4 g because the effects with 6 and 5 g seemed quite significant, and it was tempting to assume that 4 g would also work and would certainly be easier to use under real-life circumstances. In particular, 6 g is quite a large amount of cinnamon compared with the quantity generally used in real life. However, recently, it has been shown that 1 and 3 g of cinnamon did not influence blood glucose [28], whereas insulin was still affected. Therefore, considering all available data, one may now conclude that 1 to 4 g of cinnamon is not a sufficient dose to reduce the blood glucose IAUC [14,15,28].

Apart from the total amount of cinnamon, one may also compare the carbohydrate/cinnamon ratio because the blood glucose-lowering power might be related to the blood glucose increase. The rice puddings used in the studies of Hlebowicz et al [14,28] provided 48 g of carbohydrates by using 1, 3, or 6 g of cinnamon, resulting in a carbohydrate/cinnamon ratio of 48, 16, and 8. Solomon and Blannin [15] provided 5 g of cinnamon together with a 75-g oral glucose tolerance test, resulting in a ratio of 15. The ratio in our study was 19. Obviously, the studies with the lowest ratio [14,15] were the ones with a significant outcome, with the blood glucose-lowering effect of cinnamon clearly being largest in the study by Hlebowicz et al [14] with a ratio of 8. This

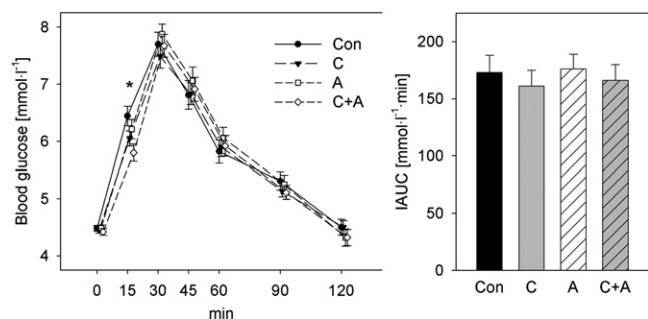


Fig. 1. Blood glucose and its IAUC for the control (Con), cinnamon (C), acetic acid (A), and the combined cinnamon + acetic acid (C + A) trial. The IAUC was calculated geometrically, ignoring areas below the fasting value [23]. Statistical analysis was performed with SAS for windows using mixed model analysis of variance for repeated measures, with Bonferroni correction, and with a random subject effect. Data are presented as mean \pm SE. Values of $P < .05$ were considered to indicate statistical significance. *Significant difference ($P = .002$) between Con and C + A.

indicates the existence of a dose-response effect and suggests a carbohydrate/cinnamon ratio of approximately 15 or lower to achieve a significant blood glucose-lowering effect.

In contrast to other studies [21,22,27], we did not see an effect of acetic acid on blood glucose. We used 1.68 g (28 mmol) of acetic acid together with 75 g of carbohydrates, resulting in a carbohydrate/acetic acid ratio of 45. Brighenti et al [27] and Liljeberg and Bjorck [22] observed a significantly reduced blood glucose IAUC by adding 1.02 and 1.08 (17 and 18 mmol) of acetic acid to white bread providing 50 g of carbohydrates, resulting in a ratio of 49 and 46, respectively. The only study with different doses of acetic acid or vinegar within the same study is the one by Ostman et al [21], and reduced blood glucose was observed 30 minutes postprandially when 1.08, 1.38, or 1.68 g (18, 23, or 28 mmol) acetic acid provided as vinegar was added to white bread providing 50 g of carbohydrates. Ebihara and Nakajima [19] reported no effect of 3.0 g (50 mmol) acetic acid on the blood glucose IAUC added to a 50-g sucrose drink, although the blood glucose peak was delayed with vinegar. Consequently, and in contrast to cinnamon, there did not seem to be an evident dose effect. Because the glycemic index and therewith the glycemic potential of the different test meals (white bread or sucrose drink) is about the same [29], the most apparent difference between the studies was the food matrix with which the acetic acid or vinegar was ingested; for example, the white bread also contains protein, some few fat, and dietary fibers and micronutrients. Sucrose provides 50% of the carbohydrate load as fructose. However, to our knowledge, there is no evident explanation as to why acetic acid might work more or less in different contexts. Further studies addressing this issue may bring more insights.

3.2. Satiety

The integrated area under the satiety response did not differ (main effect of cinnamon: $F = 0.74$, $P = .393$; main effect of acetic acid: $F = 3.55$, $P = .064$; interaction cinnamon * acetic acid: $F < 0.01$, $P = .959$) between the trials (Fig. 2). At 15 minutes, there was a main effect of cinnamon ($F = 4.73$, $P = .033$) on satiety scores with a significant difference (post hoc, $P = .026$) between the cinnamon + acetic acid trial (satiety score, 13.7 ± 0.7) compared with the control trial (12.8 ± 0.7). The main effect of acetic acid ($F = 3.90$, $P = .052$) and the interaction cinnamon * acetic acid ($F = 0.04$, $P = .849$) was not significant. At 30 minutes, there were main effects of cinnamon ($F = 4.19$, $P = .044$) and acetic acid ($F = 7.77$, $P = .007$) with a significant difference (post hoc, $P = .006$) between the cinnamon + acetic acid trial (satiety score, 13.1 ± 0.5) compared with the control trial (12.8 ± 0.7). The interaction cinnamon * acetic acid was not significant ($F = 0.3$, $P = .585$).

Satiety was significantly increased 15 and 30 minutes postprandially in the cinnamon + acetic acid trial compared with the control trial, whereas the isolated cinnamon and acetic acid trial did not differ from any other trial at any time

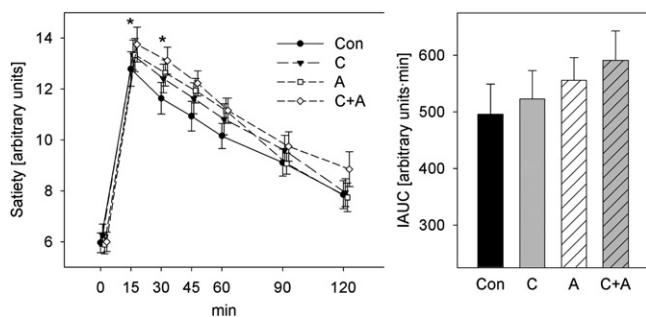


Fig. 2. Satiety and its IAUC for the control (Con), cinnamon (C), acetic acid (A), and the combined cinnamon + acetic acid (C + A) trial. The IAUC was calculated geometrically, ignoring areas below the fasting value [23]. Statistical analysis was performed with SAS for windows using mixed model analysis of variance for repeated measures, with Bonferroni correction, and with a random subject effect. Data are presented as mean \pm SE. Values of $P < .05$ were considered to indicate statistical significance. *Significant difference ($P = .026$ and $P = .006$ at 15 and 30 minutes) between Con and C + A.

point. Ostman et al [21] reported increased satiety when acetic acid was added as vinegar to white bread. Regarding cinnamon, Hlebowicz et al [14,28] did not find any effect on satiety with either 1, 3, or 6 g of cinnamon, corresponding with the results of our study. Whether the different food matrix played a role regarding the satiety outcome with acetic acid remains speculative. Interestingly, the effect on satiety 15 minutes postprandially in the combined cinnamon + acetic acid trial might indicate a potential combined effect. Furthermore, there might be a trend for an increased satiety IAUC in the combined trial. However, as subjective satiety can also be influenced by food liking or palatability [30], the satiety outcome should be interpreted with caution. We did not assess palatability, and it cannot be excluded that the different meal versions were more or less palatable to each individual subject.

The glucostatic theory suggests that increased blood glucose values are associated with increased satiety, at least in the short term [31]. Accordingly, we would rather expect reduced satiety in the combined cinnamon + acetic acid trial. However, satiety is influenced by a myriad of signals [32,33]. Therefore, it is questionable whether the slightly lower blood glucose rise from 0 to 15 minutes had any relevant influence on satiety. As we observed rather increased satiety in the cinnamon + acetic acid trial, the glucostatic effect might not have played a dominant role.

In conclusion, 4 g of cinnamon or 28 mmol (1.68 g) of acetic acid had no effect on blood glucose IAUC. However, there was a slight but significant reduction of blood glucose and satiety 15 minutes after meal ingestion and on satiety at 30 minutes when cinnamon and acetic acid were combined. The absence of an interaction effect indicates that the 2 substances work independently and may produce an additive effect when used in combination. The absent effect of cinnamon on its own in comparison to other studies [14,15,28] may be explained by the carbohydrate/cinnamon ratio. Together with the results of others [14,15,28], our data

indicate that the carbohydrate/cinnamon ratio might be a factor determining the blood glucose-lowering potential of cinnamon. Certainly, the conclusion about the influence and interaction of cinnamon and acetic acid on blood glucose and satiety is limited by the fact that we could detect only small effects in our study. Whether larger doses of cinnamon and acetic acid may result in a more substantial effect on their own and consequently also in a more substantial additive effect, which results in more significant and relevant effects on the blood glucose or satiety IAUC, needs to be determined in further studies.

Acknowledgment

We would like to thank the Swiss Foundation for Nutrition Research for funding this study.

References

- [1] American Diabetic Association. Economic costs of diabetes in the U.S. in 2007. *Diabetes Care* 2008;31:596-615.
- [2] Wang Y, Beydoun MA, Liang L, Caballero B, Kumanyika SK. Will all Americans become overweight or obese? Estimating the progression and cost of the US obesity epidemic. *Obesity (Silver Spring)* 2008;16: 2323-30.
- [3] Liu S, Willett WC, Stampfer MJ, Hu FB, Franz M, Sampson L, et al. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J Clin Nutr* 2000;71: 1455-61.
- [4] Jenkins DJ, Wolever TM, Taylor RH, Barker H, Fielden H, Baldwin JM, et al. Glycemic index of foods: a physiological basis for carbohydrate exchange. *Am J Clin Nutr* 1981;34:362-6.
- [5] Mente A, de KL, Shannon HS, Anand SS. A systematic review of the evidence supporting a causal link between dietary factors and coronary heart disease. *Arch Intern Med* 2009;169:659-69.
- [6] Riccardi G, Rivellese AA, Giacco R. Role of glycemic index and glycemic load in the healthy state, in prediabetes, and in diabetes. *Am J Clin Nutr* 2008;87:269S-74S.
- [7] Barclay AW, Petocz P, Millan-Price J, Flood VM, Prvan T, Mitchell P, et al. Glycemic index, glycemic load, and chronic disease risk—a meta-analysis of observational studies. *Am J Clin Nutr* 2008;87: 627-37.
- [8] Brand-Miller J, Millan-Price J, Steinbeck K, Caterson I. Carbohydrates—the good, the bad and the whole grain. *Asia Pac J Clin Nutr* 2008;17 (Suppl 1):16-9.
- [9] Collier G, O'Dea K. The effect of coingestion of fat on the glucose, insulin, and gastric inhibitory polypeptide responses to carbohydrate and protein. *Am J Clin Nutr* 1983;37:941-4.
- [10] Foster-Powell K, Holt SH, Brand-Miller JC. International table of glycemic index and glycemic load values: 2002. *Am J Clin Nutr* 2002; 76:5–56.
- [11] Spiller GA, Jensen CD, Pattison TS, Chuck CS, Whittam JH, Scala J. Effect of protein dose on serum glucose and insulin response to sugars. *Am J Clin Nutr* 1987;46:474-80.
- [12] Mettler S, Lamprecht-Rusca F, Stoffel-Kurt N, Wenk C, Colombani PC. The influence of the subjects' training state on the glycemic index. *Eur J Clin Nutr* 2007;61:19-24.
- [13] Mettler S, Vaucher P, Weingartner PM, Wenk C, Colombani PC. Regular endurance training does not influence the glycemic index determination in women. *J Am Coll Nutr* 2008;27:321-5.
- [14] Hlebowicz J, Darwiche G, Bjorgell O, Almer LO. Effect of cinnamon on postprandial blood glucose, gastric emptying, and satiety in healthy subjects. *Am J Clin Nutr* 2007;85:1552-6.

- [15] Solomon TP, Blannin AK. Effects of short-term cinnamon ingestion on in vivo glucose tolerance. *Diabetes Obes Metab* 2007;9:895-901.
- [16] Imparl-Radosevich J, Deas S, Polansky MM, Baedke DA, Ingebritsen TS, Anderson RA, et al. Regulation of PTP-1 and insulin receptor kinase by fractions from cinnamon: implications for cinnamon regulation of insulin signalling. *Horm Res* 1998;50:177-82.
- [17] Khan A, Safdar M, Ii Khan MM, Khattak KN, Anderson RA. Cinnamon improves glucose and lipids of people with type 2 diabetes. *Diabetes Care* 2003;26:3215-8.
- [18] Solomon TP, Blannin AK. Changes in glucose tolerance and insulin sensitivity following 2 weeks of daily cinnamon ingestion in healthy humans. *Eur J Appl Physiol* 2009;105:969-76.
- [19] Ebihara K, Nakajima A. Effect of acetic acid and vinegar on blood glucose and insulin responses to orally administered sucrose and starch. *Agric Biol Chem* 1988;52:1311-2.
- [20] Johnston CS, Buller AJ. Vinegar and peanut products as complementary foods to reduce postprandial glycemia. *J Am Diet Assoc* 2005;105:1939-42.
- [21] Ostman E, Granfeldt Y, Persson L, Bjorck I. Vinegar supplementation lowers glucose and insulin responses and increases satiety after a bread meal in healthy subjects. *Eur J Clin Nutr* 2005;59:983-8.
- [22] Liljeberg H, Bjorck I. Delayed gastric emptying rate may explain improved glycaemia in healthy subjects to a starchy meal with added vinegar. *Eur J Clin Nutr* 1998;52:368-71.
- [23] Brouns F, Bjorck I, Frayn KN, Gibbs AL, Lang V, Slama G, et al. Glycaemic index methodology. *Nutr Res Rev* 2005;18:145-71.
- [24] Mettler S, Steiner K, Colombani PC. Influence of test interval length on the variability of glycemic response tests. *Eur J Clin Nutr* 2009, doi: 10.1038/ejcn.2009.97 [Epub ahead of print August 19].
- [25] Campbell JE, Glowczewski T, Wolever TM. Controlling subjects' prior diet and activities does not reduce within-subject variation of postprandial glycemic responses to foods. *Nutr Res* 2003;23:621-9.
- [26] Haber GB, Heaton KW, Murphy D, Burroughs LF. Depletion and disruption of dietary fibre. Effects on satiety, plasma-glucose, and serum-insulin. *Lancet* 1977;2:679-82.
- [27] Brighenti F, Castellani G, Benini L, Casiraghi MC, Leopardi E, Crovetti R, et al. Effect of neutralized and native vinegar on blood glucose and acetate responses to a mixed meal in healthy subjects. *Eur J Clin Nutr* 1995;49:242-7.
- [28] Hlebowicz J, Hlebowicz A, Lindstedt S, Bjorgell O, Hoglund P, Holst JJ, et al. Effects of 1 and 3 g cinnamon on gastric emptying, satiety, and postprandial blood glucose, insulin, glucose-dependent insulinotropic polypeptide, glucagon-like peptide-1, and ghrelin concentrations in healthy subjects. *Am J Clin Nutr* 2009;89:815-21.
- [29] Atkinson FS, Foster-Powell K, Brand-Miller JC. International tables of glycemic index and glycemic load values: 2008. *Diabetes Care* 2008;31:2281-3.
- [30] Sorensen LB, Moller P, Flint A, Martens M, Raben A. Effect of sensory perception of foods on appetite and food intake: a review of studies on humans. *Int J Obes Relat Metab Disord* 2003;27:1152-66.
- [31] Chaput JP, Tremblay A. The glucostatic theory of appetite control and the risk of obesity and diabetes. *Int J Obes (Lond)* 2009;33:46-53.
- [32] Woods SC. The control of food intake: behavioral versus molecular perspectives. *Cell Metab* 2009;9:489-98.
- [33] Hlebowicz J. Postprandial blood glucose response in relation to gastric emptying and satiety in healthy subjects. *Appetite* 2009;53:249-52.