Effects of multiple herb formula SEC-22 supplementation on dietary intake, picky eating behaviors, and growth indices in thin preschool children

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BACKGROUND/OBJECTIVES: Thin children may have insufficient intake of energy and nutrients, resulting in reduced immune function and growth. This study aimed to identify the effects of multiple herb formula SEC-22 supplementation on growth, dietary changes, and picky eating behaviors in thin children.

SUBJECTS/METHODS: A double-blind, randomized clinical trial was conducted on 79 children aged 2-5 years with poor appetites, BMI percentile < 25, and without any illness. Subjects were given either SEC-22 (n = 35) or placebo (n = 44) for 2 months and followed for an additional 2 months. Three-day dietary records, questionnaires on picky eating behaviors, and anthropometric measures were collected.

RESULTS: Energy, carbohydrate intake, and feeding difficulty improved in both groups during the intervention period. However, changes were maintained only in the SEC-22 group after 2 months of follow-up post-supplementation. ‘Frequency of trying to feed’ was improved in the SEC-22 group compared to the placebo group after the first month of follow-up (P < 0.05). Intakes of potassium and thiamine were improved in the SEC-22 group compared to the placebo group after the first month of intervention (P < 0.05). ‘Frequency of food reward’, eating amount, and intakes of carbohydrate, potassium, and vitamin C showed significant improvement compared to the placebo group after the second month of follow-up (P < 0.05).

CONCLUSIONS: These results suggest that SEC-22 supplementation can improve parental feeding difficulty resulting from insufficient eating amount or picky eating as well as increase nutrient intake in thin children. Although these improvements were observable at least 2 months after supplementation, effects beyond this time frame need to be confirmed.

Keywords: Underweight, picky eating, thin children, feeding difficulty, herb extracts

INTRODUCTION

Early childhood is a critical time for physical and intellectual development, as well as development of the muscular, skeletal, nervous systems [1]. Anthropometric measures such as height and weight are the most practical means for evaluating nutritional status. In preschool children, sufficient energy and nutrient intake are very important for immune function, brain, and bone development. Early studies on underweight children have focused on only extreme cases, defined as a BMI less than the 5th percentile [2], and attributed the main cause of underweight status to lack of food intake due to poverty or illness [3-5]. Little research has been published on thin children without any apparent disease. However, thin children deserve attention and care since they may consume an inadequate amount of energy or other nutrients, which may lead to poor growth and development. If thin children chronically consume less than their Estimated Energy Requirements (EER), they are at greater risk of hindered physical growth and intellectual development [6]. Furthermore, long-term malnutrition can interfere with potential growth and may have a negative effect on cognitive development such as learning performance and concentration.

Bhagwalia and colleagues stated that mild underweight status, defined as being thinner than the median, deserves greater attention as a useful signal of changing health conditions among preschool children [7]. Fawzi and colleagues showed that lower weight-for-height is associated with rising subsequent mortality even between the underweight threshold (< -2SD) and median [8]. There have been several studies on
the use of nutritional supplements for increasing the weight of underweight children [9-11]. There is also evidence that prokinetic agent therapy, which enhances gastrointestinal motility, might be beneficial to children with poor appetites and delayed gastric emptying [12]. Thin children may exhibit diseases relating to impaired digestion such as functional dyspepsia. Talley [13] and Tack [14] showed that early satiety is associated with a lower BMI. Picky eating is a possible risk factor for thinness or underweight status [15,16]. Children with eating problems may gain less weight, and children with picky eating behaviors may be at increased risk of being underweight. Bad eating habits in early childhood are known to increase risk of disease in adulthood [17].

In Korean medicine, thin children with a chronic poor appetite may be diagnosed as having a weakened digestive system and are prescribed herbal extracts to improve their digestive system [18,19]. Medical help is often sought for children with poor appetite and growth, even though they may not be thin or underweight. However, there are few studies that have verified the effects of herbal extracts on the growth and eating behaviors of thin children. In this study, we used multiple herb formula SEC-22, which is formulated from eight herbs and used in Korean medicine for improving weakened digestive systems. We conducted a clinical trial to identify the effects of SEC-22 on growth, dietary changes, and eating behaviors in thin children.

SUBJECTS AND METHODS

Extract preparation
SEC-22 was prepared from aqueous extracts of eight food-grade herbs. The composition of SEC-22 is shown in Table 1. Herbs were purchased from Omniherb in Daegu, Korea. These eight herbs were root of *Herbs were purchased from Omniherb in Daegu, Korea. These grade herbs. The composition of SEC-22 is shown in Table 1.

| Herbs                   | Scientific Name               | Dose (g/day/15 kg) |
|-------------------------|-------------------------------|--------------------|
| Shanzha                 | Fruit of Crapega pinnatifida BUNG var. typica SCHNEIDER | 4.67               |
| Baihu                   | Root of Atractylodes japonica KOIZUMI | 3.73               |
| Chenpi                  | Dried pericarpium of Citrus unshiu MARKOVICH | 2.80               |
| Mably                   | Sprout of Hordeum vulgare LINNE | 2.80               |
| Sharen                  | Fruit of Amomum xanthioides WALLICH | 1.87               |
| Shengjiang              | Root of Zingiber officinale ROSECO | 1.40               |
| Dazao                   | Dried fruit of Zizyphus Jujuba FRUCTUS | 1.40               |
| Luzong                  | Antler of Cervus elaphus LINNE | 0.47               |
| Crystalline fructose    |                                | 12.00              |

Table 1. Composition of multiple herb formula SEC-22

Study design
An age-stratified, double-blind, and randomized clinical trial was conducted from July, 1, 2011 to April 30, 2013. The number of subjects necessary to achieve 80% power with an effect size of 40% was estimated to be 48 children per group using a two-sample test based on previous data. A total of 108 participants were recruited from childcare centers in Seoul, South Korea, and 79 subjects finished the study. Anthropometric measures were collected at Kim Kijoon BOM medicine clinic in Seoul, Korea. The experimental group was supplemented with SEC-22, and the placebo group was given a placebo without SEC-22 for 2 months. Each group was observed and followed for an additional 2 months after the supplementation period.

Subject selection
Subjects were recruited following the inclusion and exclusion criteria established before starting the study. Eligibility for participating in the study were as follows: 24-72 months of age, without chronic rhinitis, suffering from common cold less than four times per year, BMI percentile below 15, BMI percentile between 15 and 25 if suffering from poor appetite for more than 6 months, and estimated energy intake under -1.0 standard deviation of EER in 3-day dietary records. Additionally, any children with conditions described in the Morley study of 1997, including starvation, diseases, and premature birth were excluded [20]. Twins or children taking drugs or herbs that affect weight within 2 weeks of beginning the study were also excluded. Of the 108 eligible participants initially recruited, 79 subjects (35 SEC-22 group, 44 placebo group) completed the study. There were no significant differences in baseline characteristics between the two groups. The mean age of the SEC-22 and placebo groups were 4.3 and 4.0 years, respectively. The proportions of male children in the SEC-22 and placebo groups were 44% and 51%, respectively. Two-thirds of subjects consumed less than their estimated energy requirement (EER) at baseline.

The protocol was approved by the Seoul National University Institutional Review Board (SNUIRB, IRB No. 1106/001-001), and written informed consent was obtained from all subject’s caregivers.

Data collection
During the 4-month study period, the child and caregiver visited the clinic every month. Three-day dietary records, questionnaires on eating behavior, and anthropometric measures were collected each month. Height and weight were measured to one decimal place using a stadiometer and balance (InBody J05, Biospace co. Ltd., Seoul, Korea). Z-scores for height-for-age (HAZ), weight-for-age (WAZ), weight-for-height (WFH), and BMI-for-age (BAZ) were calculated using the reference data from 2007 Korea Pediatrics standard growth charts.

Dietary records were collected from caregivers who were responsible for childcare. Three-day dietary records (i.e. two-
weekdays and one weekend day, in the absence of disease such as cold) were collected every month. Dietary energy, carbohydrates, proteins, fats, vitamins, and minerals were estimated using DES (Diet Evaluation System, DES-Korea co., Seoul, Korea). Total energy intakes were calculated using the Atwater factor. Eating time was recorded in minutes. We modified the picky eating questionnaire used by Carruth [21] and evaluated responses using a 7-point Visual Analogue Scale (VAS) with higher points indicating a greater degree of picky eating behavior.

**Statistical analysis**

Student’s t-test was used to determine differences between the SEC-22 and placebo groups. Paired t-test was used to determine differences from baseline values within groups. All statistical analyses were carried out using SAS (Statistical Analysis System v9.1.3, SAS Institute, Cary, NC, USA). Changes in picky eating behaviors compared to baseline visit during the study period (n = 79)

**RESULTS**

Picky eating behaviors

During the intervention period, average meal duration decreased in both groups. These improvements returned to baseline in the placebo group after the second month of follow-up, whereas they continued to improve in the SEC-22 group until the second month of follow-up (Table 2). Among eating behaviors, ‘Frequency of trying to feed’ and ‘frequency of food reward’ improved in the SEC-22 group compared with the placebo group during the intervention period, but there was no significant difference between the two groups. However, during the follow-up period, while the placebo group returned to baseline, the SEC-22 group continued to improve. ‘Frequency of trying to feed’ showed statistically significant improvement compared to the placebo group during the follow-up period (P < 0.05) and ‘frequency of food reward’ showed significant differences between the SEC-22 and placebo groups during the follow-up period (P < 0.05).

| Variables                        | SEC-22 (n = 35) | Placebo (n = 44) | Change from baseline during treatment period | Change from baseline during follow-up period |
|----------------------------------|-----------------|------------------|---------------------------------------------|---------------------------------------------|
|                                  | Baseline        | 1 month          | 2 months                                    | 1 month                                     | 2 months                                    |
| Average meal duration (min/%)    | 34.9 ± 15.5     | -1.9 ± 11.6      | -6.2 ± 11.1*                                | -6.7 ± 12.4*                                | -6.1 ± 13.3*                                |
|                                  | 33.1 ± 14.2     | -5.1 ± 13.3*     | -3.9 ± 10.8*                                | -4.6 ± 12.1*                                | -1.9 ± 12.2                                 |
| Eating problem                   | 4.7 ± 1.5       | -0.5 ± 1.3*      | -0.9 ± 2.0*                                | -1.1 ± 1.9*                                 | -1.0 ± 1.7*                                 |
|                                  | 4.5 ± 1.7       | -0.4 ± 1.4       | -0.4 ± 1.2*                                | -0.7 ± 1.5*                                 | -0.6 ± 1.5*                                 |
| Appetite                         | 4.8 ± 1.2       | 0.3 ± 1.2*       | 0.4 ± 1.3*                                 | 0.7 ± 1.3*                                 | 0.6 ± 1.1*                                 |
|                                  | 4.9 ± 1.1       | 0.6 ± 1.1*       | 0.4 ± 1.2*                                 | 0.7 ± 1.2*                                 | 0.4 ± 1.2*                                 |
| Undereating frequency            | 4.5 ± 1.3       | -0.1 ± 1.8       | -0.3 ± 1.9                                 | -0.5 ± 2.0                                 | -0.6 ± 1.9                                 |
|                                  | 4.5 ± 1.7       | -0.3 ± 1.2       | -0.5 ± 1.3*                                | -0.6 ± 1.7                                 | -0.5 ± 2.0                                 |
| Frequency of trying to feed      | 5.3 ± 1.5       | -0.4 ± 1.8       | -0.9 ± 1.5*                                | -1.2 ± 1.6*                                | -1.2 ± 1.6*                                |
|                                  | 4.9 ± 2.0       | -0.2 ± 1.1       | -0.5 ± 1.4*                                | -0.4 ± 1.4**                               | -0.4 ± 1.7**                               |
| Frequency of food reward         | 3.6 ± 1.5       | -0.7 ± 1.8*      | -0.7 ± 2.0*                                | -0.8 ± 1.8*                                | -1.0 ± 1.6*                                |
|                                  | 3.4 ± 1.8       | -0.5 ± 1.7       | -0.3 ± 1.6                                 | -0.3 ± 1.3                                 | -0.2 ± 1.8**                               |
| Frequency of preparing special food | 3.5 ± 1.8     | -0.3 ± 1.1       | -0.4 ± 1.3                                 | -0.4 ± 1.4                                 | -0.4 ± 1.7                                 |
|                                  | 3.5 ± 1.9       | -0.1 ± 1.5       | -0.4 ± 1.3                                 | -0.2 ± 1.2                                 | -0.4 ± 1.4                                 |
| Frequency to try new foods       | 4.6 ± 1.4       | 0.1 ± 1.4        | 0.1 ± 1.7                                 | 0.1 ± 1.6                                 | 0.1 ± 1.6                                 |
|                                  | 5.0 ± 1.4       | 0.0 ± 1.3        | -0.1 ± 1.3                                 | -0.4 ± 1.8                                 | -0.2 ± 1.7                                 |
| Willingness to try new foods     | 4.7 ± 1.7       | 0.0 ± 1.3        | 0.2 ± 1.9                                 | -0.1 ± 2.0                                 | 0.0 ± 2.0                                 |
|                                  | 4.9 ± 1.6       | -0.2 ± 1.4       | -0.1 ± 1.4                                 | -0.2 ± 1.3                                 | -0.3 ± 1.5                                 |
| Food variety                     | 4.2 ± 1.8       | -0.3 ± 1.2       | -0.7 ± 1.6*                                | -0.6 ± 1.6*                                | -0.7 ± 1.7*                                |
|                                  | 4.0 ± 2.0       | -0.2 ± 1.2       | -0.1 ± 1.4                                 | -0.5 ± 1.5*                                | -0.1 ± 1.4                                 |

Mean ± SD.

SEC-22: Multiple herb formula composed of eight food-grade herbs,

1) What is the average meal duration of your child during the previous month?
2) To what extent do you consider your child to have a feeding problem? Rated on 7-point scale with 7 = to a great extent and 1 = not at all.
3) Does your child have a good appetite? Rated on 7-point scale with 7 = to a great extent and 1 = not at all. Positively worded questions were reverse scored.
4) In general, at the end of each meal, how often has your child eaten the amount you think he/she should eat? Rated on 7-point scale with 7 = always or almost always and 1 = never or almost never.
5) How often do you attempt to persuade your child to eat a certain type of food? Rated on 7-point scale with 7 = always or almost always and 1 = never or almost never. Positively worded questions were reverse scored.
6) How often do you provide a food reward for eating a food you think your child should eat? Rated on 7-point scale with 7 = always or almost always and 1 = never or almost never.
7) How often do you prepare a special food for your child because he/she does not like what the rest of the family is eating? Rated on 7-point scale with 7 = always or almost always and 1 = never or almost never.
8) How often do you prepare a special food for your child because he/she does not like what the rest of the family is eating? Rated on 7-point scale with 7 = always or almost always and 1 = never or almost never. Positively worded questions were reverse scored.
9) How often do you provide food variety to your child? Rated on 7-point scale with 7 = extremely willing and 1 = almost never or never. Positively worded questions were reverse scored.
10) Overall, to what extent does your child like a wide variety of foods from those that you think he/she should eat? Rated on 7-point scale with 7 = to a great extent and 1 = not at all. Positively worded questions were reverse scored.

* Difference from baseline values was significant by paired t-test (P < 0.05)
** Significantly different from placebo group by student’s t-test (P < 0.05)
Table 3. Changes in nutrient intakes by 3-day dietary record during the study period

| Variables              | SEC-22 (n = 35) | Placebo (n = 44) | Baseline | Change from baseline during treatment period | Change from baseline during follow-up period |
|------------------------|-----------------|-----------------|----------|---------------------------------------------|---------------------------------------------|
|                        |                  |                 |          | 1 month | 2 months | 1 month | 2 months |            |            |
| Energy (kcal/day)      | 1,191 ± 299.7    | 1,167.9 ± 275.7 | 131 ± 390* | 116 ± 307* | 87 ± 326 | 137 ± 380* |
| Eating amount (g/day)  | 1,050.8 ± 308.8  | 1,069.7 ± 249.6 | 101 ± 339 | 77 ± 216 | 28 ± 65 | 99 ± 313 |
| Carbohydrate (g/day)   | 179.9 ± 45.1     | 173.8 ± 43.9    | 21.8 ± 61.9* | 17.8 ± 48.2* | 16.6 ± 53.1 | 27.2 ± 58* |
| % energy(1) SEC-22    | 58.9 ± 5.5       | 57.9 ± 5.9      | 0.6 ± 6.3 | 0.4 ± 5.8 | 0.9 ± 5.8 | 1.9 ± 6.4 |
| % energy(1) Placebo   | 49.8 ± 13.9      | 50.1 ± 15.7     | 3.4 ± 15.5 | 3.7 ± 13.5 | 3.1 ± 14.1 | 4.4 ± 15.5 |
| Protein (g/day)        | 49.8 ± 13.9      | 50.1 ± 15.7     | 3.4 ± 15.5 | 3.7 ± 13.5 | 3.1 ± 14.1 | 4.4 ± 15.5 |
| % energy(1) SEC-22    | 24.9 ± 4.5       | 25.5 ± 4.5      | -0.2 ± 5.2 | -0.1 ± 4.8 | -0.8 ± 4.9 | -1.4 ± 6.2 |
| % energy(1) Placebo   | 24.9 ± 4.5       | 25.5 ± 4.5      | -0.2 ± 5.2 | -0.1 ± 4.8 | -0.8 ± 4.9 | -1.4 ± 6.2 |
| Calcium (mg/day)       | 407.2 ± 131.0    | 459.4 ± 216.3   | 57.5 ± 286.7 | 30.0 ± 173.5 | -16.9 ± 136.8 | 36.8 ± 175.6 |
| Iron (mg/day)          | 346.6 ± 126.6    | 347.4 ± 10.4    | 3.2 ± 14.5 | 3.4 ± 13.1 | 1.1 ± 12.8 | 2.5 ± 17.8 |
| % energy(1) SEC-22    | 8.7 ± 3.5        | 9.2 ± 6.1       | 0.8 ± 3.9 | 0.5 ± 3.1 | 0.1 ± 3.5 | 0.8 ± 4.0 |
| % energy(1) Placebo   | 8.7 ± 3.5        | 9.2 ± 6.1       | 0.8 ± 3.9 | 0.5 ± 3.1 | 0.1 ± 3.5 | 0.8 ± 4.0 |
| Potassium (mg/day)     | 1,525.9 ± 466.4  | 1,693.2 ± 681.9 | 225.2 ± 687.3 | 107.4 ± 465.9 | 16.6 ± 431.9 | 219.7 ± 526.3* |
| Vitamin A (µg RE/day) | 385.5 ± 197.1    | 495.8 ± 216.3   | 247.4 ± 140.8 | -38.0 ± 212 | -10.9 ± 186.7 | -374.2 ± 209.4 |
| Vitamin C (mg/day)     | 54.7 ± 28.9      | 67.6 ± 49.6     | 11.7 ± 44.8 | -11.7 ± 53.1 | -8.4 ± 46.6 | -9.4 ± 51.9* |
| Thiamine (mg/day)      | 0.7 ± 0.2        | 0.8 ± 0.7       | 0.1 ± 0.3* | 0.1 ± 0.3* | 0.1 ± 0.3* | 0.1 ± 0.3* |
| Riboflavin (mg/day)    | 0.9 ± 0.3        | 1.0 ± 0.4       | 0 ± 0.4 | 0 ± 0.4 | 0 ± 0.4 | 0 ± 0.4 |
| Niacin (mg NE/day)     | 8.3 ± 3.0        | 8.8 ± 3.6       | 0.8 ± 3.4 | 1.1 ± 2.8* | 0.6 ± 2.8 | 1.2 ± 3.4* |

Mean ± SD.

SEC-22: Multiple herb formula composed of eight food-grade herbs

(1) Percentage of total energy intake (% energy) was calculated by using Atwater factor (Carbohydrate = 4 kcal/g, Protein = 4 kcal/g, Fat = 9 kcal/g).

* Difference from baseline values was significant by paired t-test (P < 0.05)

** Significantly different from placebo group by student’s t-test (P < 0.05)

Table 4. Changes in Growth Indices during the Study Period

| Variables               | SEC-22 (n = 35) | Placebo (n = 44) | Baseline | Change from baseline during treatment period | Change from baseline during follow-up period |
|-------------------------|-----------------|-----------------|----------|---------------------------------------------|---------------------------------------------|
|                        |                  |                 |          | 1 month | 2 months | 1 month | 2 months |            |            |
| Height-for-age (z score)| -0.144 ± 0.800  | -0.149 ± 0.892  | -0.043 ± 0.116 | -0.004 ± 0.165 | 0.005 ± 0.178 | -0.039 ± 0.168 |
| Weight-for-age (z score)| -1.210 ± 0.625  | -1.191 ± 0.871  | 0.035 ± 0.271 | 0.085 ± 0.234* | 0.064 ± 0.248 | 0.082 ± 0.280 |
| Weight-for-height (z score)| -1.745 ± 0.596 | -1.667 ± 0.581 | -0.005 ± 0.333 | 0.058 ± 0.376 | -0.014 ± 0.432 | -0.031 ± 0.530 |
| BMI-for-age (z score)   | -1.661 ± 0.600  | -1.616 ± 0.575  | 0.118 ± 0.360 | 0.152 ± 0.366* | 0.074 ± 0.397 | 0.158 ± 0.373* |

Mean ± SD.

SEC-22: Multiple herb formula composed of eight food-grade herbs

* Difference from baseline values was significant by paired t-test (P < 0.05)
improvement compared to the placebo group after the second month of follow-up ($P < 0.05$). There was no significant difference in ‘eating problem’, ‘appetite’, ‘undereating frequency’, or food variety-related questions between the groups (Table 2).

**Dietary intake**

Dietary intake showed a similar pattern as picky eating behaviors. Energy, carbohydrate, protein, and lipid intakes as well as eating amounts increased in both groups during the intervention period. Intakes returned to baseline in the placebo group after the second month of follow-up, whereas they continued to increase in the SEC-22 group during the follow-up period. Compared with the placebo group, intakes of several vitamins and minerals in the SEC-22 group increased during both the intervention and follow-up periods. Carbohydrate intake significantly increased compared to the placebo group after the second month of follow-up. From the questionnaires given to caregivers, there was no significant improvement in ‘appetite’ or ‘undereating frequency’ of picky eating behaviors. However, there was a significant increase in the amount of food eaten in the SEC-22 group compared to the placebo group based on actual data obtained from dietary records. There was no significant difference in protein or fat intake between the two groups. Potassium intake significantly increased compared to the placebo group after the first month of intervention and second month of follow-up. There were significant increases in vitamin C and thiamine intakes in the SEC-22 group compared to the placebo group after the second month of follow-up and first month of the intervention period, respectively (Table 3).

**Growth indices**

There was greater improvement in WAZ, WFH, and BAZ compared to baseline values after the second month of intervention and follow-up period only in the SEC-22 group. However, there was no significant difference in growth indices between the two groups (Table 4).

**DISCUSSION**

Although not underweight, thin children with poor appetites are at risk for insufficient intake of energy and other nutrients. At the beginning of our study, two-thirds of subjects with BMIs lower than the 25th percentile reported an average energy intake below their EER. If children continue to eat an inadequate amount of food, they become at risk for stunted growth and negative health outcomes [22,23]. Even if children are not underweight, some evidence suggests that thinness can be problematic. Two other studies have noted that mild underweight, some evidence suggests that thinness can be problematic [22,23].

In the questionnaire on picky eating behaviors, appetite and eating problems were improved in both the SEC-22 and placebo groups. While average meal duration in the placebo group decreased during the treatment period and then returned to baseline level after the second month of follow-up, average meal duration in the SEC-22 group showed a tendency to maintain improvement into the second month of follow-up. The items ‘frequency of food reward’ and ‘frequency of trying to feed’ are questions about parental difficulty in child feeding. Feeding difficulty showed greater improvement in the SEC-22 group than the placebo group during the intervention period. During the follow-up period, this improvement persisted in the SEC-22 group. Carbohydrate intake increased in both groups during the intervention period and remained significantly elevated in the SEC-22 group. These patterns are similar to changes in the feeding difficulty of eating behaviors. Since rice is a main dietary staple for most Koreans, increasing the amount of food eaten will likely increase carbohydrate intake as well. Intake of most vitamins and minerals showed greater improvement only in the SEC-22 group during the whole study period, which can be attributed to improvements in eating amount and picky eating behavior. We believe that the increase in eating amount contributed to significant improvement of carbohydrate, vitamin C, potassium, and thiamine intakes in the SEC-22 group compared to the placebo group. This result suggests that SEC-22 could improve digestion as well as decrease abdominal discomfort in children, resulting in improvement of eating behaviors and more pleasant mealtime for caregivers and children.

These results were partly due to improvement of digestion through the function of extract components, which have been demonstrated to affect digestion [24]. Dried fruit of *Crataegus pinnatifida*, which contains lipase and enhances pepsin activity, has been used to treat indigestion in Korean medicine since it promotes digestion of protein and fat as well as enhances the contractility of rat gastric and intestinal smooth muscle strips [25,26]. The median lethal doses of *Crataegus pinnatifida* in mice and rats were found to be 1.85 and 3.38 g/kg, respectively [27]. Root of *Atractylodes japonica* has been used to help digestion and has been shown to improve gastrointestinal tract activity with no observed toxicity up to a dose of 4 g/kg in animal testing [28,29]. Dried pericarpium of *Citrus unshiu* may aid digestion by relaxing gastric smooth muscle and promote gastric juice secretion by increasing amylase activity [30]. Sprout of *Hordeum vulgare* is rich in α-amylase and β-amylase and may improve digestion of carbohydrates [31]. There have been no documented reports of the toxicity of dried pericarpium of *Citrus unshiu* and sprout of *Hordeum vulgare*. Fruit of *Amomum xanthioides* has been used in the treatment of abdominal pain and indigestion and may ameliorate gastric ulcers and gastritis as well as promote peristalsis [32,33]. No signs of toxicity up to a dose of 25 g/kg were observed in a previous animal study [34]. Root of *Zingiber officinale* has been used frequently for treatment of dyspepsia, gastroparesis, and slow motility symptoms and may speed up gastric transit of foods [35-38]. *Zingiber officinale* has been listed as “Generally Recognized as Safe” (GRAS) by the US FDA, and its median lethal dose in rats is 170 g/kg [39,40]. Dried fruit of *Zizyphus Jujuba* has been used along with root of *Zingiber officinale* for purposes related to gastrointestinal health and digestion in traditional Korean medicine [41]. No signs of toxicity were observed up to a dose of 150 g/kg in mice [42]. Antler of *Cervus elaphus* was shown to play a role in bone healing by promoting the synthesis of
proteins and nucleic acids in animal testing [33].

Shim and the colleagues suggested that picky eating behaviors consist of two behavioral dimensions (i.e. eating amount and variety of diet) [43]. The results of this study show that supplementation of SEC-22 improved the eating amount component in picky eating behaviors, although there was no change related to preference for specific flavor and texture of foods (e.g. ‘frequency of preparing special food’, ‘frequency to try new foods’, ‘willingness to try new foods’, and ‘food variety’). These findings represent that supplementation with SEC-22 did not alter thin children’s food preferences, such as flavor and texture, but did have an effect on eating amount. In addition, improvements induced by SEC-22 were not only immediate but also maintained for at least 2 months. This maintenance of improved nutritional intake after intervention may benefit long-term growth. Shim and colleagues reported that preschool children with picky eating behaviors and insufficient intake show faltering linear growth, whereas those with picky eating behaviors of limited variety do not. Therefore, SEC-22 supplementation may help picky eaters’ linear growth by improving the amount of food eaten. In the current study, there was no significant change between the two groups in HAZ, although a 4 months study period is not enough to observe a significant change related to preference for specific flavor and texture of foods. In addition, there was no significant change between the two groups in WAZ, WFH, or BAZ as indicators of short-term nutritional status. However, P values of WAZ, WFH, and BAZ after the second month of follow-up were 0.093, 0.069, and 0.090 respectively. There was greater improvement in WAZ, WFH, and BAZ compared to baseline values after the second month of intervention and follow-up only in SEC-22 group.

This study has several limitations. First, as these results of picky eating behaviors and dietary records were based on questionnaires administered by caregivers, they may be errors. Second, as eating behaviors and dietary intake generally have some large variations, long-term study of a larger sample size is required to identify an exact effect on linear growth. This study included just 2 months of treatment and 2 months of follow-up. Thus, a study of longer duration is likely required to identify whether or not SEC-22 has an effect on growth outcomes in the aspect of linear growth. On the other hand, this study, to the best of our knowledge, is the first intervention study to investigate therapeutic effects on picky eating and dietary behaviors of thin children. Since there have been few studies on thin children without any illness or starvation, this study could provide insights into thin children with poor appetites or picky eaters in terms of feeding and amount of eating. While thin children can gain weight by increasing their eating amount, nutrition education targeted to caregivers and children regarding healthy dietary behaviors may be helpful for promoting appropriate growth.

In conclusion, supplementation with multiple herb formula SEC-22 may be effective in improving eating amount and nutrient intakes or carbohydrates, vitamin C, potassium, and thiamine in thin children. This study also showed that SEC-22 supplementation is effective in improving parental feeding difficulty resulting from eating small amounts of food and picky eating. The results of this study suggest that supplementation with multiple herbal extracts based on Korean traditional medicine may be beneficial in improving diet intake, growth, and eating behaviors in thin children.

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