INTRODUCTION

The sedentary lifestyle of the current modern society coupled with more frequent consumption of high-fat and/or high-sugar foods has led to an elevated proportion of people with high body fat. According to the National Health and Nutrition Examination Survey, a significant increase was observed for obesity among men and women from 1999 to 2010, with more than 2/3 of adults in the US being considered overweight.[1] This unhealthy body composition is associated with low quality of life and several other conditions.[2] Thus, due to the high prevalence of overweight people and negative impact on health, ways of improving body composition are needed.

Thermogenesis is the physiological process of generating heat. An important site of thermogenesis is the brown adipose tissue (BAT).[3] BAT generates heat in response to cold temperatures for protection against hypothermia, as well as in response to feeding for dissipation of excess energy from food.[1,4] Since BAT can convert energy into heat, this body region can be considered a site for active metabolism. Particularly, BAT has been considered an organ that burns off excess fat, with an area of recent intense research, and an interesting target for improving body composition.[5,6]

Diet-induced thermogenesis, and a potential stimulation of fat metabolism, can be achieved by consumption of certain foods. Capsinoids, which consist of capsaicin, capsiate, and dihydrocapsiace, are the naturally occurring spicy components in Capsicum annuum peppers, and Improves Body Composition in Mice. Phcog Res 2018;10:37-43.
and known to activate thermogenesis via β3-adrenergic receptors and upregulation of uncoupling protein 1 (UCP1), a downstream signal from β3-adrenergic receptors in BAT. In clinical studies, capsinoid administration reduced body weight and fat. The seed extract of *Irvingia gabonensis*, also known as African mango, was shown to reduce body weight and fat in clinical trials by potentially modulating PPARγ and leptin genes. Similarly, the root extract of the plant *Coleus forskohlii*, extensively known for its stimulation of intracellular cyclic adenosine monophosphate production, increases UCP1 mRNA and protein in vitro and reduces weight gain and body fat in rodents and humans. Finally, *P*-synephrine, the natural stimulant present in *Citrus aurantium* and other citrus fruits, increases energy expenditure in humans.

Extensive research has also demonstrated that whey protein supplementation promotes satiety, improves body composition, and enhances weight loss. Particularly, previous published preclinical research on the currently tested whey protein supplement revealed significant effects on biomarkers of fat burning, metabolism, and satiety in rats. Due to this potential synergistic effect of whey protein and thermogenic foods, a novel supplement containing thermogenic food ingredients was tested alone and in combination with a whey protein supplement for effects on body composition and thermogenesis in this current pilot study in mice. The primary aim of the current study was to assess whether a combination of the above-mentioned food ingredients (novel blend) reduces the gain in body weight and fat that is caused by high-fat diet. Furthermore, it was hypothesized that the addition of whey protein supplementation would improve the benefits of the novel blend in reducing body weight and fat without altering muscle mass. To test these hypotheses, we assessed body weight, fat mass, and muscle mass before and after treatment with novel blend alone or in combination with whey protein in mice fed a high-fat diet. We further carried out experiments to explore the potential mechanism by which novel blend attenuates body weight and fat gain. These experiments suggest that novel blend attenuates body weight and fat gain in response to high-fat diet mainly via stimulation of thermogenesis in BAT rather than reduction in appetite in mice.

**MATERIALS AND METHODS**

**Subjects**

C57BL/6j male mice (The Jackson Laboratory, Bar Harbor, ME, USA) initially aged 4 weeks old were ear notched for identification and housed in individually and positively ventilated polysulfonate cages with high-efficiency particulate absolute-filtered air. The animal room was lighted entirely with artificial fluorescent lighting, with controlled 12 h light/dark cycle (6 am to 6 pm light). The normal temperature and relative humidity were 22°C ± 4°C and 50% ± 15%, respectively. Food and water were available *ad libitum*. Food consumption was measured twice a week. All experiments were performed by The Jackson Laboratory, approved by The Jackson Laboratory Institutional Animal Care and Use Committee, and conducted in accordance with the NIH guide for care and use of animals.

**Study protocol**

Animals (*n* = 12 per group) were placed on a 60% high-fat diet at wean age (4 weeks of age) and remained on high-fat diet throughout the study. High-fat diet was supplied by Research Diets, Inc., and irradiated prior to shipment to The Jackson Laboratory. At 8 weeks of age, baseline measures were collected as described below, and subsequently animals were randomly assigned to receive daily dosing by oral gavage of vehicle, the novel blend alone or in combination with whey protein supplement. At 12 weeks of age, posttreatment measures were collected as described below.

**Supplements**

The test article is a blend that contains African mango (*I. gabonensis*) seed extract (daily human equivalent dose of 300 mg; Nutragenesis, Vermont, USA), citrus fruit extract from *Citrus aurantium*, *Citrus sinensis*, and *Citrus paradisi* standardized to 5% synephrine and 80% bioflavonoids (daily human equivalent dose of 1000 mg; Novel Ingredients, NJ, USA), *Coleus forskohlii* root extract 10% forskolin (daily human equivalent dose of 500 mg; Suan Farma, NJ, USA), dihydrocapsiate (2.4 mg daily human equivalent dose; Glanbia, Ireland), and red pepper (*Capsicum annuum*) fruit extract 2% capsinoids (1.56 mg daily human equivalent dose). The novel blend was dissolved in 20-mL 0.5% carboxymethyl cellulose at 250 mg/kg. Control group received 20-mL 0.5% carboxymethyl cellulose. The human equivalent dose was calculated per ingredient as described by Reagan-Shaw et al., 2008. Safety of the novel blend was first evaluated in an acute maximum tolerated dose study (data not presented) in which 12 ICR mice were placed on 60% fat diet for 8 days and subsequently treated with 125, 250, or 500 mg/kg of the novel supplement by oral gavage daily for 5 days. No observable adverse event was noted at any given dose. The middle dose of 250 mg/kg was selected for the current study. This experiment was independently performed and analyzed by Wasatch Scientific (Murray, Utah, USA).

Protein supplement consisted of 4LifeTransform® PRO-TF (4Life Research, LLC, UT, USA), a blend containing whey protein concentrate, extensively hydrolyzed whey and egg white protein, bovine colostrum, and egg yolk extract. Protein supplement was administered once daily via oral gavage 4 h apart from novel blend treatment at the human equivalent dose of 10 g (2000 mg/kg mouse dose) dissolved in 10-mL deionized water. Novel blend was administered in the morning and protein supplement was administered in the afternoon. Due to a limited amount of gavage material a mouse can take, the supplements were not administered at the same time. The choice of administration of whey protein in the afternoon was to match previous rodent study that demonstrated that this particular whey protein supplement administered in the early afternoon to rats produces significant effects on markers of body composition. Future studies are necessary to evaluate the impact of the timing of administration of novel blend on body composition.

**Body weight and composition**

Body weight was measured three times a week for the entire course of the study. Just prior to treatment (baseline) and after 4 weeks of treatment, body weights, fat mass, and lean muscle mass were measured using dual-energy X-ray absorptiometry (DEXA). Mice were anesthetized via gaseous anesthetic (isoflurane) for approximately 10 min during recording. Body weights shown in Figure 1a and body weights at week 4 in Figure 1b were assessed via DEXA.

**Thermogenesis**

Surface thermal imaging of BAT and tail regions were obtained using the FLIR A6703sc thermal camera and ResearchIR software (FLIR Systems, OR). Mice were anesthetized via gaseous anesthetic (isoflurane) and fur removed from the subscapular region and at the base of tail using a small electric shaver. During this procedure, mice were set on a heated platform (37°C) to maintain body temperature. The following day, mice were again anesthetized, placed on heated platform, and temperature reading was recorded over the course of 0–120 min. Outcome measures were obtained before and after 4 weeks of treatment. Mitochondrial UCP1 protein expression was assessed via Western blot from isolated intrascapular BAT harvested after the final thermal
imaging scan (~2½ h postfinal dose) and snap-frozen on dry ice. Mitochondria were isolated from BAT using Abcam Mitochondrial Isolation Kit (ab110168, Abcam, MA, USA). Protein quantification was determined using DC™ Protein Assay (BioRad Life Science Research, CA, USA). UCP1 protein quantification was determined using ProteinSimple Wes™ system (ProteinSimple, CA, USA) using 0.5-μg protein loading, Ucp1 antibody at 1:100 dilution, and Cox 4 antibody (mitochondrial housekeeping) at 1:100 dilution.

**Leptin levels**
Plasma level of leptin was assessed using Mouse Metabolic Kit (K15124C-3) from Meso Scale Diagnostics, MD. Whole blood was collected from mice via retro-orbital eye bleed (~200 μl) into BD P800 vacutainers and processed in a refrigerated centrifuge set to 4°C and spun at 14,000 rpm for 10 min to obtain plasma. Leptin level was determined using Mouse Leptin Assay Kit (K15124C-3, Meso Scale Diagnostics, MD) following the manufacturer’s instructions. Leptin levels were expressed as mean values ± standard error of the mean.

**Statistical analysis**
Statistical analyses were conducted using Statistica software (Dell, Oklahoma, USA). The baseline and posttreatment outcome measures were analyzed using one-way ANOVA followed by Newman–Keuls post hoc test for determination of significance among groups. Within-group comparisons were obtained using paired t-tests. Difference among groups was considered significant if the probability of type I error was <5% (P < 0.05).

**RESULTS**

**Body weight**
All animals received high-fat diet throughout the study, and as expected and shown in Figure 1, all groups gained weight over time (P < 0.05). However, the amount of weight gain differed among groups. Results presented in Figure 1a reveal that animals on high-fat diet treated with the novel blend weighed significantly less than animals on high-fat diet treated with vehicle control at the end of 4 weeks of daily oral supplementation (P = 0.0168 vs. control). The addition of whey protein supplementation led to a further reduction in body weight gain [Figure 1a; P = 0.0028 vs. control]. As shown in Figure 1b, within-group comparison analysis of body weight change revealed that animals treated with vehicle control gained significant amounts of weight at weeks 2, 3, and 4 in comparison to baseline; whereas, a significant amount of weight gain was observed only at weeks 3 and 4 in animals treated with the novel blend alone, and at week 4 in animals treated with the combination of novel blend and whey protein (*P < 0.05 vs. baseline). Similarly, between-group comparison revealed that body weight gain was greater in animals treated with vehicle control at weeks 3 and 4 in comparison to animals treated with the novel blend alone, and at weeks 2, 3, and 4 in comparison to animals treated with the combination of novel blend and whey protein (*,b,P < 0.05).

**Body composition**
Body composition was assessed to investigate whether the reduction in body weight gain was due to reduction in fat mass, muscle mass, or both. Results presented in Figure 2a demonstrate that, despite all animals gaining fat over time (*P < 0.05 vs. baseline), animals that received the novel blend alone and in combination with the whey protein supplement had significantly less fat mass than animals that received vehicle control (*P < 0.05). Analysis of fat mass change from baseline demonstrated that novel blend alone reduces fat mass gain in comparison to vehicle control [Figure 2b; *P < 0.05]. The addition of whey protein supplement further reduced fat mass gain [Figure 2b; a,b *P < 0.05 vs. control and novel blend alone]. Lean mass was not significantly different among groups at baseline and at the end of the study [Figure 2c]. However, within-group comparison showed that the novel blend + whey protein supplement group had a reduction in lean mass (*P < 0.05 vs. baseline). Between-group comparison of lean mass change from baseline similarly revealed that the novel blend + whey protein supplement group lost lean mass at the end of 4 weeks [Figure 2d; a,b *P < 0.05 vs. control and novel blend alone].

**Fat metabolism and thermogenesis**
As an approach to understand the potential mechanism by which novel blend alone and in combination with whey protein supplementation reduces body weight and fat gain, the end points of fat metabolism and thermogenesis were assessed. The novel blend alone and in combination with whey protein supplementation led to significantly greater BAT temperature than animals that received vehicle control [Figure 3a and d; *P < 0.05]. Additionally, data revealed that the novel blend alone increased BAT temperature to a greater extent than the novel blend + whey protein supplement [Figure 3a and d; a,b *P < 0.05 vs. novel blend alone]. Representative image of thermal imaging data is shown in Figure 3b. Thermal imaging data at baseline are shown in Figure 3a and d. As shown in Figure 3c, in contrast to the thermal imaging data, as shown in Figure 4, protein expression in BAT of the thermogenic marker UCP1 was...
significantly greater in animals that received novel blend in combination with whey protein supplement (\( ^* P < 0.05 \)), but no significant effect in UCP1 was found in the novel blend alone group.

**Figure 2:** The novel blend alone or in combination with whey protein supplement attenuated body fat gain in high-fat diet with small change in lean mass. Data are expressed as mean values ± standard error of the mean (a) total fat mass, (b) fat mass change from baseline, (c) total lean mass, and (d) lean mass change from baseline. Within-group comparison: *Indicate values significantly different from baseline (\( P < 0.05 \)). Between-group comparison: groups that do not share a common letter are statistically different (\( P < 0.05 \)).

**Figure 3:** The novel blend alone or in combination with whey protein supplement increased thermal imaging of brown adipose tissue. (a) Data are expressed as mean values ± standard error of the mean of 0–120 min brown adipose tissue thermal imaging change from baseline. (b) Representative image of thermal imaging data depicting the region of interest of brown adipose tissue positive and negative (tail). Means ± standard deviation at each time point from 30–120 min are shown for brown adipose tissue thermal imaging collected at (c) baseline, and (d) at the end of the study. Groups that do not share a common letter are statistically different (\( P < 0.05 \)).

**Food consumption**

As shown in Table 1, no treatment effect was found among groups and in comparison to baseline on the food consumed. The amount
of food consumed by the novel blend + whey protein supplement group had a tendency to be less in comparison to control and novel blend alone groups, but these effects were not statistically different (P > 0.05).

Leptin levels
Pre-/post-comparisons of leptin levels in plasma revealed significant treatment effect of the novel blend + whey protein supplement in comparison to vehicle control and novel blend alone [Table 2. \(^*\) \(^*\) P < 0.05].

DISCUSSION

Current data reveal that 4-week oral administration to mice of a novel blend stimulates thermogenesis and attenuates the gain in body weight and fat in response to a high-fat diet. The positive effects on body weight, fat, and thermogenesis were improved when the novel blend was administered in combination with a whey protein supplement. No significant effects of novel blend alone were observed on lean muscle mass and plasma leptin levels. However, a reduction in lean muscle mass and leptin levels was observed in mice treated with novel blend + whey protein supplement.

Previous research has revealed that oral administration of *I. gabonensis* and *C. forskohlii* reduces body weight gain. In a clinical trial with overweight adults, *I. gabonensis* seed extract administered before lunch and dinner for 10 weeks reduced body weight in comparison to placebo control. In a 6-week study with young rats fed a high-fat/high-sugar diet, oral administration of *C. forskohlii* root extract attenuated body weight gain in comparison to high-fat/high-sugar diet alone in as early as 1 week. Similarly, in the current investigation, oral administration to mice of a novel blend that contains *I. gabonensis* and *C. forskohlii* attenuated body weight gain after 3 weeks in comparison to high-fat diet alone.

Similar to novel blend alone, novel blend + whey protein supplement reduced body weight gain in response to high-fat diet. Particularly, the reduction in body weight gain was greater in novel blend + whey protein supplement group than that in novel blend alone group. Furthermore, no difference in food consumption was found among groups and thus the significant effect of novel blend and whey protein supplement on body weight gain was likely not due to reduction in food consumption.

The current study also revealed that the novel blend alone or in combination with whey protein supplement reduces fat mass gain in response to high-fat diet. These data resemble previous research conducted on the individual ingredients in the novel blend and in whey protein supplements. In clinical studies, *I. gabonensis* seed extract, *C. forskohlii* capsinoids, *C. forskolin*, and whey protein administration showed reduction in total body fat in comparison to placebo. Furthermore, this finding is in agreement with previous clinical studies demonstrating that whey protein, particularly whey hydrolysate, reduces body fat. Protein supplementation, without an exercise component, has also been shown to stimulate muscle protein synthesis in rats and increase muscle mass in humans. In contrast, muscle mass was reduced in the novel blend + whey protein supplement group in comparison to novel blend alone and control groups. These effects potentially occurred due to the significant greater reduction in body weight gain observed in this group.

The mechanism through which the novel blend reduced fat mass can be in part explained by its thermogenic effect. Previous research has demonstrated that capsinoids and forskolin increase BAT temperature and the protein and mRNA expression of the thermogenic biomarker UCP1. Furthermore, previous study demonstrated that oral administration of the whey protein supplement used in the current investigation increases other fat metabolism markers, namely, phospho-HSL and PGC-1α in rats. In accordance with these prior studies, in the current investigation, the novel blend increased thermal...
imaging of BAT in comparison to vehicle control and this effect remained significant when the novel blend was administered with a whey protein supplement. In addition, the thermogenic biomarker UCP1 was increased in the novel blend + whey protein supplement group, but unexpectedly not in the novel blend alone. Unpublished data suggest that a higher dose of novel blend might be necessary for upregulation of UCP1 protein.

The satiety hormone leptin was investigated as another possible mechanism for the reduction in body weight gain. Previous clinical and preclinical studies have demonstrated that bitter orange reduces hunger cravings.[14] *I. gabonensis* and capsinoids reduce blood leptin levels,[10,18] and *Coleus forskohlii* reduces food intake.[16,25] Furthermore, whey protein has also shown to reduce leptin levels in rodents,[19] although not in humans.[10] In the current study, blood leptin levels at posttreatment were different in the novel blend + whey protein group in comparison to control and novel blend alone groups. However, since no significant effect was found in the novel blend-alone group, any effect in leptin levels may be due to the whey protein supplement as opposed to the novel blend. Another possibility for the lack of effect in blood leptin in the novel blend-alone group is that blood leptin levels were not significantly increased with 4 weeks of high-fat diet as seen in the within-group comparisons of posttreatment versus baseline in all the three groups. Further studies on the effects of novel blend on blood leptin during high-fat diet are needed to elucidate this issue.

**CONCLUSIONS**

In conclusion, oral administration to mice of a novel blend containing *I. gabonensis*, citrus fruit extract, *C. forskohlii*, dihydrocapsiate, and red pepper stimulated thermogenesis and attenuated the gain in body weight and fat in response to high-fat diet without affecting muscle mass. The novel blend increased thermal imaging of BAT, indicating that improvement in body composition potentially occurred due to a fat-burning effect. Furthermore, reduction in body weight and fat gain improved when novel blend was administered in combination with whey protein supplement. Particularly, novel blend + whey protein supplement increased UCP1 protein expression in BAT in addition to augmentation of BAT thermal imaging, suggesting that protein supplement provides a synergistic fat-burning effect.

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**Conflicts of interest**

All of the authors are currently employees of the funding organization.

**REFERENCES**

1. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. JAMA 2012;307:491-7.
2. CDC. Adult Obesity Causes & Consequences. 16 June, 2015 edition. Division of Nutrition, Physical Activity, and Obesity. National Center for Chronic Disease Prevention and Health Promotion; 2015. Available from: https://www.cdc.gov/obesity/adult/causes.html. [Last accessed on 2017 Oct 12].
3. Cannon B, Nedergaard J. Brown adipose tissue: Function and physiological significance. Physiol Rev 2004;84:277-359.
4. Calderon-Dominguez M, Mir JP, Fuchu R, Weber M, Serra D, Herrero L, et al. Fatty acid metabolism and the basis of brown adipose tissue function. Adipocyte 2016;5:98-118.
5. Kajimura S. Engineering fat cell fate to fight obesity and metabolic diseases. Keio J Med 2015;64:65.
6. Merlin J, Evans BA, Dehvari N, Sato M, Bengtsson T, Hutchinson DS, et al. Could burning fat start with a brite spark? Pharmacological and nutritional ways to promote thermogenesis. Mol Nutr Food Res 2016;60:18-42.
7. Kawada T, Watanabe T, Takaishi T, Tanaka T, Iwai K. Capsaicin-induced beta-adrenergic action on energy metabolism in rats: Influence of capsaicin on oxygen consumption, the respiratory quotient, and substrate utilization. Proc Soc Exp Bioi Med 1986;183:250-6.
8. Masuda Y, Haramizu S, Oki K, Ohnuki K, Watanabe T, Yazawa S, et al. Upregulation of uncoupling proteins by oral administration of capsaïate, a nonpungent capsaïcin analog. J Appl Physiol (1985) 2003;95:2408-15.
9. Kawabata F, Inoue N, Yazawa S, Watanabe T, Inoue K, Fushiki T, et al. Effects of CH-19 sweet, a non-pungent cultivar of red pepper, in decreasing the body weight and suppressing body fat accumulation by sympathetic nerve activation in humans. Biosci Biotechnol Biochem 2005;69:3234-35.
10. Ngondjie JL, Etohoudo BC, Nyangongo CB, Mtoubung CM, Oben JE. IGOB131, a novel seed extract of the West African plant *Irvingia gabonensis*, significantly reduces body weight and improves metabolic parameters in overweight humans in a randomized double-blind placebo controlled investigation. Lipids Health Dis 2009;8:7.
11. Azantsa B, Kuate D, Chakokam R, Paga G, Bartholomew B, Nash R. The effect of extracts of *Irvingia gabonensis* (IGOB131) and Dicrostachys *glomerata* (Dyoglomerata™) on body weight and lipid parameters of healthy overweight participants. Funct Foods Health Dis 2015;5:200-8.
12. Ngondi JL, Oben JE, Minka SR. The effect of *Irvingia gabonensis* seeds on body weight and blood lipids of obese subjects in Cameroon. Lipids Health Dis 2005;4:12.
13. Oben JE, Ngondi JL, Blum K. Inhibition of *Irvingia gabonensis* seed extract (IOB131) on adipogenesis as mediated via down regulation of the PPARgamma and leptin genes and up-regulation of the adiponectin gene. Lipids Health Dis 2008;7:44.
14. Galmozzi A, Sonne SB, Altshuler-Keylin S, Hasegawa B, Shinoda K, Luinten IH, et al. Thermomouser. An in vivo model to identify modulators of UCP1 expression in brown adipose tissue. Cell Rep 2014;9:1584-93.
15. Shivasarasad HN, Gopalakrishna S, Mariyanna B, Thekkoott M, Reddy R, Tipseswamy BS, et al. Effect of *Coleus forskohlii* extract on cafeteria diet-induced obesity in rats. Pharmacognosy Res 2014;6:42-5.
16. Henderson S, Magu B, Rasmussen C, Lancaster S, Kerksick C, Smith P, et al. Effects of *coleus forskohlii* supplementation on body composition and hematological profiles in mildly overweight women. J Int Soc Sports Nutr 2005;2:54-62.
17. Godard MP, Johnson BA, Richmond SR. Body composition and hormonal adaptations associated with forskolin consumption in overweight and obese men. Obes Res 2005;13:1335-43.
18. Stohs SJ, Preuss HG, Keith SC, Keith PL, Miller H, Kaats GR, et al. Effects of p-synephrine alone and in combination with selected bioflavonoids on resting metabolism, blood pressure, heart rate and self-reported mood changes. Int J Med Sci 2011;8:295-301.
19. Pathak B, Gougeon R, Center MN. Thermic effect of *Citrus aurantium* in obese subjects. Montreal: Royal Victoria Hospital McGill Nutrition and Food Science Center; 2005.
20. Kalman D, Feldman S, Martinez M, Krieger DR, Tallon MJ. Effect of protein source and resistance training on body composition and sex hormones. J Int Soc Sports Nutr 2007;4:4.
21. Miller PE, Alexander DD, Perez V. Effects of whey protein and resistance exercise on body composition: A meta-analysis of randomized controlled trials. J Am Coll Nutr 2014;33:163-75.
22. Tahavorang A, Vafa M, Shifard F, Gohari M, Heydari I. Whey protein preloads are more beneficial than soy protein preloads in regulating appetite, calorie intake, anthropometry, and body composition of overweight and obese men. Nutri Res 2014;34:856-61.
23. Mobley CB, Fox CD, Ferguson BS, Pascoe CA, Healy JC, McAdam JS, et al. Effects of protein type and composition on postprandial markers of skeletal muscle anabolism, adipose tissue lipolysis, and hypothalamic gene expression. J Int Soc Sports Nutr 2016;12:14.
24. Reagen-Shaw S, Nihal M, Ahmad N. Dose translation from animal to human studies revisited. FASEB J 2008;22:689-61.
25. Han LK, Morimoto C, Yu RH, Okuda H. Effects of *Coleus forskohlii* on fat storage in overweight rats. Yakugaku Zassi 2005;125:449-53.
26. Lockwood CM, Roberts MD, Dalvo VJ, Smith-Ryan AE, Kendall KL, Moon JR, et al. Effects of hydrolyzed whey versus other whey protein supplements on the physiological response to 8 weeks of resistance exercise in college-aged males. J Am Coll Nutr 2017;36:16-27.
27. Ohnuki N, Niwa S, Maeda S, Inoue N, Yazawa S, Fushiki T, et al. CH-19 sweet, a non-pungent cultivar of red pepper, increased body temperature and oxygen consumption in humans. Biosci Biotechnol Biochem 2001;65:2033-6.
28. Haramizu S, Kawabata F, Masuda Y, Ohnuki K, Watanabe T, Yazawa S, et al.
Capsinoids, non-pungent capsaicin analogs, reduce body fat accumulation without weight rebound unlike dietary restriction in mice. Biosci Biotechnol Biochem 2011;75:95-9.

29. Pezeshki A, Fahim A, Cheilikani PK. Dietary whey and casein differentially affect energy balance, gut hormones, glucose metabolism, and taste preference in diet-induced obese rats. J Nutr 2015;145:2236-44.

30. Kinsey AW, Eddy WR, Madzima TA, Panton LB, Arciero PJ, Kim JS, et al. Influence of night-time protein and carbohydrate intake on appetite and cardiometabolic risk in sedentary overweight and obese women. Br J Nutr 2014;112:320-7.