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ARTICLE

Effect of Daily Exposure to an Isolated Soy Protein Supplement on Body Composition, Energy and Macronutrient Intake, Bone Formation Markers, and Lipid Profile in Children in Colombia

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ABSTRACT

A soy protein–based supplement may optimize bone health, support physical growth, and stimulate bone formation. This study aimed to assess the effect of a daily soy protein supplement (SPS) on nutritional status, bone formation markers, lipid profile, and daily energy and macronutrient intake in children. One hundred seven participants (62 girls), ages 2 to 9, started the study and were randomly assigned to lunch fruit juice with ($n = 57$, intervention group) or without ($n = 50$, control group) addition of 45 g (230 Kcal) of a commercial SPS during 12 months; 84 children (51 girls, 33 boys) completed the study (45 and 39 intervention and control, respectively). Nutritional assessment included anthropometry and nutrient intakes; initial and final blood samples were taken; insulin-like growth factor-I (IGF-I), osteocalcin, bone specific alkaline phosphatase (BAP), insulin-like growth factor binding protein-3 (IGFBP-3), cholesterol, triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were analyzed. Statistically significant changes ($p < .05$) in body mass index and weight for age Z scores were observed between groups while changes in body composition were not. Changes in energy, total protein, and carbohydrate intakes were significantly higher in the intervention group ($p < .01$). Calorie intake changes were statistically significant between groups ($p < .001$), and BAP decreased in both groups, with values within normal ranges. Osteocalcin, IGFBP-3, and lipid profile were not different between groups. IGF-I levels and IGF/IGFBP-3 ratio increased significantly in both groups. In conclusion, changes in macronutrient and energy intake and nutritional status in the intervention group compared to control group may ensure harmonious and adequate bone health and development.

KEYWORDS

child; Colombia; dietary supplements; nutritional status; soybean proteins

Introduction

Soybean is widely used as a source of protein. Soy protein–based formulas account for about 25% of total infant formulas used in the United States (Bathia and Greer, 2008). In pediatric formulas and nutritional supplements, the purpose is to supplement the daily diet to ensure proper growth and development and prevent disease. The nutritional composition of a

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supplement based on soy protein isolate also includes sugars, vitamins, minerals, and other nutrients (Rossen et al., 2016). In addition, they are fortified with micronutrients such as iron, calcium, phosphorus, magnesium, zinc, manganese, copper, potassium, and so on, and vitamins A, C, D, E, K, and B (B1, B2, B6, B12, niacin, folic acid, biotin, and pantothenic acid). The formulas are fortified with minerals to compensate binding phytates that may be present as contaminants (National Toxicology Program, 2010).

The main concerns about the use of soy protein nutritional supplements are protein digestibility and balanced concentration of essential amino acids, biological quality of the protein, high levels of aluminum, presence of phytates, and content of phytoestrogens (Boland et al., 2009).

The nutritional quality of soy protein (SP) as assessed by PDCASS (protein digestibility corrected amino acid score) and DIASS (digestible indispensable amino acid score) has been determined to be similar to milk protein concentrate (MPC) or whey protein isolate (WPI). Moreover, when dietary indispensable and conditionally indispensable amino acids are analyzed, true ileal amino acid digestibility varied considerably following the same pattern within the protein sources (SP, MPC, or WPI) (Rutherfurd et al., 2015).

Phytates (hexa-and penta-inositol phosphate) are potent inhibitors of mineral absorption and bind divalent minerals, such as calcium, magnesium, iron, and zinc. Phytoestrogens are plant-derived compounds of nonsteroidal structure. The molecular weights and structural characteristics are similar to those of 17 β-estradiol. The estrogenic activity of isoflavones is associated with the structural similarity, which may enable them to bind to specific β-estrogen receptors and exert estrogenic or antiestrogenic actions. However, the estrogenic potential of isoflavones is weak compared to estradiol (Setchell, 1998).

A recent meta-analysis of cross-sectional, case-control, cohort studies or clinical trials carried out in children fed soy infant formula (SIF) compared with those fed cow's milk formula (CMF) or human formula (HM) concluded that growth patterns, bone health, and metabolic, reproductive, immune, endocrine, and neurological functions in children fed SIF are similar to those observed in children fed CMF or HM (Vandenplas et al., 2014). Although the evidence, analysis, and literature review raise no clinical concerns with respect to nutritional adequacy of soy protein–based formulas, further studies are needed to support these statements.

Most of the epidemiological and clinical studies have been done on infants or Asian populations and have been the basis for other research in Western countries (Messina, 2010). Several analytical studies show that soy produced in Asia differs in its composition of macro- and micronutrients from the soy produced and consumed in the United States and other Western countries (Cassidy et al., 2006). In Asian countries, soy foods are generally minimally processed; evidence suggests that 10% of the Asian population consumes as much as 25 g of soy protein per day, and about 30% of total soy foods consumed by Asians is in the form of fermented foods (Messina et al., 2006). Americans eat much more processed forms of soy (e.g., soy flour, textures vegetable protein, and isolated soy protein). Soy protein isolate is the sole source of protein in infant formulas and soy dietary supplements (Klein et al., 2010). It has been reported that soybeans from China had higher crude protein content compared to soy produced in countries such as Brazil, Argentina, and the United States, while soy protein-processed products from the United States had a higher protein content than those produced in other countries (Karr-Lilienthal et al., 2004). It is known that soy protein composition differs chemically and varies with the soybean strain, when it is harvested, where it is grown, and how it is stored, processed, and analyzed; in addition, it is absorbed and modified differently in the gastrointestinal tract (Klein et al., 2010). Moreover, in dose-response studies in humans, it is not easy to estimate the amount of soy or soy protein needed

to exert a physiological effect on individuals. For example, the dose-dependent relationship between soy protein and low-density lipoprotein (LDL) cholesterol (Padhi et al., 2015), the effect of consuming different amounts of soy protein isolate on postprandial glycemic control in healthy humans (Kashima et al., 2016), and the high intake of soy foods have also been associated with a small reduction in breast cancer risk in Asian countries (Bilal et al., 2014).

There are few epidemiological or clinical studies in the literature performed in pediatric populations older than two years monitoring nutritional formulas or supplements based on soy protein to assess the physiological effects of consumption (Joeckel and Phillips, 2009). The formulas and supplements based on isolated soy protein for infant and children populations are used for economic, religious, and philosophic reasons. In addition, soy protein–based supplements may be a valid option to feed term-born infants if breastfeeding is not possible and if CMF is not tolerated (Vandenplas et al., 2011).

A recent cohort study did not find group differences when comparing effects on reproductive organ volumes and structural characteristics in five-year-old children who were fed CMF or SIF as infants (Andres et al., 2015). Literature reports about soy effects on children older than two years are either not available or not explicitly separated from the evidence in younger children.

The present study aimed to assess the effect of daily 12-month soy protein supplement (SPS) intake on nutritional status, bone formation markers, lipid profile, and daily energy and macronutrient intake in healthy preschoolers and schoolchildren two-to-nine years old from low-income Colombian families.

Materials and methods

Based on a sample size calculation, a randomized controlled trial (RCT) was designed to detect clinically relevant changes in nutritional status, anthropometric variables, or bone metabolism markers ($n = 150$ to account for possible subjects lost for follow-up). A convenience sample of children (aged 2–9 years) in preschool or attending public schools and participating in three community dining rooms in Bogota were enrolled from June to September 2012. All participants were from low-income families; they were healthy prepuberal children (Tanner 1) according to normal standards established by the World Health Organization (WHO), born at term (> 37 weeks), and with normal weight at birth (> 2,500 g).

Enrollment, randomization, and blinding

Appointments were assigned to receive 10 to 12 parents each day; informed consent was obtained from them as well as from children age 7 or older. Pediatric and nutritional assessments were then performed and children were screened for eligibility according to the inclusion criteria; to classify nutritional status, WHO growth reference standards were followed. Allocation concealment was kept in sealed folders until blood samples were taken from eligible children, a code was assigned, and laboratory staff did not know the participants' group assignments. Participants were randomly assigned, using a computer-generated random number sequence, either to an intervention group that received the lunch fruit juice with addition of a commercial preparation of SPS during 12 months or to the control group that consumed the lunch juice and a drink based on whole milk. A staff member in each dining room involved in the intervention was aware of group assignments, prepared, delivered, and registered supplement record adherence daily.

Table 1. Nutritional supplement composition.

Kcal per 45 g serving	230	:
	Kcal from fat:100	% daily value
Total fat	11 g	17
Saturated	1.5 g	8
Trans fat	0 g	
Protein	7 g	14
Total carbohydrates dietary fiber	24 g	8
Sugars	< 1 g	0
	24 g	
Sodium	105 mg	4
Potassium	208 mg	8
Vitamin A		10
Vitamin C		40
Vitamin D		30
Vitamin E		20
Vitamin B1		40
Vitamin B2		25
Vitamin B3		25
Vitamin B6		30
Vitamin B12		25
Vitamin K		10
Pantothenic acid		25
Folic acid		20
Biotin		25
Calcium		20
Iron		20
Magnesium		10
Iodine		15
Phosphorus		25
Zinc		20
Selenium		8
Cooper		15
Manganese		30
Chromo		15
Molybdenum		15
Chloride		8
Choline	68 mg	
Carnitine	2 mg	
Taurine	16 mg	
Inositol	18 mg	

Intervention

Forty-five grams of soy protein supplement, which provides 230 kcal (flavors: strawberry, chocolate, and vanilla), was dissolved in 190 cm^3 of the menu fruit juice and administered Monday–Saturday for 12 months. The control group received the menu fruit juice and a drink based on whole milk.

On Sundays, the parents or caretakers were given the supplement powder to give to the children in a similar way. Nutritionists performed home visits randomly on Sundays to verify supplement consumption, adherence, and perception of participants and to give dietary advice to parents and caregivers (for supplement composition, see Table 1).

Nutritional assessment

Anthropometric measures were obtained by a trained nutritionist at 0, 6, and 12 months of the study, using standardized methods, which refer to routine anthropometric protocol followed by the trained nutritionist according to WHO (World Health Organization, 1995). Child height was measured to the nearest 0.1 cm using a Seca 213 mobile stadiometer. Weight

was measured to the nearest 0.1 kg on a Tanita UM-051 scale (Tanita Corporation of America, Inc), with a tare function and the children wearing only shorts and a T-shirt. Body mass index (BMI) was obtained according to the formula (weight (kg)/height (m^2). Height, weight, and BMI Z scores were calculated using World Health Organization (WHO) Anthroplus software (version 1.0.4). The triceps skinfold thickness (T) was measured using a Harpenden Skinfold Caliper. Upper arm circumference (C) was measured using a Lufkin W606PM Anthropometric Tape. Upper arm muscle area (M), arm muscle circumference (CM), upper arm area (A), and upper arm fat area (F) were derived from measures using usual procedures. All estimates were calculated for each participant; age and gender-specific percentiles were used as reference for each of the variables (Frisancho, 1981).

Nutrient and food intakes were assessed using food frequency questionnaire and 24-hour dietary recall answered by a parent or caregiver during a weekday and a weekend day. Types of foods included 18 types of cereals and cereal products, 14 types of meat products, 20 types of fruits, 13 types of vegetables, 9 types of legumes, 11 types of beverages, 5 types of dairy products; information regarding snacks and other items was collected. Diet composition was analyzed according to each nutrient according to the Colombian nutrient database for standard reference (ICBF, 2015). The nutrient intake of each child was assessed according to the estimated average requirement (EAR) and acceptable macronutrient distribution range (AMDR) defined by the American National Academy of Sciences (Murphy and Poos, 2002).

Morning blood samples were taken from fasting children at the beginning and end of the study; serum was obtained, aliquoted, and kept at -70°C; it was analyzed for IGF-I, osteocalcin, bone specific alkaline phosphatase (BAP), insulin-like growth factor binding protein-3 (IGFBP-3), total cholesterol, triglycerides, and LDL and HDL cholesterol. IGF-I and IGFBP-3 were measured by Elisa (Diasource, USA); osteocalcin and BAP activity were measured by Elisa (IDS, UK). Serum concentrations of triglycerides, total cholesterol, and LDL and HDL cholesterol were measured enzymatically using commercial kits (Spinreact, USA)

Statistical analysis was performed using descriptive statistics (mean, median, and standard deviation). Significant differences among groups were assessed by homogeneity contrasts of quantitative variables followed by analysis of variance (ANOVA) for factors with repeated and not repeated measures. *RWizard* statistical program was used. A p value of $< .05$ was considered significant; p values were obtained assuming sphericity. Mauchly test was used to test sphericity; when it was significant, the p value was obtained by Greenhouse-Geisser and Huynh-Feldt corrections for departure from sphericity.

The study followed local and international ethical guidelines and was approved by the ethical committee of the Faculty of Sciences at the Pontificia Universidad Javeriana Columbia. Written consent was obtained from each participant's parent or legal caretaker. Written assent was also obtained from children older than 7 years of age.

Results

One hundred seven children were enrolled and randomly assigned to the intervention group ($n = 57$) or the control group ($n = 50$); 84 participants finished the study (45 in the intervention group and 39 in the control group). Reasons to withdraw from the study were unrelated to the study (the most common was relocation of the family within the city; others were absence for more than two weeks due to school vacation, complaints of the parents about not observing visible physical changes compared to those in the control group, some family-related children in the control group wanted to drink the supplement and vice versa, and in

Table 2. General characteristics of the study participants.

	Intervention ($n = 57$)		Control ($n = 50$)	
	Boys ($n = 24$)	Girls ($n = 33$)	Boys ($n = 21$)	Girls ($n = 29$)
Age (years)				
Mean ± SD	7.8 ± 2.0	6.99 ± 1.78	7.1 ± 2.0	6.77 ± 1.78
Median	8.6	7.4	8.0	6.8
range	2.0–9.9	2.2–9.5	2.6–9.6	2.3–9.9
2–6 years (%)	6 (25%)	12 (36%)	7 (33%)	15 (52%)
7–9 Years (%)	18 (75%)	21 (64%)	14 (67%)	14 (48%)
Body weight (kg)				
Mean ± SD	25.7 ± 5.9	22.6 ± 5.5	22 ± 4.8	21.9 ± 4.20
Median	26	23.4	23.6	21.6
Range	11.4–35.6	13–32	10–35	13–32
WFA *z* score	−0.002 ±0.59	−0.04 ± 0.96	0.05 ± 0.61	−0.09 ± 0.63
Height (m)				
Mean ± SD	1.23 ± 0.13	1.17 ± 0.13	1.17 ± 0.11	1.16 ± 0.10
Median	1.17	1.2	1.22	1.16
Range	0.83–1.44	0.89–1.36	0.84–1.41	0.89–1.36
HFA *z* score	−0.44 ± 0.61	−0.49 ± 0.74	−0.85 ± 0.44	−0.64 ± 0.65
Body mass index				
Mean ± SD	16.5 ± 1.29	16.0 ± 1.14	16.9 ± 1.2	16.2 ± 1.14
Median	16.3	16.1	16.7	16.1
Range	14.9–19.7	14.4–19.2	14.2–18.1	14.4–19.2
BMIFA *z* score	0.38 ± 0.67	0.22 ± 0.76	0.79 ± 0.73	0.44 ±0.73
T (mm^2)				
Mean ±SD	9.66 ± 2.7	10.79 ± 2.6	8.9 ± 2.1	10.21 ± 2.09
Median	9.6	10	9	10
Range	6–15	7–17	7–18	7–17
Percentile 10th–85th (*n*)	24	33	21	29
C (mm)				
Mean ± SD	180 ± 15.4	176 ± 20	173 ± 17.3	169.4 ± 13.3
Median	180	180	175	170
Range	143–216	146–203	143–220	128–203
Percentile 10th–85th (*n*)	24	33	21	28
M (mm^2)				
Mean ± SD	1,810 ± 367	1,647 ± 349	1,692 ± 200	1,502 ± 247
Median	1,761	1,809	1,723	1,453
Range	990–2,774	988–2,096	842–2,417	988–2,096
Percentile 10th–85th (*n*)	23	23	23	29
F (mm^2)				
Mean ± SD	808 ± 281	867 ± 288	713 ± 200	785 ± 199
Median	736	816	723	773
Range	460–1,435	567–1,498	461–1,806	567–1,498
Percentile 10th–85th (*n*)	23	31	19	29

WFA = weight for age; HFA = height for age; BMIFA = body mass index for age; T = triceps skinfold thickness; C = upper arm circumference; M = upper arm muscle area; F = upper arm fat area; percentile (n) = number of participants within this interval; SD – standard deviation.

one case a mother associated the increase of the boy sweating with the supplement intake). Characteristics of the sample are shown in Table 2.

Anthropometric parameters

The increase in height, weight, BMI, and growth velocity during 12 months was the expected in both groups, control and intervention, without reaching a significant difference between them when presented in means and SD. When expressed as Z score, statistically significant changes in weight for age and BMI for age were observed ($p < .01$) (Table 3). There were no statistically significant changes in body composition parameters: triceps skinfold thickness, mid-upper arm circumference, mid-upper arm muscle area, and mid-upper arm fat area. Arm

Table 3. Anthropometric and body composition parameters.

	Intervention ($n = 45$)		Control ($n = 39$)		
	Beginning	End	Beginning	End	p value
Weight (g)	23 ± 5.8	26.5 ± 2.7	23 ± 4.4	26 ± 3.4	0.5
WFA *z* score	− 0.028 ± 0.84	0.08 ± 0.86	− 0.03 ± 0.63	− 0.15 ± 0.68	0.01
Height (m)	1.2 ± 0.13	1.27 ± 0.03	1.2 ± 0.13	1.28 ± 0.05	0.1
HFA *z* score	− 0.47 ± 0.69	− 0.34 ± 0.71	− 0.72 ± 0.58	− 0.56 ± 0.80	0.1
BMI (kg/m^2)	16.1 ±1.2	16.6 ± 1.8	16.8 ±1.3	16.3 ± 1.5	0.09
BMIFA *z* score	0.58 ± 0.75	0.20 ± 0.81	0.28 ± 0.73	0.29 ± 0.8	0.01
Growth velocity (Cm/y)	6.82 ±2.3	7.16 ±4.5	6.39 ±2.09	6.43 ± 2.97	0.43
T (mm)	10.5 ± 2.7	11.3 ± 3.6	10.1 ±2.3	10.6 ± 2.5	0.94
C (mm)	177.8 ± 20.8	192 ± 29.1	173.2 ± 15.2	184.6 ± 18.2	0.64
M (mm^2)	1,690 ± 388	1,985 ± 658	1,607 ± 316	1,833 ± 337	0.46
F (mm^2)	859 ± 293	1,014 ± 436	800 ± 209	904 ± 274	0.86

WFA = weight for age; HFA = height for age; BMIFA = body mass index for age; T = triceps skinfold thickness; C = upper arm circumference; M = upper arm muscle area; F = upper arm fat area. p value corresponds to ANOVA for change differences between control and intervention groups.

anthropometry according to the classification of Frisancho ranged from the 10th to the 85th percentile, and the differences between groups were not statistically significant.

Energy and macronutrient intakes

An overview of energy and macronutrient intakes is provided in Table 4, together with the difference between the measures at the beginning and at the end of the study.

There was a statistically significant difference ($p < .001$) between groups in the change in caloric intake, and a more homogeneous variation, represented as a smaller standard deviation, 131 in the intervention group compared to 383 in the control group

Mean daily protein intake (P intake) was similar in both groups at the beginning and at the end of the trial. Despite this, the slightly higher change in the intervention group, together with a more homogenous range of protein intake (a smaller standard deviation), resulted in a statistically significant difference ($p < .001$).

Mean daily carbohydrate intake (CH intake) showed an increase in the intervention group and a decrease in the controls, with a significant difference between groups ($p < .001$). Changes in mean daily fat intake (F intake) were statistically significant between the two groups, with a higher increase in the intervention group ($p < .001$). Analyses for saturated fat, monounsaturated fat, and polyunsaturated fat did not show statistically significant differences between groups.

There was no statistically significant difference between groups in the change between initial and final values in any of the parameters shown in Table 5. Serum bone specific alkaline phosphatase levels showed a statistically significant decrease, similar in both groups after a year (45 ± 33 µg/L and 24 ± 47 µg/L intervention and control groups, respectively, $p < .01$), but initial and final values were within normal reference ranges (Table 5). Osteocalcin and IGFBP-3 levels were similar at the beginning and end, both within the reference values for the age ranges.

Serum levels of IGF-1 increased similarly and significantly in both groups as expected ($p < .001$) (Table 5). The concentrations, when analyzed by age intervals, are within the normal ranges of reference for age (data not shown). Serum ferritin levels increased similarly and significantly in both groups after a year ($p < .005$), but values were within normal reference range.

Table 4. Values and changes in energy and macronutrient intakes (mean ± standard deviation).

	Intake			AMDR (% of energy)		
	Intervention ($n = 45$)	Control ($n = 39$)	p value	Intervention ($n = 45$)	Control ($n = 39$)	p value
Energy (kca/day)						
Initial	1,808 ± 438	1,988 ± 567	< .001			
End	1,974 ± 434	2,024 ± 533				
Change	166 ± 131	36.9 ± 383				
Protein (g/day)						
Initial	58.8 ± 16.6	63.8 ± 20.1	< .001	13.0 ± 2.1	12.9 ± 1.7	.009
End	63.6 ± 16	66.4 ± 21.6		12.9 ± 1.8	13.0 ±1.7	
Change	4.8 ± 4.6	2.6 ± 13.4		− 0.1 ± 0.6	0.2 ± 1.9	
Vegetable protein (g/day)						
Initial	22.5 ± 7.3	24.8 ± 9.1	< .001			
End	28.6 ± 8.0	27.3 ± 10.6				
Change	6.1 ± 4	2.4 ± 9.1				
Carbohydrate (g/day)						
Initial	242 ± 70	276.3 ± 96.4	< .001	54.3 ± 9.5	55.3 ± 7.7	.3
End	260 ± 67	275.3 ± 89.4		53.4 ± 8.2	54.1 ± 8.0	
Change	17.8 ± 23.6	− 1.0 ± 87.9		− 0.9 ± 5.4	− 1.2 ± 9.7	
Total fat (g/day)						
Initial	65.6 ± 21.3	70.4 ± 21.4	< .001	32.6 ± 7.3	32.2 ± 7.0	.002
End	73.4 ± 21.6	71.6 ± 21.3		33.4 ± 6.8	32.3 ± 7.2	
Change	7.8 ± 6.2	1.2 ± 19		0.8 ± 1.1	0.2 ± 8.1	
Saturated fat (g/day)						
Initial	18.9 ± 7.3	19.5 ± 6.9	.91	9.45 ± 3.06	8.90 ± 2.5	.2
End	18.93 ± 7.3	19.72 ± 7.8		8.51 ± 2.81	9.01 ± 3.0	
Change	0.04 ± 0.27	0.21 ± 7.0		− 1.1 ± 2.2	0.11 ± 0.6	
Monounsaturated fat (g/day)						
Initial	17.57 ± 6.54	19.97 ± 7.43	.12	8.84 ± 2.88	9.07 ± 2.46	.77
End	18.29 ± 7.62	19.35 ± 7.53		8.17 ± 2.72	8.80 ± 2.72	
Change	0.72 ± 5.20	− 0.62 ± 7.2		− 0.85 ± 2.32	− 0.27 ± 2.86	
Polyunsaturated fat (g/day)						
Initial	14.88 ± 6.5	16.43 ± 6.45	.22	7.39 ± 2.58	7.56 ± 2.80	.65
End	14.76 ± 6.19	16.21 ± 5.30		6.65 ± 2.25	7.44 ± 2.16	
Change	− 0.11 ± 1.84	− 0.21 ± 7.1		− 0.68 ± 0.97	− 0.12 ± 3.53	

AMDR = acceptable macronutrient distribution range.

Discussion

This study presents the results of daily soy protein–based nutritional supplement intake for 12 months on body composition, markers of bone metabolism, lipid profile, and intake of energy and macronutrients in children between 2 and 9 years of age.

Table 5. Serum measurements (mean ± standard deviation).

	Intervention ($n = 45$)		Control ($n = 39$)	
	Beginning	End	Beginning	End
BSAP (μg/L)	144.8 ± 38.1	99.4 ± 31.6	134.1 ± 37.9	110 ± 42.3
Osteocalcin (ng/mL)	31 ± 12.6	31.3 ± 10.1	30.4 ± 13	31.2 ± 10.3
IGF-I (ng/mL)	144.5 ± 47.3	234.5 ± 24.6	142.1 ± 48.6	241.7 ± 26.7
IGFBP-3 (ng/mL)	7,303 ± 2,606	7,483 ± 1,301	7,406 ± 2,456	7,581 ± 1,603
Ferritin (ng/mL)	44.4 ± 17.2	64.1 ± 35.4	50.1 ± 23.7	61.9 ± 27.5
Total protein	7.4 ± 0.8	6.8 ± 0.9	7.5 ± 0.6	7.2 ± 0.9
Albumin	4.4 ± 0.6	4.0 ± 0.7	4.4 ± 0.5	4.1 ± 0.6
Cholesterol	161 ± 45.2	145.3 ± 26.6	156.6 ± 34.1	143.2 ± 26.3
HDL	55.3 ± 7.7	46.1 ± 17	56.2 ± 9.1	46.3 ± 11.7
LDL	86.8 ± 42.3	83.6 ± 31.6	82.7 ± 30.9	89.7 ± 33.3
Triglycerides	95.3 ± 37.9	96.6 ± 41.6	88.2 ± 26.8	93.7 ± 33.14

The growth patterns of the World Health Organization for children 2–18 years of age are followed in Colombia to assess growth and to monitor nutritional status. The fact that we do not have local nutritional standards is a limitation, as is the loss of individuals for follow-up (22%), which was similar in the intervention and control groups. In addition, macronutrient intake, which was evaluated at the beginning of the trial, midway, and at the end, was not then regularly followed either at home or at school. A limited sample size and the fact that all the participants came from a single city are other concerns. Childhood growth is influenced by internal and external factors: genetic, lifestyle, and nutrition. Changes in lifestyles and nutrition can modify trends in height, weight, and body mass index (Hernandez et al., 2015). In our study, the gain in size during the 12 months was similar for both groups and according to the reference standards. When discriminated by gender, the analysis of variance to find differences between the control group and intervention values for weight gain were not significant (boys: $p = .75$; girls: $p = .5$; data not shown). Similarly, the analysis of BMI mean changes for 12 months showed no significant difference between the two groups. The observed decrease in the control group remains in the normal range and does not involve changes in the classification by WHO standards for malnutrition or overweight. The analysis of changes in BMI for age and body weight for age Z scores during 12 months suggests that there was a significant effect of the supplement intake on the nutritional status. Changes in the growth rate were as expected, without an acceleration of growth. Results of the changes in body composition variables (weight for age and BMI for age) lead us to conclude that the consumption of the nutritional supplement for 12 months may have a significant effect on body composition mainly at the expense of body weight gain without involving changes in the adequate nutritional status. A recent published study showed no differences in body weight or body composition when comparing a meat diet of chicken and beef with a vegetarian diet primarily of soy protein (Neacsu et al., 2014).

In our study, the growth and development of children who received the nutritional supplement based on soy protein for 12 months were similar to those of the control children who consumed the cow's milk–based drink. These results agree with those published on infant populations that compare growth and development of children consuming infant formula based on soy protein to growth and development of children who consumed a formula based on milk protein (Andres et al., 2015; Vandenplas et al., 2014).

The concern of pediatricians when recommending the use of a nutritional supplement based on soy protein is on possible hormonal effects of the exposure of children to phytoestrogens contained in these formulas (McCarver et al., 2011). Isoflavones are phytoestrogens. The isoflavones are bound to the proteins through noncovalent forces and co-precipitate with the soy protein isolate during the process. Isoflavone content in soy can be obtained both as aglycone (genistein, daidzein, and glycitein) and glycone forms (linked through a glycosidic sugar: genistin, daidzein, and glycitin) (Setchell, 1998). In the case of aglycone forms, genistein content is between 52% to 61%, followed by daidzein 31% to 42%, and glycitein 5% to 9%. In nutritional supplements, most of the isoflavones are in a glycoside form; once in the gastrointestinal tract, the action of specific bacteria β-glucosidases hydrolyzes them to release the aglycone forms, which are then biologically active (Vitale et al., 2013).

In this study, the daily average consumption of isoflavones in the soy protein nutritional supplement was 0.130 mg/kg body weight/day. Genistein and genistin, 0.036 and 0.056 mg/kg body weight/day, respectively, were the most abundant, followed by daidzein and daidzin, 0.015 and 0.020 mg/kg body weight/day, respectively. This value is below those reported in other studies, where the range has been from 1.6 to 8.0 mg/kg body weight/day (Setchell et al., 1997). According to the U.S. National Toxicology Program, total isoflavone intake by

infants exclusively fed soy formula was estimated at 2.3–9.3 mg/kg bw/day in the United States; in Brazil it was estimated at 9.2–34.9 mg/kg body weight/day (Fonseca et al., 2014). In Italian children aged 5–8 years, the total isoflavone intake was estimated at 1.2 mg/kg body weight/day (Morandi et al., 2005). Therefore, in accordance with the recommendation of the expert panel on the use of nutrition based on soy protein of the National Toxicology Program of the U.S. National Institutes of Health (NIH) supplements, we can suggest the safe use of this nutritional supplement because of its low level of isoflavones (McCarver et al., 2011).

Bone metabolism in children is directed to bone growth and remodeling. Bone remodeling during formation and resorption are closely linked. Serum biochemical markers of bone metabolism are classified according to the process of formation and resorption. BAP, osteocalcin, and procollagen peptides I are markers of bone formation (Tuchman et al., 2008).

In the present study, the decrease observed in serum levels of BAP, 30% in the intervention group and 18% in the control group, remained within the normal range for age. It is known that dietary protein enhances the production of IGF-I, a bone trophic growth factor that promotes osteoblast formation and bone growth, which was increased significantly in both groups, with no differences between them (Minuto et al., 2005). Serum levels of IGFBP-3, a binding protein also regulated by protein intake, remained unchanged in both groups. Similarly, no changes in osteocalcin levels were found, which remained within normal limits. These findings and the subsequent increase in the IGF-I/IGFBP-3 ratio indicate that dietary protein contributes to bone health and normal metabolism without deleterious changes in bone formation.

Several recently published studies have analyzed the relationship between soy protein and lipid profile in normal adult population, postmenopausal women, or people with a metabolic disorder (type II diabetes, hypercholesterolemia, dialysis). Few studies have concentrated on children. The first meta-analysis, published in 1995, included 38 studies involving children and adults and suggested that soy protein consumption was associated with significantly decreased levels of serum cholesterol, LDL cholesterol, and triglycerides and nonsignificant increase in HDL cholesterol concentrations. It was suggested that soy phytoestrogens could be responsible for these hypocholesterolemic effects (Anderson et al., 1995). Another meta-analysis, published in 2005, indicated that consumption of soy protein containing isoflavones was associated with a significant decrease in total cholesterol, LDL cholesterol, and triglycerides and a significant increase in HDL cholesterol. Changes were related to gender, initial concentrations, and dietary model. This study found that the higher the content of isoflavones in protein isolate, the greater the effects on changes in lipids; in addition, longer periods of consumption were associated with higher HDL effects (Zhan and Ho, 2005). In 2007, another meta-analysis (Fulgoni, 2008) concluded that soy protein with or without isoflavones significantly improves the lipid profile; in addition, soy isoflavones significantly decreased total cholesterol and LDL cholesterol and caused no change in HDL cholesterol and triglycerides. In our study, which is in the child population, we find no trend or significant change in serum total cholesterol, HDL and LDL cholesterol, or triglycerides, in either the control or the intervention group. One of the possible explanations may lie in the low isoflavone content of the supplement used.

In developing countries, supplementing school feeding programs with soy protein may be an alternative to improve the nutritional and cognitive indicators of the child population, as evidenced by a recent study that evaluated anthropometric and cognitive performance for one year in schoolchildren given a nutritional supplement based on corn and soy protein. The results showed a significant increase in learning indicators and in achieving greater muscle mass, obtained from the measurement of the upper half circumference of the arm (Nkhoma et al., 2013).

Macronutrient consumption can be analyzed in several ways: g/day, g/kg according to reference dietary intakes (DRIs) or as a percentage of calories. Another measure of macronutrient intake is the range of acceptable macronutrient distribution (AMDR), which was the method used in this study. Protein intake for both groups was within the recommended range (5%–20%); changes in intake were higher for the group consuming the nutritional supplement. Similarly, carbohydrate and total fat intakes were within the recommended range (45%–65% and 25%–35%, respectively); however, the changes in the consumption of these macronutrients were also significantly higher in the group that consumed the supplement. Since intake of fatty acids is difficult to measure with dietary questionnaires, serum measurements are proposed as biomarkers of intake. A recent longitudinal study in school-age children from Bogota, Colombia, showed, for example, that trans fatty acids were not associated with weight or linear growth during a median of 2.5 years of follow-up (Baylin et al., 2015).

Intake analysis showed a statistically significant increase in calorie intake changes between groups ($p < .001$), 166 ± 131 kcal/day in the intervention group versus 36.9 ± 383 in the control group, which was at the expense of higher protein, carbohydrate, and fat intakes but always within the range recommended for each age. The energy density in the soy protein supplement is provided by the macronutrients, which might have a significant impact on daily energy intake. In this study, the energy density might be associated with body composition, mainly with the body weight gain observed in the intervention group. The observation of a more homogeneous variation in calorie and macronutrient intake represented in a smaller standard deviation in the intervention group is of particular interest. The soy protein supplement was dissolved in a volume of 190 mL of fruit juice; the effect of the energy density, macronutrient content, timing of consumption, and volume of the supplement preload on energy intake and its influence on satiety needs to be further studied.

It has been recently shown that the consumption of a high-protein afternoon snack, containing soy protein, improves appetite control, satiety, and diet quality in adolescents while beneficially influencing aspects of mood and cognition (Leidy et al., 2015). More research is needed to evaluate the effects of soy proteins on appetite, satiety, and food intake.

The daily soy protein–based supplement intake for 12 months in preschoolers and schoolchildren showed that changes in macronutrient and energy intake were more uniform than in the control group; harmonious growth, evidenced in changes in BMI for age and weight for age Z scores, biochemical parameters of protein metabolism, and nutrition could ensure adequate development, nutritional status, and optimal bone health.

Declaration of interest

The authors declare no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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