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Case report

Ephedrae Herba in combination with herbal medicine (Zhizichi decoction and Phellodendri Cortex) for weight reduction: a case series

Eunji Lee^{a,b}, Sang-Hoon Yoon^{a,b}, Hyunho Kim^{b,c}, Young Doo Kim^d, Jungtae Leem^{b,c,*}, Jinbong Park^{e,*}^a Chung-Yeon Korean Medicine Hospital, Gwangju, Republic of Korea^b Chung-Yeon Central Institute, Gwangju, Republic of Korea^c Dongshin Korean Medicine Hospital, Seoul, Republic of Korea^d Jaonmi Korean Medicine Clinic, Seoul, Republic of Korea^e Department of Pharmacology, College of Korean Medicine, Kyung Hee University, Seoul, Republic of Korea

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ABSTRACT

Backgrounds: Ephedrae Herba is widely used to treat obesity. There is a concern for adverse events (AEs) using it and we need to develop strategies to attenuate it without its effectiveness for weight-reducing potential. We investigated the effects of a combination of Ephedra Herba with Zhizichi decoction and Phellodendri Cortex (Anmyungambi (AMGB) decoction) in reducing the incidence of Ephedra Herba-related AEs.

Methods: We performed a retrospective chart review from a clinical case series of patients visiting the Jaonmi Korean Medicine Clinic (Seoul, Korea). The inclusion criteria was patients who were prescribed AMGB decoction, (containing Ephedrae Herba, Phellodendri Cortex, and Zhizichi decoction [Gardeniae Fructus, and Glycine Semen Preparata] in different proportions) for weight reduction. Exclusion of Phellodendri Cortex in the original AMGB preparation was allowed; conventional medications, acupuncture, and dietary supplements were not allowed. The primary outcome was absolute weight loss at the end of treatment.

Results: Twenty-seven patients (6 men and 21 women), aged 18–75 years (mean age, 42.6 ± 11.1 years) and the average treatment duration was 39.4 days. Absolute weight loss at the end of treatment was 4.49 ± 2.40 kg. Fifteen patients lost more than 5% weight (55.6%). Treatment >45 days resulted in significantly greater weight loss compared to treatment <30 days ($p < 0.001$). Not severe AEs were reported in 16 patients including constipation, fatigue, etc.

Conclusion: A combination of Ephedra Herba with Zhizichi decoction and Phellodendri Cortex may be a safe and effective treatment for weight reduction in obese and overweight patients.

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1. Introduction

Obesity is fast becoming a global healthcare problem with the increase in prevalence by more than double from 1980 to 2014.¹ In addition, obesity is usually associated with increased mortality² as it impairs the function of many organs, such as the kidneys and causes diabetes and other chronic diseases of the gastrointestinal

and cardiovascular systems.^{3,4} However, the existing weight loss strategies are often difficult to implement or unsuccessful.⁵

Obesity is treated with medications such as phentermine, orlistat, topiramate ER, and liraglutide and/or with surgical procedures such as adjustable gastric banding, sleeve gastrectomy, and Roux-en-Y gastric bypass.⁵ However, the drugs used to control obesity are usually associated with many adverse effects (AEs).

Because of these limitations of conventional therapies, traditional East Asian medicine treatments are widely used and many clinical studies have been conducted.⁶ One of the most commonly prescribed medicinal herb for the treatment of obesity is Ephedrae Herba.^{7,8} It contains ephedrine as the main active ingredient and is known to reduce weight by causing appetite loss and enhancing body metabolism, especially lipid metabolism, resulting in decrease in body fat and blood lipids.⁹ However, Ephedrae Herba is also associated with several AEs, such as increase

* Corresponding authors at: Dongshin Korean Medicine Hospital, 351, Omok-ro, Yangcheon-gu, Seoul 07999, Republic of Korea; Department of Oriental Pharmacology, Kyung Hee University, 26 Kyunghedae-ro, Hoegi-dong, Dongdaemun-gu, Seoul 02447, Republic of Korea.

E-mail addresses: julcho@naver.com (J. Leem), thejinbong@khu.ac.kr (J. Park).

* ORCID: <https://orcid.org/0000-0003-3300-5556>.

in the tone of sympathetic nerves resulting palpitation, tremor, and insomnia.¹⁰ Additionally, ephedrine is associated with the occurrence of dysrhythmia, sinus tachycardia, hypertension, palpitations, headaches, hyperactivity, anxiety, and gastrointestinal irritability.¹¹ Due to its poor safety profile, the use of ephedrine as supplementary or functional food was banned by the US Food and Drug Administration (FDA) in 2004¹² and is currently not allowed as a food additive in Korea. In 2007, clinical guidelines for the use of Ephedrae Herba were developed and its prescription was only allowed by licensed traditional Korean Medicine physicians.¹³

Since about 60% of the AEs due to ephedrine-type alkaloids are related to cardiovascular/autonomic nervous system symptoms,⁸ it is important to reduce the toxicity of Ephedrae Herba via combination with other medicinal herbs to allow safe long-term treatment of the drug. Zhizichi decoction (Chijasitang) is a popular herbal medicine prescribed for insomnia, depression, and anxiety in eastern Asia.¹⁴ Phellodendri Cortex is another herbal medicine used for weight reduction, which acts by decreasing glucose tolerance and exerting a differentiation-inhibitory effect on adipocytes.^{15,16} A combination of Ephedra Herba with Zhizichi decoction and Phellodendri Cortex has shown a beneficial effect on weight reduction while decreasing AEs of Ephedrae Herba in clinical practice and named it as Anmyungambi (AMGB) decoction. The aim of this retrospective chart review study was to explore the safety and effectiveness of AMGB decoction for weight reduction using data from real-world clinical setting.

2. Methods

2.1. Study design and participants

This chart review was conducted in the Jaonmi Korean Medicine Clinic, a primary Korean medical care clinic. Patients meeting the following the inclusion criteria were included: (1) aged more than 18 years and less than 75 years, (2) prescribed AMGB decoction for weight reduction, and (3) with initial treatment date ranging from January 1, 2011 to September 30, 2018. Exclusion criteria were: (1) weight not measured during the follow-up period and (2) AMGB decoction not taken for more than two weeks.

2.2. Intervention

AMGB decoction consisted of Glycine Semen Preparata, Gardeniae Fructus, Phellodendri Cortex, and Ephedrae Herba. The usual daily prescription doses of each herb in the real-world clinical practice are 1–8 g, 1–4 g, 0.5–8 g, and 0.5–8 g, respectively. In our chart review, we allowed inclusion of two additional medicinal herbs from the original AMGB preparation. While cases that excluded Phellodendri Cortex were considered, cases that excluded Ephedrae Herba and Zhizichi decoction (Glycine Semen Preparata and Gardeniae Fructus) were not considered. In other words, only exclusion of Phellodendri Cortex from original AMGB were allowed in our review. AMGB decoction was orally administered three times daily before meals.

2.3. Data collection and outcome measurements

The following baseline characteristics were considered: age, sex, weight, concomitant diseases (e.g., hypertension, hyperlipidemia, diabetes), existing medications, and treatment duration. The primary outcome was absolute weight loss (in kg) at the end of treatment. The secondary outcomes were: (1) the ratio of responders (patients with body weight loss compared to baseline), (2) weight reduction ratio from baseline (%), (3) clinically meaningful weight loss (the ratio of participants with weight loss over 5%¹⁷), and (4) AEs, including their incidence, types, causality, and severity.

2.4. Statistical analysis

Descriptive analysis was conducted for the patients' baseline characteristics. Categorical variables were presented as the frequency and ratio (%), while continuous variables were presented as the mean \pm standard deviation (SD). Paired *t*-test and independent *t*-test were done for intra- and inter-group comparisons, respectively of continuous variables for both primary and secondary outcomes. The effect of different treatment durations (short-term, <30 days and long-term, >45 days) on weight loss was evaluated using independent *t*-test. The SPSS Statistics for Windows, Version 26.0. (Armonk, NY: IBM Corp) was used for the statistical analysis.

2.5. Safety assessment

Safety was assessed based on incidence of AEs during the treatment period, as stated in the medical record. Incidence rates of all AEs and serious AEs were considered. AE severity was assessed based on the Common Terminology Criteria for AEs version 5.0 (CTCAEs).¹⁸ Causality assessment followed the WHO-Uppsala Monitoring Center (WHO-UMC) causality assessment system.¹⁹ AE severity and causality were determined by an independent investigator and discussed with a practitioner when additional information was needed.

2.6. Ethical consideration

This study was exempt from ethical approval and informed consent by the Chung-Yeon Korean Medicine Hospital Institutional Review Board on October 1, 2018 (CY-IRB 2018-09-003).

3. Results

3.1. Baseline characteristics

From January 2011 to September 2018, 1,085 patients visited the Jaonmi Korean Medicine clinic for weight reduction treatment. A total of 34 patients were prescribed AMGB decoction, amongst which 7 patients were excluded as the exact dosage was not described in their medical record. We included 27 patients (21 women and 6 men, average age of 42.56 ± 11.11 years; average body weight, 71.07 ± 11.58 kg). Five of them had hypertension and two had hyperlipidemia.

3.2. Individual dosage information and absolute/relative weight reduction

Data regarding individual starting and final doses of AMGB decoction, treatment duration, weight before and after treatment, total weight loss (kg), and the weight loss ratio (%) are shown in Table 1. The actual daily doses of medicinal herbs used in AMGB decoction were: Glycine Semen Preparata (A), 4–8 g; Gardeniae Fructus (B), 2–5 g; Phellodendri Cortex (C), 0–12 g; Ephedrae Herba (D), 2–9 g. Treatment duration ranged from a minimum of 15 days to a maximum of 75 days. The absolute weight loss ranged from 1 kg to 9.7 kg, and the weight loss ratio ranged from 1.54% to 12.47%.

All patients lost more than 1 kg and the responder (patients with weight loss) rate was 100%. Body weight decreased from 71.07 ± 11.58 kg to 66.59 ± 10.45 kg after treatment and the average weight loss (4.49 ± 2.40 kg) was statistically significant ($p < 0.001$ by paired *t*-test). Fifteen patients (55.6%) had a clinically meaningful weight loss (over 5%), while 12 patients (44.4%) showed weight loss of less than 5%.

Table 1
Individual Clinical Data of Patients Treated With AMGB Decoction for Weight Reduction

No.	Sex	Age (years)	Daily dosage (initial) A-B-C-D (g)	Daily dosage (final) A-B-C-D (g)	Treatment duration (days)	Weight before treatment (kg)	Weight after treatment (kg)	Total weight loss (kg)	Weight loss ratio (%)
1	F	24	4-2-1-3	4-2-1-5	60	77.8	68.1	9.7	12.47
2	F	34	4-2-3-3	4-2-3-3	60	83.8	75	8.8	10.50
3	F	39	4-2-6-6	4-2-6-6.3	75	94.1	85.5	8.6	9.14
4	F	42	8-5-0-7 (E 1 g, F 12 g)	8-5-0-7 (E 1 g)	60	69	61.4	7.6	11.01
5	M	32	4-2-1-3 (F 8 g)	4-2-1-3 (F 8 g)	45	78	70.5	7.5	9.62
6	F	55	4-2-1-3 (F 9 g)	4-2-3-3.3 (F 9 g)	45	66.3	60	6.3	9.50
7	F	43	8-5-12-9	8-5-12-9	60	82	76	6	7.32
8	M	43	8-5-12-9	8-5-12-9	75	79	73	6	7.59
9	M	62	8-5-12-9	4-2.5-6-4.5	45	77	71	6	7.79
10	M	58	4-2-1-3	4-2-1-4	30	89.7	84.4	5.3	5.91
11	F	37	8-5-12-9	8-5-12-9	30	70	65	5	7.14
12	F	28	4-2-1-3	4-2-1-3 (G 3 g)	75	56.5	52	4.5	7.96
13	F	32	4-2-1-3 (F 8 g)	4-2-1-3 (F 8 g)	30	59.3	55	4.3	7.25
14	F	51	4-2-3-3	4-2-5-4	30	76	72	4	5.26
15	M	20	4-2-1-3	4-2-1-4	30	82.2	78.2	4	4.87 ^a
16	F	50	4-2-4.5-4.5	4-2-4.5-4.5	15	62	58.6	3.4	5.48
17	F	63	4-2-1-3	4-2-1-3	15	71.4	68.2	3.2	4.48 ^a
18	F	53	4-2-5-5	4-2-5-5	45	62	59	3	4.84 ^a
19	F	40	4-2-4.5-4.5	4-2-6-5.5	30	71	68	3	4.23 ^a
20	M	58	4-2-3-3	4-2-3-3	45	81.3	79	2.3	2.83 ^a
21	F	37	4-2-4-2	4-2-4-4	30	85.8	83.6	2.2	2.56 ^a
22	F	35	8-5-8-5	8-5-8-5	30	53.7	51.5	2.2	4.10 ^a
23	F	42	4-2-3-3	4-2-4-4 (H 16 g)	30	56	54	2	3.57 ^a
24	F	35	4-2-2-3	4-2-2-3	15	50.5	48.5	2	3.96 ^a
25	F	53	6-3-12-6	6-3-12-6	30	63.2	61.3	1.9	3.01 ^a
26	F	41	4-2-1-3	4-2-1-3	15	56.5	55	1.5	2.65 ^a
27	F	42	4-2-2-3	4-2-2-3	15	65	64	1	1.54 ^a

^a Weight loss less than 5%.

AMGB, Anmyungambi decoction. AMGB decoction consisted of Glycine Semen Preparata, Gardeniae Fructus, Phellodendri Cortex, and Ephedrae Herba. A, Glycine Semen Preparata; B, Gardeniae Fructus; C, Phellodendri Cortex; D, Ephedrae Herba; E, Coptidis Rhizoma; F, Tritici Fructus Levis; G, Rhei Radix et Rhizoma; H, Gypsum Fibrosum.

Table 2
Comparison of Weight loss Based on the Treatment Duration

Treatment duration (number of patients)	Weight before treatment (kg)	Weight after treatment (kg)	Weight loss (kg)
More than 45 days (n = 12)	75.56 ± 9.95	69.21 ± 9.16	6.36 ± 2.17
Less than 30 days (n = 15)	67.48 ± 11.56	64.48 ± 10.93	3.00 ± 1.26

3.3. Difference in weight loss according to treatment duration

In the group of 12 patients who took AMGB decoction for more than 45 days, 10 patients (83.3%) lost over 5% of their body weight. On the other hand, only 5 patients (33.3%) in the group taking the medication for less than 30 days lost more than 5% weight (Table 2). The difference in weight loss between the two groups was statistically significant ($p < 0.001$ by independent t -test).

3.4. Safety assessment

In total, 28 AEs were recorded in 16 out of 27 patients as follows: constipation ($n = 6$), fatigue ($n = 4$), headache ($n = 2$), nausea ($n = 2$), dizziness ($n = 2$), hot flashes ($n = 2$), abdominal fullness ($n = 1$), numbness ($n = 1$), urinary tract stone ($n = 1$), edema ($n = 1$), insomnia ($n = 1$), body aches ($n = 1$), feeling of hunger ($n = 1$), reduction in urine output ($n = 1$), increased thirst ($n = 1$), and drowsiness ($n = 1$). The data indicated that only one patient had insomnia, while none had palpitation or hypertension, which are the commonly reported AEs for herbal decoction containing Ephedrae Herba. The most frequent AEs in the analyzed patient population were constipation and fatigue. The causality of all AEs was assessed as probable/likely, according to the WHO-UMC causality assessment system. All AEs were of Grade 1 (mild) severity, except for one urinary stone case, qualified as Grade 2 (moderate).

4. Discussion

We analyzed the chart of 27 patients who were treatment with AMGB decoction and they showed the significant weight reduction. We also found that longer treatment with AMGB was more effective. Among the 28 AEs, the incidences of those related to the autonomic nervous system and cardiovascular system were relatively low and no serious AEs were observed.

One systematic review showed that herbal medicines showed more weight loss effect of 4.03 kg (95% CI: 2.22–5.85) or 2.76 kg (95% CI: 1.61–3.83), respectively, compared to the placebo or lifestyle modification group. In our study, AMGB decoction decreased 4.49 ± 2.40 kg which is comparable to the previous review.⁶ In our case series, AMGB decoction showed a clinically meaningful weight reduction rate (5% loss) of 56%, despite a relatively short treatment period (15–75 days). This result is comparable to that of the existing conventional drugs (37–73%).¹⁷

In this study, we investigated whether AMGB decoction could attenuate AEs caused by Ephedrae Herba. A recent study indicated that Zhizichi decoction (Chijiasitang) has anti-depressant effects associated with reducing appetite,²⁰ anti-stress effects,¹⁴ and anti-insomnia effect.²¹ In a cross-over RCT ($n = 12$), use of Ephedrae Herba extract resulted in an increase in the adverse event ratio of insomnia and increased pulse by 25% and 33%, respectively.²² Similarly, in a retrospective review, the use of Ephedrae Herba for weight reduction led to AEs such as palpitation (13.7%), insomnia (10.8%), and dry mouth (9.4%).²³ However, our study reported rela-

atively low adverse event ratio of insomnia (1/27, 3.7%) and thirst (1/27, 3.7%), which indicated that AMGB decoction reduced the side effects of Ephedrae Herba. Thus, it could be assumed that the AMGB decoction might attenuate the AEs of Ephedrae Herba. However, these results should be interpreted with caution taking into consideration the facts that data is retrospective and the number of included patients is relatively small.

Results from this retrospective review indicated that among the AEs observed in 16 AMGB-treated patients, constipation and fatigue were the most common. On the other hand, AEs related to the autonomic nervous system and cardiovascular system, such as insomnia, anxiety, hypertension, arrhythmia, and palpitation were not frequent, and no severe AEs were observed. Thus, the treatment with AMGB decoction succeeded in its primary goal to reduce major AEs, i.e., disturbances of the autonomic nervous and cardiovascular systems.

Our study has several strengths. In Jaonmi clinic, the patients were recommended to walk only about an hour, and to refrain from drinking and eating late. Therefore, the effects of AMGB decoction on weight loss were assessed without interference of confounding factors such as very strict lifestyle changes, exercise, acupuncture, and supplementary functional food.

Our study also has several limitations. We only reported weight loss and weight reduction ratio. Due to the limitation of retrospective review, we could not acquire body height and body mass index. However, a weight loss of more than 5% is considered clinically meaningful in obesity treatment.¹⁷ Although more outcome variables are needed in future studies, weight loss is a notable outcome for obesity treatment.

Conclusion

In conclusion, the results of this study indicate that AMGB decoction may be a relatively safe and effective treatment for weight reduction without serious AEs. Therefore, it may be utilized as a new treatment strategy to control AEs caused by Ephedrae Herba. However, more rigorous studies should be done to confirm this conclusion.

Author contributions

Conceptualization: JL and JP. Data curation: YK. Formal analysis: SY. Investigation: YK. Methodology: HK. Project administration: SY and EL. Resources: YK. Software: JL. Validation: EL. Visualization: JL. Writing - original draft: EL and JL. Writing - review & editing: JL and JP. Funding acquisition: JL. Supervision: HK.

Conflict of interest

The authors have no conflicts of interest to declare.

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Ethical statement

This study was exempt from ethical approval and informed consent by the Chung-Yeon Korean Medicine Hospital Institutional Review Board on October 1, 2018 (CY-IRB 2018-09-003).

Data availability

Data are available upon request to the corresponding authors or the first author.

References

- World Health Organization. *Global status report on noncommunicable diseases 2014*. Geneva, Switzerland: WHO Press, World Health Organization; 2014.
- Prospective Studies Collaboration, Whitlock G, Lewington S, Sherliker P, Clarke R, Emberson J, et al. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet Lond Engl* 2009;373(9669):1083–96. [http://dx.doi.org/10.1016/S0140-6736\(09\)60318-4](http://dx.doi.org/10.1016/S0140-6736(09)60318-4).
- Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. *N Engl J Med* 1995;332:621–8. <http://dx.doi.org/10.1056/NEJM199503093321001>.
- Greenway FL. Physiological adaptations to weight loss and factors favouring weight regain. *Int J Obes* 2015;39:1188–96. <http://dx.doi.org/10.1038/ijo.2015.59>.
- Bray GA, Frühbeck G, Ryan DH, Wilding JPH. Management of obesity. *Lancet* 2016;387:1947–56. [http://dx.doi.org/10.1016/S0140-6736\(16\)00271-3](http://dx.doi.org/10.1016/S0140-6736(16)00271-3).
- Sui Y, Zhao HL, Wong VCW, Brown N, Li XL, Kwan AKL, et al. A systematic review on use of Chinese medicine and acupuncture for treatment of obesity. *Obes Rev Off J Int Assoc Study Obes* 2012;13(5):409–30. <http://dx.doi.org/10.1111/j.1467-789X.2011.00979.x>.
- Song Y-K, Lim H-H. Clinical application of ma huang in the obesity treatment. *J Soc Korean Med Obes Res* 2007;7:1–7.
- Song M-Y, Kim H-J, Lee M-J. The safety guidelines for use of Ma-huang in obesity treatment. *J Korean Orient Assoc Study Obes* 2006;6:17–27.
- Astrup A, Breum L, Toubro S, Hein P, Quaade F. Ephedrine and weight loss. *Int J Obes Relat Metab Disord J Int Assoc Study Obes* 1992;16:715.
- Boozer CN, Daly PA, Homel P, Solomon JL, Blanchard D, Nasser JA, et al. Herbal ephedra/caffeine for weight loss: a 6-month randomized safety and efficacy trial. *Int J Obes Relat Metab Disord J Int Assoc Study Obes* 2002;26(5):593–604. <http://dx.doi.org/10.1038/sj.ijo.0802023>.
- Fleming RM. Safety of ephedra and related anorexic medications. *Expert Opin Drug Saf* 2008;7:749–59. <http://dx.doi.org/10.1517/14740330802510915>.
- Food and Drug Administration, HHS. Final rule declaring dietary supplements containing ephedrine alkaloids adulterated because they present an unreasonable risk. Final rule. *Fed Regist* 2004;69:6787–854.
- Kim H, Han C-H, Lee E-J, Song Y-K, Shin B-C, Kim Y-K. A clinical practice guideline for Ma-huang (*Ephedra sinica*) prescription in obesity. *J Soc Korean Med Obes Res* 2007;7:27–37.
- Jung S, Kim J, Lee G, Lyu Y, Kang HW. A study of the anti-stress effects of Chijiasitang in mice. *J Orient Neuropsychiatry* 2017;28:183–93.
- Ikarashi N, Tajima M, Suzuki K, Toda T, Ito K, Ochiai W, et al. Inhibition of preadipocyte differentiation and lipid accumulation by Oregedokuto treatment of 3T3-L1 cultures. *Phytother Res PTR* 2012;26(1):91–100. <http://dx.doi.org/10.1002/ptr.3493>.
- Ma Y, Kim H, Han Y, Kim H, Oh J. Effects of cortex phellodendri on the metabolic function in experimental mouse model of obesity. *J Korean Orient Intern Med* 2015;36:447–57.
- Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. *JAMA* 2014;311:74–86. <http://dx.doi.org/10.1001/jama.2013.281361>.
- National Cancer Institute. *Grading: general characteristics of the CTCAE (common terminology criteria for adverse events) grading (severity) scale*; 2012. https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf.
- World Health Organization (WHO)-Uppsala Monitoring Centre. *The use of the WHO-UMC system for standardized case causality assessment*; 2012. http://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausality_assessment.pdf.
- Zhang H, Xue W, Wu R, Gong T, Tao W, Zhou X, et al. Rapid antidepressant activity of ethanol extract of *Gardenia jasminoides* Ellis is associated with upregulation of BDNF expression in the hippocampus. *Evid Based Complement Alternat Med* 2015;2015:1–8. <http://dx.doi.org/10.1155/2015/761238>.
- Kuratsune H, Umigai N, Takeno R, Kajimoto Y, Nakano T. Effect of crocetin from *Gardenia jasminoides* Ellis on sleep: a pilot study. *Phytomed Int J Phytother Phytopharm* 2010;17:840–3. <http://dx.doi.org/10.1016/j.phymed.2010.03.025>.
- Odaguchi H, Sekine M, Hyuga S, Hanawa T, Hoshi K, Sasaki Y, et al. A double-blind, randomized, crossover comparative study for evaluating the clinical safety of ephedrine alkaloids-free ephedra herb extract (EFE). *Evid-Based Complement Altern Med ECAM* 2018;2018:4625358. <http://dx.doi.org/10.1155/2018/4625358>.
- Jo D-H, Lee S, Lee J-D. Effects of Gambisan in overweight adults and adults with obesity: a retrospective chart review. *Medicine (Baltimore)* 2019;98:e18060. <http://dx.doi.org/10.1097/MD.00000000000018060>.