

Chapter 31

Effect of Dietary Taurine and Arginine Supplementation on Bone Mineral Density in Growing Female Rats

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Abstract The purpose of this study was to determine the effect of arginine or taurine alone and taurine plus arginine on bone mineral density (BMD) and markers of bone formation and bone resorption in growing female rats. Forty female SD rats (75 ± 5 g) were randomly divided into four groups (control, taurine, arginine, taurine + arginine group) and treatment lasted for 9 weeks. All rats were fed on a diet and deionized water. BMD and bone mineral content (BMC) were measured using PIXImus (GE Lunar Co, Wisconsin, USA) in spine and femur. The serum and urine concentrations of calcium and phosphorus were determined. Bone formation was measured by serum osteocalcin and alkaline phosphatase concentrations, and the bone resorption rate was measured by deoxypyridinoline cross-links. Femur BMD was significantly increased in the group with taurine supplementation and femur BMC/weight was significantly increased in the group with arginine + taurine supplementation. Rats fed an arginine or taurine supplemental diet increased femur BMD or femur BMC, but a taurine + arginine-supplemented diet does not have a better effect than arginine or taurine alone in the spine BMD. The femur BMC, expressed per body weight, was higher in arginine + taurine group than in the taurine or arginine group. The results of this study suggest that taurine + arginine supplementation may be beneficial on femur BMC in growing female rats. Additional work is needed to clarify the interactive effects between the taurine and arginine to determine whether dietary intakes of arginine and taurine affect bone quality in growing rats.

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Abbreviations

ALP	Alkaline phosphatase
DPD	Deoxypyridinoline
Arg	Arginine
Tau	Taurine
Arg + Tau	Arginine + taurine
DPD/Cr	Creatinine excretion
AI	Adequate intake
BMD	Bone mineral density
BMC	Bone mineral content
FER	Food efficiency ratio
SBMD	Spine bone mineral density
SBMC	Spine bone mineral content
FBMD	Femur bone mineral density
FBMC	Femur bone mineral content

31.1 Introduction

The increase in the life span will be associated with future increases in the prevalence of chronic disease. Osteoporosis is one of the major health problems, particularly with the gradual aging of the population. There is a growing emphasis on osteoporosis prevention. So timing of intervention will be important where the maximum benefit may be in prevention rather than therapy of osteoporosis. To ease the future burden of osteoporosis, focusing on prevention will be the key, and this should include dietary interventions to stimulate bone formation (Mundy 2006). Nutrition is important for the formation and maintenance of bone mineral density (BMD) and for the prevention of osteoporosis. A variety of dietary factors such as calcium, vitamin D, phosphate, magnesium, and protein can influence bone. It is also likely that a variety of other dietary factors such as vitamin K, caffeine, and fluoride have the potential to affect bone. Evidence suggests that some amino acids may benefit bone health. Arginine supplementation is used in several disease states. Under normal physiological conditions, arginine is a semi-essential amino acid that is derived both from endogenous and dietary sources. And arginine is well tolerated at intravenous, intra-arterial, or oral doses not exceeding 30 g/day (Luiking and Deutz 2007). The estimated daily intakes of arginine in the US diet is about 5.4 g (Visek 1986), whereas the total arginine whole-body production and consumption are 25 g/day and protein breakdown is a major endogenous source of arginine (Luiking and Deutz 2007). Arginine supplementation has been shown to have an effect on femur bone mineral content (BMC) in growing female rats (Choi 2007a) and OVX rats (Choi 2009). Taurine supplementation has been shown to

have an effect on femur BMC in OVX rats (Choi and DiMarco 2009). Although it is expected that taurine and arginine act synergistically on bone, the effect of taurine and arginine simultaneously on bone has not been studied. The objective of the present study was to investigate the effect of taurine and arginine supplementation with measures of spine and femur BMD and bone markers in growing female rats.

31.2 Methods

31.2.1 Materials

Forty-eight 6-week-old, female Sprague–Dawley rats were purchased from Bio Genomics, Oriental, Seoul, Korea. On arrival at our lab, rats were acclimated for 5 days to a standard laboratory nonpurified diet (Samyang, Seoul, Korea). After acclimation, the rats were divided into four groups through the use of a randomized complete block design, with blocks determined by initial body weight, as follows: a casein-based diet (control), a casein-based diet with an arginine (Arg), a casein-based diet with a taurine (Tau), and a casein-based diet with an arginine and taurine (Arg+Tau). Rats were individually housed in stainless steel cages in a room with controlled temperature (23°C) and humidity (55%) and were given free access to the experimental diets and water. Rats were maintained at 12-h light (07:00–19:00 h) and dark cycle. The compositions of the experimental diets are shown in Table 31.1. For 9 weeks, rats were fed experimental powdered diets. The experimental diet groups were fed similar diets which were supplemented with arginine or/and taurine. Blood samples were collected from the abdominal aorta and serums were separated at 3,000 rpm for 20 min. Serums were stored at –70°C until analysis. Serum concentrations of alkaline phosphatase (ALP) and osteocalcin were measured. Serum calcium and phosphate were also measured. Serum ALP and osteocalcin and urinary DPD cross-link value were measured as markers of bone formation and resorption. ALP activity was reported as units per liter (U/L). The concentration of urine deoxypyridinoline (DPD) was measured with an enzyme immunoassay that preferentially recognizes the free form of DPD (CLIA, Pyrilinks-D DPC, USA). DPD was corrected for creatinine excretion (DPD/Cr). The concentration of serum osteocalcin was measured with an osteocalcin kit (IRMA, OSTEO-RIACT, Cis Bio, Saclay, France), which recognizes the intact form of osteocalcin. Serum ALP activity was measured with a kit from Enzymatic assay (Prueauto S ALP) following the manufacturer's instructions.

BMD and BMC were measured using PIXImus (GE Lunar Co, Wisconsin, USA) in spine and femur on 9 weeks after feeding. The experimental protocol was approved by Institutional Animal Care and Use Committee (IACUC) in Keimyung University and conformed to the Guide for the Care and Use of Laboratory Animals.

Table 31.1 Composition of control and experimental diets (g/kg diet)

Ingredient	Control	Arg	Tau	Arg + Tau
Casein ^a	200	200	200	200
Corn starch	529.486	523.486	509.486	503.486
Sucrose	100	100	100	100
Soybean oil	70	70	70	70
α -Cellulose ^b	50	50	50	50
Min-mix ^c	35	35	35	35
Vit-mix ^d	10	10	10	10
L-Cystine ^e	3	3	3	3
Choline ^f	2.5	2.5	2.5	2.5
TBHQ ^g	0.014	0.014	0.014	0.014
Arginine ^h		6.6		6.6
Taurine ⁱ			20	20

^aCasein, Maeil Dairy industry Co. Ltd., 480 Gagok-Ri, JinwiMyun, Pyungtaek-City, Kyunggi-Do, Korea

^b α -Cellulose, Sigma Chemical Co., St. Louis, Mo, USA

^cMineral-mix, AIN-93G-Mx, Teklad Test Diets, Madison, Wisconsin, USA

^dVitamin-mix, AIN-93-VM, Teklad Test Diets, Madison, Wisconsin, USA

^eL-Cystine, Sigma Chemical Co., St. Louis, MO, USA

^fCholine bitartate, Sigma Chemical Co., St. Louis, MO, USA

^g*Tert*-butyl hydroquinone, Sigma-Aldrich Inc., St. Louis, MO, USA

^hL-Arginine: Sigma A8094, Japan

ⁱTaurine, Dong-A Pham Co. Ltd., 434-4 Moknae-dong., Ansan-City, Korea

31.2.2 Statistics Analysis

Analysis of variance (ANOVA) was performed on the means to determine whether there were significant ($p < 0.05$) differences among the groups. When ANOVA indicated statistical significance, the Duncan's multiple comparisons test was used to determine which means were significantly different. SAS package (version 9.12, Institute Inc., Cary, NC, USA) was used for all statistical analyses. Results are expressed as means \pm SD. Values were reported as significant have p -values < 0.05 .

31.3 Results and Discussion

31.3.1 Weight Gain, Food Intake, and Food Efficiency Ratio

Tables 31.2 and 31.3 show the weight at beginning, weight at sacrifice, weight gain, food intake, and FER of rats fed on experimental diets. Body weight gain and food intake of rats fed the experimental diets did not differ from those of rats fed the control. This finding is in agreement with what Sugiyama and coworkers (Sugiyama et al. 1989) reported that taurine supplementation had no influence on

Table 31.2 Body weight changes of experimental rats for 9 weeks

Variables	Control	Arg	Tau	Arg + Tau
Initial weight (g)	75.9 ± 2.9 ^{1, a, 2}	75.4 ± 3.1 ^a	75.1 ± 2.9 ^a	75.7 ± 2.5 ^a
Final weight (g)	301.9 ± 21.5 ^a	296.9 ± 20.1 ^a	307.8 ± 19.4 ^a	303.9 ± 23.2 ^a
Weight gain (g)	225.9 ± 22.5 ^a	221.4 ± 18.5 ^a	232.6 ± 18.8 ^a	228.2 ± 22.3 ^a

¹Mean ± SD²Values with different superscripts within the row are significantly different at $p < 0.05$ by Duncan's multiple range test**Table 31.3** Food intake and FER of rats fed during experimental period

Variables	Control	Arg	Tau	Arg + Tau
Food intake (g/day)	19.91 ± 1.52 ^{1, a, 2}	19.37 ± 2.13 ^a	20.15 ± 1.96 ^a	19.50 ± 1.70 ^a
FER	0.18 ± 0.02 ^a	0.18 ± 0.02 ^a	0.19 ± 0.02 ^a	0.19 ± 0.02 ^a

¹Mean ± SD²Values with different superscripts within the row are significantly different at $p < 0.05$ by Duncan's multiple range test

the weight gain and food intake of the animals. Table 31.2 shows that all experimental groups were fed diets containing Arg, Tau, and Arg + Tau. No difference was observed in weight of rats because of diet. Food intake was not affected by diet. FER of the rats were similar.

31.3.2 Serum Ca and P Concentrations

The concentrations of serum Ca and P were not significantly different among the experimental groups (Table 31.4). Mean serum calcium was 9.41 ± 0.39 mg/dl, 9.50 ± 0.16 mg/dl, 9.59 ± 0.30 mg/dl, and 9.44 ± 0.30 mg/dl for control, Arg, Tau, and Arg + Tau, respectively. Mean serum phosphate was 6.34 ± 0.86 mg/dl, 6.60 ± 0.42 mg/dl, 6.36 ± 0.29 mg/dl, and 6.98 ± 0.76 mg/dl for control, Arg, Tau, and Arg + Tau, respectively. The mean serum calcium and phosphate concentrations were within the normal range.

31.3.3 Urine Calcium, Phosphorus, Deoxyypyridinoline, Creatinine, and Cross-Link Value

Urinary calcium and phosphate excretion were not significantly different (Table 31.5). Arginine and/or taurine supplementation did not have a measurable effect on urinary calcium and phosphate excretion. Urinary calcium excretion in the experimental diet group tended to be less in the arginine- or taurine-supplemented group than in the un-supplemented group, although urinary calcium excretion was not significantly different between the four groups. The amount of urine calcium

Table 31.4 Serum calcium and phosphorus concentrations of rats fed experimental diets

Variables	Control	Arg	Tau	Arg + Tau
Ca (mg/dl)	9.41 ± 0.39 ^{1, a, 2}	9.50 ± 0.16 ^a	9.59 ± 0.30 ^a	9.44 ± 0.30 ^a
P (mg/dl)	6.34 ± 0.86 ^a	6.60 ± 0.42 ^a	6.36 ± 0.29 ^a	6.98 ± 0.76 ^a

¹Mean ± SD²Values with different superscripts within the row are significantly different at $p < 0.05$ by Duncan's multiple range test**Table 31.5** Urinary calcium and phosphorus excretion of rats fed experimental diets

Variables	Control	Arg	Tau	Arg + Tau
Ca (mg/day)	0.38 ± 0.14 ^{1, a, 2}	0.35 ± 0.06 ^a	0.36 ± 0.15 ^a	0.36 ± 0.11 ^a
P (mg/day)	17.48 ± 4.39 ^a	18.33 ± 2.28 ^a	19.55 ± 3.09 ^a	19.51 ± 3.31 ^a

¹Mean ± SD²Values with different superscripts within the row are significantly different at $p < 0.05$ by Duncan's multiple range test**Table 31.6** Serum ALP and osteocalcin concentration of rats fed experimental diets

Variables	Control	Arg	Tau	Arg + Tau
ALP (µg/l)	50.7 ± 11.0 ^{1, a, 2}	57.7 ± 18.4 ^a	61.4 ± 18.3 ^a	59.0 ± 10.7 ^a
Osteocalcin (ng/ml)	30.14 ± 3.80 ^a	31.29 ± 4.72 ^a	32.57 ± 6.92 ^a	28.25 ± 5.06 ^a

¹Mean ± SD²Values with different superscripts within the row are significantly different at $p < 0.05$ by Duncan's multiple range test

was lower in the arginine-supplemented group than in the control group. No significant differences in calcium excretion were observed. Urinary excretion of phosphate was greater in the taurine- or arginine-supplemented group than in the un-supplemented group, but the difference was not significant. Fasting urinary phosphate excretion was similar in all groups, too. Urinary calcium and phosphate excretion were nearly identical in all study groups.

31.3.4 Bone Markers

Serum concentrations of ALP and osteocalcin, a marker of bone formation, were not significantly different among groups (Table 31.6). Urinary bone resorption markers, cross-link value, decreased among experimental groups, but the difference was not significant (Table 31.7). Urine DPD and cross-link value were lower in the Arg + Tau-supplemented groups than in the control group and Tau and Arg + Tau groups lower in the cross-link value than in the Arg group among supplemented groups, but the difference was not significant. Choi and Seo (2006) reported that taurine supplementation increased the femur BMD, and decreased urinary calcium excretion in male rats. They also found that taurine supplementation significantly reduced concentrations of not only DPD and cross-link value. Hip fractures are the most costly of all fracture types, resulting in significant mortality, morbidity, functional consequences, and

Table 31.7 Urine deoxypyridinoline, creatinine, and cross-link value of rats fed experimental diets

Variables	Control	Arg	Tau	Arg + Tau
Deoxypyridinoline (nM)	852.6±100.0 ^{1, a, 2}	728.4±223.1 ^a	605.0±175.3 ^a	621.3±204.3 ^a
Creatinine (mM)	6.0±0.0 ^a	6.1±0.4 ^a	6.0±0.6 ^a	5.9±0.6 ^a
Cross-link value (nM/mM)	142.10±16.67 ^a	121.40±37.19 ^a	100.44±23.57 ^a	103.24±30.81 ^a

¹Mean±SD²Values with different superscripts within the row are significantly different at $p < 0.05$ by Duncan's multiple range test

socioeconomic burden (Inderjeeth et al. 2012). The health effects of arginine or taurine have been studied principally in relation to diabetes (Wells et al. 2005) or anti-inflammatory effects (Schuller-Levis and Park 2003). However, no positive effects of taurine on BMD were found in the ovariectomized rats fed a calcium-deficient diet (Choi 2009). Calcium and vitamin D are key nutrients necessary for bone health. In addition to calcium and vitamin D, vitamin K, magnesium, potassium, and vitamin C may also play a role in optimizing bone health (Nieves 2005). However, most older children and adolescents in the United States do not meet the adequate intake (AI) for calcium (Fulgoni et al. 2004). Clinical trials have shown that calcium supplementation in children can increase BMD. High protein may exert detrimental effect on bone density when calcium is low (Heaney 2007). In light of our interest in the effect of taurine and arginine on the BMD, we have taken the opportunity to examine the relation between taurine and arginine supplementation and BMD.

31.3.5 Bone Mineral Density and Bone Mineral Content

BMD and BMC were measured using PIXImus (GE Lunar Co, Wisconsin, USA) in spine and femur. The data obtained from BMD and BMC of the experimental diets are shown in Table 31.8. The spine BMC and BMD were not significantly different among the experimental groups. Rats fed taurine diet (2.0%) or arginine diet (2.0%) had no significant difference in spine and femur BMD and BMC than those fed control diet in female fed an appropriate diet. Supplementation with arginine and taurine did not significantly alter calcium excretion or markers of bone turnover in this study. Taurine (2%) was added to the food from 8 to 18 weeks of age. In one study (Choi 2007a, b), arginine supplementation markedly increased BMD in female rats. This confirms that arginine supplementation increased of bone in female rats, too. Results of this study are also consistent with the previous study (Choi 2007a, b). To our knowledge, the present study was the first attempt to supplement the amino acids of diet. This study showed that arginine and taurine supplementation is acceptable to growing female rat with enough calcium. Arginine and taurine supplementation did not affect urinary calcium excretion. This finding supports earlier studies by us (Choi 2007a, b) that taurine or arginine supplementation in diet did not increase urinary calcium excretion in rats, as long as the amount of calcium in the diet is enough. Skeletal bone mass reaches over 90% of its maximum by age 18

Table 31.8 Spine BMD and BMC of rats fed experimental diets at 9 weeks

Variables	Control	Arg	Tau	Arg + Tau
SBMD (g/cm ²)	0.156±0.007 ^{1, a, 2}	0.157±0.012 ^a	0.162±0.007 ^a	0.159±0.004 ^a
SBMD (g/cm ²)/Wt (kg)	0.517±0.025 ^a	0.524±0.021 ^a	0.532±0.021 ^a	0.521±0.033 ^a
SBMC (g)	0.519±0.049 ^a	0.550±0.071 ^a	0.563±0.041 ^a	0.539±0.048 ^a
SBMC (g)/Wt (kg)	1.757±0.072 ^a	1.831±0.168 ^a	1.841±0.048 ^a	1.733±0.107 ^a

¹Mean±SD²Values with different superscripts within the row are significantly different at $p < 0.05$ by Duncan's multiple range test

(earlier in females) but does not peak until age 25–30, at some point in mid-life (Heaney et al. 2000). Body weight relationships were statistically significant between the BMC of the femoral neck (Wheatley 2005). The taurine-supplemented group had higher spine BMC than did the un-supplemented group (0.563 ± 0.041 g compared with 0.519 ± 0.049 g). We also analyzed our results after correcting for body weight, because weight can affect mechanical factors such as increased loading associated with changes to bone tissue, and increased weight can encourage mineralization and alter bone microarchitecture (Frost 2000).

In the Arg group, spine BMC increased by 6.0%, femur BMD increased by 2.6%, and femur BMC increased by 5.2% and these differences were significantly different from those in the control group ($p < 0.05$). But spine BMD of the Arg group was similar to that of the control group. After feeding of taurine supplementation for 9 weeks, serum calcium and phosphorus concentrations tended to decrease slightly. Compared with the control group, the Tau group significantly increased the FBMD at 9 weeks after taurine supplementation. Compared with the control group, the Arg+Tau group increased the FBMD ($p < 0.05$) (Table 31.9). Despite a slightly greater FBMD of the Arg and Arg+Tau group, this increase of FBMD tended to increase the amount of FBMC from the Arg+Tau group (Table 31.9). The femur BMC, expressed per body weight, was lower in the rats fed control diet than in the supplemented groups. The femur BMC when expressed as kilogram per body weight was significantly greater in the Arg+Tau group than in the Arg- or Tau-supplemented groups. The results of the current investigation confirm data reported previously indicating that bone mass is increased in rats receiving long-term Arg or Tau. Compared with control group, rats given Tau supplementation group had higher values for both femur and femur per weight BMC, as suggested previously by Choi and DiMarco (2009).

Taurine is a potent antioxidant and prevents tissue injury as a result of antioxidation (Wong et al. 2009). No serious side effects were found with taurine supplementation in study by Nakaya et al. (2000) nor in the studies by Azuma et al. (1992) and Takahashi et al. (1998). Even though a small amount of taurine is synthesized in liver in humans (Garcia and Stipanuk 1992) the main source of taurine is from ingestion of foods of animal origin (Yu et al. 1998). Also meat intake has been positively associated with incidence and mortality of chronic diseases, including heart disease (Micha et al. 2010) and osteoporosis. Excess

Table 31.9 Femur BMD and BMC of rats fed experimental diets at 9 weeks

Variables	Control	Arg	Tau	Arg + Tau
FBMD (g/cm ²)	0.196±0.008 ^{1, a, 2}	0.201±0.011 ^{ab}	0.207±0.008 ^b	0.200±0.005 ^{ab}
FBMD (g/cm ²)/Wt (kg)	0.653±0.029 ^a	0.683±0.040 ^a	0.679±0.028 ^a	0.657±0.040 ^a
FBMC (g)	0.425±0.019 ^a	0.447±0.031 ^a	0.448±0.033 ^a	0.455±0.024 ^a
FBMC (g)/Wt (kg)	1.413±0.060 ^a	1.472±0.059 ^{ab}	1.466±0.060 ^{ab}	1.485±0.07 ^b

¹Mean±SD²Values with different superscripts within the row are significantly different at $p < 0.05$ by Duncan's multiple range test

protein intake is risk factors for osteoporosis. So without the increase of meat intake, supplementation of taurine is the better idea to protect bone. In a previous study, our rat model also confirmed that supplementation of a taurine diet increases femur BMC. In a previous publication by our group, it was shown that a taurine-supplemented diet could significantly increase the femur BMC in growing male rats (Choi and Seo 2006). To improve osteoporosis prevention strategies, a better understanding of nutrition-related risk is needed. Higher animal protein intakes have been reported to be associated with increased risk of diabetes (Sluijs et al. 2010). Of the many factors that affect BMD, nutrition is considered an important factor (Choi and Jo 2003; Kim and Kim 1983). In Western countries, a sizeable proportion of the population has adopted a vegetarian diet. According to previous studies in the European Union, the proportion of self-reported vegetarians in the general population is 5% (Heys and Gardner 1999). Whether vegetarian diets confer benefit or harm to bone health is a contentious issue. Ecologic studies found an inverse association between the incidence of hip fracture and vegetarian protein intake, such that countries with a high intake of vegetable protein had a lower risk of hip fracture (Newsholme and Leech 1983; Windmueller and Spaeth 1981). Whereas some data suggest that a raw vegetarian diet is associated with lower bone mass (Ho-Pham et al. 2009), other studies have found no such association (Chung 2001; Chen et al. 2003; Park et al. 2001). There was no significant effect of arginine or taurine on urinary ca excretion, osteocalcin, and spine BMD with appropriate diets. Generally, it is calcium that is the limiting nutrient in the diets of North America and Asia (Thacher et al. 2006). Taurine supplementation has been shown to have a positive effect on bone in OVX rats with appropriate calcium (Choi and DiMarco 2009). But there was no positive effects in the ovariectomized rats fed a calcium-deficient diet (Choi 2009). Thus the effects of amino acids depend on the content of calcium in the diet. Level of calcium in diet with taurine or arginine to be studied to bone health by virtue of their (taurine or arginine) beneficial effect. These data suggest that it would be worthwhile to explore further link between dietary arginine, taurine, and markers of bone health. Future work should also focus on the role of particular amino acid in regulating bone metabolism.

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References

- Azuma J, Sawamura A, Awata N (1992) Usefulness of taurine in chronic congestive heart failure and its prospective application. *Jpn Circ J* 56:95–99
- Chen W, Nishimura N, Oda H, Yohogoshi H (2003) Effect of taurine on cholesterol degradation and bile acid pool in rats fed a high-cholesterol diet. *Taurine 5: beginning the 21st century. Adv Exp Med Biol* 526:261–267
- Choi MJ (2007a) Effects of arginine supplementation on bone mineral density in growing female rats. *Korean J Nutr* 40:235–241
- Choi MJ (2007b) Effects of arginine supplementation on bone markers and hormones in growing female rats. *Korean J Nutr* 42:1–9
- Choi MJ (2009) Effects of taurine supplementation on bone mineral density in ovariectomized rats fed calcium deficient diet. *Nutr Res Pract* 3:108–113
- Choi MJ, DiMarco NM (2009) The effects of dietary taurine supplementation on bone mineral density in ovariectomized rat. *Adv Exp Med Biol* 643:341–349
- Choi MJ, Jo HJ (2003) Effects of soy and isoflavones on bone metabolism in growing female rats. *Korean J Nutr* 36:549–558
- Choi MJ, Seo JN (2006) The effect of dietary taurine supplementation on plasma and liver lipid concentrations in rats. *J East Asian Soc Dietary Life* 16:121–127
- Chung YH (2001) The effect of dietary taurine on skeletal metabolism in ovariectomized rats. *Korean J Hum Ecol* 4:84–93
- Frost HM (2000) Utah paradigm of skeletal physiology: an overview of its insights for bone, cartilage and collagenous tissue organs. *J Bone Miner Metab* 18:305–316
- Fulgoni VL III, Huth PJ, DiRienzo DB, Miller GD (2004) Determination of the optimal number of dairy servings to ensure a low prevalence of inadequate calcium intakes in Americans. *J Am Coll Nutr* 23:651–659
- Garcia RAG, Stipanuk MH (1992) The splanchnic organs, liver and kidney have unique roles in the metabolism of sulfur amino acids and their metabolites in rats. *J Nutr* 122:1693–1701
- Heaney RP (2007) Does daily calcium supplementation reduce the risk of clinical fractures in elderly women? *Nat Rev Rheumatol* 3:18–19
- Heaney RP, Abrams S, Dawson-Hughes B, Looker A, Marcus R, Matkovic V, Weaver C (2000) Peak bone mass. *Osteoporos Int* 11:985–1009
- Heys SD, Gardner E (1999) Nutrients and the surgical patient: current and potential therapeutic applications to clinical practice. *J R Coll Surg Edinb* 44:283–293
- Ho-Pham LT, Nguyen ND, Nguyen TV (2009) Effect of vegetarian diets on bone mineral density: a Bayesian meta-analysis. *Am J Clin Nutr* 90:943–950
- Inderjeeth CA, Chan K, Kwan K, Lie M (2012) Time to onset of efficacy in fracture reduction with current anti-osteoporosis treatments. *J Bone Miner Metab* 30:493–503. doi:10.1007/s00774-012-0349-1
- Kim KL, Kim WY (1983) The effect of soy protein and casein on serum lipid, amino acid. *Korean J Nutr* 17:309–310
- Luiking YC, Deutz NEP (2007) Biomarkers of arginine and lysine excess. *J Nutr* 137(6):1662S–1668S
- Micha R, Wallace SK, Mozaffarian D (2010) Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes mellitus: a systematic review and meta-analysis. *Circulation* 121:2271–2283
- Mundy GR (2006) Nutritional modulators of bone remodeling during aging. *Am J Clin Nutr* 83:427S–430S
- Nakaya Y, Minami A, Harada N, Sakamoto S, Niwa Y, Ohnaka M (2000) Taurine improves insulin sensitivity in the Otsuka long-evans tokushima fatty rat, a model of spontaneous type 2 diabetes. *Am J Clin Nutr* 71:154–158
- Newsholme EA, Leech AR (1983) *Biochemistry for the medical sciences*. Wiley, New York
- Nieves JW (2005) Osteoporosis: the role of micronutrients. *Am J Clin Nutr* 81:1232S–1239S

- Park SY, Kim H, Kim SJ (2001) Stimulation of ERK2 by taurine with enhanced alkaline phosphatase activity and collagen synthesis in osteoblast-like UMR-106 cells. *Biochem Pharmacol* 62:1107–1111
- Schuller-Levis GB, Park E (2003) Taurine: new implications for an old amino acid. *FEMS Microbiol Lett* 226:195–202
- Sluijs I, Beulens JW, Vander A DL, Spijkerman AM, Van der Schouw YT (2010) Dietary intake of total, animal, and vegetable protein and risk of type 2 diabetes in the European prospective investigation into cancer and nutrition (EPIC)-NL study. *Diabetes Care* 33:43–48
- Sugiyama K, Ohishi A, Ohnuma Y, Muramatsu K (1989) Comparison between the plasma cholesterol-lowering effects of glycine and taurine in rats fed on high cholesterol diets. *Agric Biol Chem* 53(6):1647–1652
- Takahashi K, Azuma M, Baba A, Schaffer S, Azuma J (1998) Taurine improves angiotensin II induced hypertrophy of cultured neonatal rat heart cells. *Adv Exp Med Biol* 442:129–135
- Thacher TD, Fischer PR, Strand MA, Pettifor JM (2006) Nutritional rickets around the world: causes and future directions. *Ann Trop Paediatr* 26:1–16
- Visek WJ (1986) Arginine needs, physiological state and United diets. A reevaluation. *J Nutr* 116:36–46
- Wells BJ, Mainous AG III, Everett CJ (2005) Association between dietary arginine and C-reactive protein. *Nutrition* 21:125–130
- Wheatley BP (2005) An evaluation of sex and body weight determination from the proximal femur using DXA technology and its potential for forensic anthropology. *Forensic Sci Int* 29(147):141–145
- Windmueller HG, Spaeth AE (1981) Source and fate of circulating citrulline. *Am J Physiol* 241:E473–E480
- Wong WW, Lewis RD, Steinberg FM, Murray MJ, Cramer MA, Amato P, Young RL, Barnes S, Ellis KJ, Shypailo RJ, Fraley JK, Konzelmann KL, Fischer JG, Smith EO (2009) Soy isoflavone supplementation and bone mineral density in menopausal women: a 2-y multicenter clinical trial. *Am J Clin Nutr* 90:1433–1439
- Yu CH, Lee YS, Lee JS (1998) Some factors effect in bone density of Korean college women. *Korean J Nutr* 31:36–45