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EFFECTS OF COMPOSITION AND PREPARATION CONDITION OF FORTIFIED MILK ON ABSORPTION AND BIOAVAILABILITY OF CALCIUM IN RATS

AREZOO ERFANIAN

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By

AREZOO ERFANIAN

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfillment of the Requirements for the Degree of Doctor of Philosophy

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EFFECTS OF COMPOSITION AND PREPARATION CONDITION OF FORTIFIED MILK ON ABSORPTION AND BIOAVAILABILITY OF CALCIUM IN RATS

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December 2014

Chairman: Mohd Yazid Abd Manap, PhD
Faculty: Food Science and Technology

Calcium is an important mineral especially for the elderly. The average intake of calcium by the elderly women is below the reference nutrient intake (RNI). The amount of calcium absorption and calcium bioavailability in menopausal women is low. Therefore, the main aim of this research was to evaluate the effect of fortification and preparation condition on the absorption and bioavailability of calcium in milk powder formulas applied for ovariectomized (OVX) and OVX-osteoporosis (OS) rats. (1) skim milk powder (T1), (2) skim milk powder fortified with calcium carbonate (1300 mg), inulin (10 g), eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) (1.1 g), vitamins D_3 (10 µg), B_6 (1.5 mg) and K_1 (55 µg) (T2) and (3) skim milk fortified with calcium citrate (1300 mg), inulin (10 g), EPA + DHA (1.1g), vitamins D_3 (10 µg), B_6 (1.5 mg) and K_1 (55 µg) (T3) were formulated based on the North American and Western European dietary allowances. The ingredients were blended using high speed mixer for 5 minutes. The basal and fortified formulas were fed to OVX and OVX-OS rats and the plasma calcium, feces calcium, bone calcium content, bone breaking strength (maximum load), and bone morphology were measured to evaluate calcium absorption and bioavailability. The effect of particle size on absorption and bioavailability of calcium on OVX and OVX-OS rats was studied. Optimization on cycle and pressure of high-pressure homogenizer was done to produce T2-nano and T3-nano. *In vivo* study of calcium absorption and bioavailability in OVX and OVX-OS rats demonstrated that calcium fortification increased absorption and bioavailability. Calcium absorption and bioavailability showed a significant ($p < 0.05$) increase using T2 and T3 compared with T1 in OVX rats. Absorption and bioavailability of calcium from T2 were higher than T3 in OVX rats. The calcium absorption and bioavailability of T2-nano (absorption: 89.06% and bioavailability: 41.65%) and T3-nano (absorption: 80.22% and bioavailability: 34.82%) increased significantly ($p < 0.05$) compared with T2 (absorption: 63.54 % and bioavailability: 24.64%) and T3 (absorption: 33.66% and bioavailability: 15.94%) in OVX rats. T2-nano could enhance the calcium absorption and bioavailability better than T3-nano in OVX rats. The best milk powder for OVX rats was T2-nano with the positive effect of size reduction on absorption and bioavailability of calcium. It was observed that T2 and T3, in OVX-OS rats, had higher calcium absorption and bioavailability than T1. The calcium absorption and bioavailability were improved with consumption of T2 compared with T3 in OVX-OS rats. The results provided that absorption and bioavailability of calcium in OVX-OS rats increased with consumption of T2-nano (absorption: 82.09% and bioavailability: 30.17%) and T3-nano (absorption: 68.67% and bioavailability: 20.38%) compared with T2 (absorption: 60.54% and bioavailability: 9.74%) and T3 (absorption: 42.87% and bioavailability: 4.23%). T2-nano in OVX-OS rats had more positive effect on absorption and bioavailability of calcium than T3-nano. The best milk powder for OVX-OS rats was T2-nano with the positive effect of size reduction on calcium absorption and bioavailability. The current study revealed that OVX rats exhibited higher calcium bioavailability and absorption than OVX-OS rats. In conclusion, this study had successfully developed as a safe and effective fortified milk powder because the basal diet and compounds composed of fully natural food grade components eligible for food application. They were added under limited dosage. The formula could increase calcium absorption and bioavailability and decrease bone loss in OVX and OVX-OS rats as a model of menopause and menopause-OS women.

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KESAN KOMPOSISI DAN KONDISI PENYEDIAAN SUSU DIPERKAYA KE ATAS PENYERAPAN DAN KEBOLEHGUNAAN KALSIUM TERHADAP TIKUS

Oleh

AREZOO ERFANIAN

December 2014

Pengerusi: Mohd Yazid Abd Manap, PHD
Fakulti: Sains dan Teknologi Makanan

Kalsium adalah mineral penting kepada orang dewasa. Purata pengambilan kasium oleh wanita dewasa adalah dibawah paras pengambilan diet yang disarankan. Amaun kalsium yang diserap dan yang dapat digunakan oleh badan oleh OVX dan tikus OVX-OS. Olehitu, tujuan utama penyelidikan ini adalah untuk menilai kesan penambahan dan keadaan penyediaan keatas penyerapan dan kebolehgunaan kalsium didalam formulasi susu tepung spesifik untuk wanita menaposa. Susu tepung skim (T1, Formulasi asas), susu tepung skim yang ditambah dengan kalsium karbonat (1300 mg), inulin (10 g), EPA + DHA (1.1 g), vitamin D_3 (10 ug), B_6 (1.5 mg) dan K_1 (55 ug) (formulasi T2) dan susu skim yang ditambah dengan kalsium sitrat (1300 mg), inulin (10 mg), EPA + DHA (1.1 g), vitamins D_3 (10 ug), B_6 (1.5 mg) dan K_1 (55 ug) (formulasi T3) telah diformulasi mengikut saranan dari WHO-RNI untuk wanita menopaus. Bahan ini telah dicampurkan menggunakan pengisar berkelajuan tinggi selama 5 minit. Formulasi asas dan formulasi diperkaya telah diberikan kepada tikus OVX dan tikus OVX-OS. Kalsium plasma (mmol/l), kalsium tulang (%), kekuatan tulang pecah (N) dan struktur tulang telah diukur untuk menilai penyerapan kalsium (%) dan kebolehgunaan kalsium (%). Kesan saiz partikel keatas penyerapan dan kebolehgunaan kalsium oleh tikus OVX dan tikus OVX-OS telah dikaji. Pengoptimuman kitaran (kali) dan tekanan (bar) homogenizer tekanan tinggi telah dilakukan untuk menghasilkan formulasi T2-nano dan T3-nano. Kajian *in vivo* keatas penyerapan dan kebolehgunaan oleh tikus OVX dan tikus OVX-OS menunjukkan bahawa formulasi diperkaya kalsium meningkatkan penyerapan dan kebolehgunaan kalsium. Penyerapan dan kebolehgunaan kalsium menunjukkan peningkatan yang ketara pada tikus OVX yang diberi formulasi T2 dan T3 berbanding T1. Penyerapan dan kebolehgunaan kalsium oleh tikus OVX lebih tinggi bagi formulasi T2 berbanding T3. Penyerapan dan kebolehgunaan kalsium dari formulasi T2-nano dan T3-nano meningkat dengan ketara berbanding dengan T2 dan T3 oleh tikus OVX. T2-nano dapat meningkatkan penyerapan dan kebolehgunaan kalsium lebih dari T3-nano oleh tikus OVX. Olehitu, formulasi T2-nano untuk tikus OVX menunjukkan kesan positif untuk pengurangan saiz. Formulasi T2 dan T3 menunjukkan penyerapan dan keb oleh gunaan kalsium yang lebih tinggi oleh tikus OVX-OS berbanding dengan formulasi asas,T1. Peratus penyerapan dan kebolehgunaan kalsium meningkat dengan

pengambilan T2 berbanding dengan T3 oleh tikus OVX-OS. Keputusan ini menunjukkan bahawa penyerapan dan kebolehgunaan kalsium oleh tikus OVX-OS meningkat melalui pengambilan T2-nano dan T3-nano berbanding dengan pengambilan T2 dan T3.T2-nano memberikan kesan yanglebih positif keatas penyerapan dan kebolehgunaan kalsium oleh tikus OVX-OS. Olehitu, formulasi T2-nano member pengurangan saiz yang positif keatas tikus OVX-OS. Kajian terbaru ini menunjukkan bahawa penyerapan dan kebolehgunaan kalsium oleh tikus OVX adalah lebih tinggi berbanding oleh tikus OVX-OS. Rumusannya, kajian ini telah berjayamembangunkan formulasi susu tepung diperkaya yang selamat dan dapat meningkatkan penyerapan dan kebolehgunaan di dalam mengurangkan kehilangan jisim tulang oleh tikus OVX dan tikus OVX-OS sebagai model kepada wanita menaposa dan wanita menaposa-OS.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfillment of the requirements for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

Mohd Yazid Abd Manap, PhD
Professor
Faculty of Food Science and Technology
Universiti Putra Malaysia
(Chairman)

Mohd Hair Bejo, PhD
Professor
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Member)

Shuhaimi Bin Mustafa, PhD
Professor
Halal Products Research Institute
Universiti Putra Malaysia
(Member)

Seyed Hamed Mirhosseini, PhD
Associate Professor
Faculty of Food Science and Technology
Universiti Putra Malaysia
(Member)

BUJANG KIM HUAT, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

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Signature: ____________________

Member of Supervisory Committee: Prof. Dr. Mohd Hair Bejo

Signature: ____________________

Member of Supervisory Committee: Prof. Dr. Shuhaimi Bin Mustafa

Signature: ____________________

Member of Supervisory Committee: Assoc. Prof. Dr. Seyed Hamed Mirhosseini

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LIST OF ABBREVIATIONS

%	Percentage
<	Less than
>	More than
°C	Celsius degree
µg	Microgram
µL	Microliter
µm	Micrometer
AAS	Atomic absorption spectrophotometry
ACUC	Animal Care and Use Committee
AI	Adequate intake
ANOVA	Analysis of variance
APS	Average particle size
BMC	Bone mineral content
BMD	Bone mineral density
CCD	Central composite design
CH_3CN	Acetonitrile
CH_3OH	Methanol
CV	Coefficients of variation
d	Day
DHA	Docosahexaenoic acid
DI	Deionized
DV	Dependent variable
EAR	Estimated average requirement
ECF	Extracellular fluid
EFTEM	Energy filtered transmission electron microscopy
e.g.	For example
EPA	Eicosahexaenoic acid
et al.	And others
FA	Fatty acid
FAME	Fatty acid methyl esters
FAO	Food and agriculture organization
FRM	Final reduced model
g	Gram
GC	Gas chromatography
hrs	Hours
HCl	Hydrochloric acid
$HClO_4$	Perchloric acid
HPLC	High pressure liquid chromatography
HMF	Hydroxymethylfuraldehyde
i.e.	Meaning
I.S.	Internal standard
IV	Independent variable
kcal	Kilocalorie
kg	Kilogram
L	Liter
$LaCl_3$	Lanthanum oxide
LOD	Limit of detection
LOQ	Limit of quantification

m	Meter
mg	Milligram
min	Minute
mL	Milliliter
mm	Millimeter
MTBE	Methyl tert butyl ether
NDO	Non digestible oligosaccharide
ng	Nanogram
nm	Nanometer
NV	Normalized value
OC	Osteocalcin
OS	Osteoporosis
OVX	Ovariectomized
PDI	Polydispersity index
ppm	Parts per million
PUFA	Polyunsaturated fatty acid
RBV	Relative bioavailability value
RC	Regression coefficient
RE	Regression equation
RF	Response factor
RH	Relative humidity
RNI	Reference nutrient intake
rpm	Round per minute
RRF	Relative response factor
RRSM	Reduced response surface model
RSD	Relative standard deviation
RSE	Response surface equation
RSM	Response surface methodology
RV	Response variable
SCFAs	Short chain fatty acids
SD	Standard deviation
SEM	Standard error of the mean
S/N	Signal to noise
TEM	Transmission electron microscopy
TUIL	Tolerable upper intake level
UV	Ultraviolet
v/v	Volume per volume
WHO	World health organization
wt	Weight

CHAPTER I

INTRODUCTION

Osteoporosis is a skeletal disorder which ultimately increases the risk of bone fracture. It is one of the major health problems, and expected to increase dramatically in coming decades (National Osteoporosis Foundation, 2002). As recently reported, 1.66 million hip fractures occur each year worldwide. The incidence is predicted to increase fourfold by 2050 as the number of elderly people increases year by year (Van den *et al*., 2009). Calcium is one of the nutrients required for normal skeletal growth and mineralization. It plays an important role in regulating bone remodelling and bone mass (Matkovic *et al*., 1992). Calcium deficiency is a global public health problem, especially in developing countries (Ma *et al*., 2007). Untreated calcium deficiency can lead to severe consequences such as osteoporosis that is one of the major health problems worldwide (Hunt *et al*., 2007; Ma *et al*., 2007).

Osteoporosis, a skeletal disorder characterized by low bone strength, predisposes people to an increased risk of fracture (Finkelstein *et al*., 2006). It is increasing in the Western world and has been predicted to increase up to 300% until 2050 in Asia (Kruger *et al.,* 2003). It is a costly and debilitative disease affecting one in four women over the age of 50 and associated with significant morbidity and mortality (National Osteoporosis Foundation, 2002). Gradual loss of bone with aging is normal; however, it may be accelerated by factors such as menopause, serious health conditions or their treatment, and lifestyle factors such as inadequate diet, lack of exercise, smoking, or excessive alcohol consumption (WHO, 2004). The most common type of osteoporosis is menopausal bone loss associated with ovarian hormone deficiency, low calcium intake and bioavailability (Devine *et al*., 2004).

A sharp decrease in ovarian estrogen production is the predominant cause of rapid bone loss during the first decade after menopause (Campbell *et al*., 2001). Post-menopausal osteoporosis is a serious health problem in elderly women and is characterized by a decrease in bone mass, leading to fracture and imbalanced turnover of the bone (Tamaki *et al*., 1998); while the balance of bone formation and bone resorption is kept in the young, bone resorption exceeds bone formation due to various reasons such as menopause and ageing. In particular, the bone mass of many women after menopause decreases and the risk of fracture increases rapidly (Kanis *et al*., 1991). However, it is a disease that can be prevented by taking adequate nutrition (Grashoff, 2002; Scholz-Ahrens *et al*., 2004).

There are some solutions to this problem. For instance; increased calcium intakes can be a key way to solve this problem. Calcium balance studies demonstrated that calcium requirements increase after menopause in women. This finding, coupled with an early epidemiological study associating increased hip fracture rates with low calcium intake, strongly suggested the significance of adequate calcium intake with regard to osteoporosis particularly in post-menopausal women (Murray, 1996). Indeed, there is widespread interest in assuring adequate calcium intake at critical stages in a woman's life. Dietary calcium is essential when considering calcium requirements of the elderly since the bioavailability of calcium declines with age. Previous study on post-menopausal women showed reduction in calcium absorption led to bone loss (Swaim *et* *al*., 2008). Normally, approximately 30% of calcium in the diet is absorbed by the body and deposited in the skeleton. Improved calcium absorption could have major preventive effects on the occurrence of bone fractures and osteoporosis in the body (Looker *et al*., 1997). Milk and dairy products are the most popular and trusted sources of calcium. They can be taken for a long time, and are important to human health.

Besides the calcium content of the diet, absorption of dietary calcium in intestine is also a critical factor in determining the availability of calcium for bone development and maintenance. Calcium absorption via the intestines is usually regarded as a synonym for bioavailability (Guéguen *et al*., 2000). Bioavailability of nutrient is the proportion of dietary nutrient absorbed and utilized by certain organs. This definition considers the achievement of the nutrient to a fluid (*e.g.* blood) bathing in the site of action. In addition, the fluid can assist the nutrient to reach the site of action.

The bioavailability of a mineral depends directly on the extent in which the mineral is absorbed and distributed to the site of action and depends inversely on the extent in which it is metabolized and excreted prior to arriving at the site of action (Zeyuan *et al*., 1998). Specifically, the bioavailability of calcium from foods is an important concern because calcium intake is quite low in our diet. Most of the calcium in food is chemically bonded to other dietary constituents, and must be released in a soluble form (Ayed *et al.,* 2006).

Another way is by increasing calcium bioavailability using suitable composition. Fortification is the practice of increasing the content of essential micronutrients such as vitamins and minerals, in food to improve the nutritional quality of the food supply and provide a public health benefit with minimal risk to health (WHO, 2006). Supplements and fortified foods not only show an improved absorbability, but also are alternative sources of calcium to traditional foods. Fortified foods, such as fortified milk, can be alternative sources for women who cannot consume adequate amount of dietary calcium daily (Heaney *et al*., 2006). However, such alternative sources need to be evaluated in respect of bioavailability. It is significant to emphasize that the intestinal absorption is not essentially a reflection of calcium bioavailability to the organism because calcium should be used for bone formation and mineralization (Ranhotra *et al*., 2000). Chemically, the calcium compound utilized to fortify the food affects calcium bioavailability (Ayed *et al.*, 2006).

In addition, it is necessary to develop food components that stimulate bone formation or suppress bone resorption like prebiotics. Moreover, it is believed that omega-3 poly unsaturated fatty acids (PUFAs) have protective effects on bone mineralization (Stransky *et al*., 2009). Vitamin D is also essential for the development and maintenance of bone as it plays a significant role in assisting calcium absorption from the diet, and is influential in ensuring the proper renewal and mineralization of bone tissue (International Osteoporosis Foundation, 2006). Furthermore, vitamin B_6 has effect on mineralization of bone (Stransky *et al*., 2009). Vitamin K, a less known nutrient, is also important for bone health. The role of Vitamin K is vital in the production of specific proteins, such as osteocalcin, required in formation of bone (Zittermann, 2007). It is accepted that adequate amounts of vitamins D_3, K_1, and B_6, inulin, DHA and EPA are key elements for healthy bone development, maintenance of bone density and bone strength, and prevention of osteoporosis. These combined effects are resistive against the development of osteoporosis, a disease characterized by the dwindling of bone mass due to loss of calcium which causes pain especially in post-menopausal women (Dickinson**,** 2002).

Fortification with micro calcium particles results in low absorption efficiency than nano calcium particles. Therefore, the dosage of calcium needs to be raised to enable the optimal amount of absorption; however, a high dosage is not advantageous to the elderly (Huang *et al*., 2009). Thus, the last and the most important key solution are to increase calcium absorption and bioavailability by reducing particle size (Park *et al*., 2007). Nanotechnology is expected to resolve this issue. At nano size range, the properties of formulations may differ substantially from bulk compounds of the same composition, mostly due to the increased specific surface area, which may lead to enhance calcium absorption and bioavailability.

It is important to understand the effects of dietary calcium deficiency as well as calcium supplementation on bone health. To improve the absorption and bioavailability of dietary calcium, especially in menopausal women, four types of fortified milk powder has been developed and compared *in vivo* by OVX and OVX-OS rats as a model of menopause and menopause-OS women. It was hypothesized that the fortified milk with specific composition will improve the absorption and bioavailability of calcium in OVX and OVX-OS rats.

The main goal of this research was to investigate the effects of composition and preparation condition on the absorption and bioavailability of calcium in fortified milk powder in OVX and OVX-OS rats. The following specific objectives were also considered accordingly:

- To formulate the fortified milk powders and do proximate analysis;
- To optimize the preparation condition of calcium carbonate and calcium citrate nano fortified milk powders; and
- To evaluate the absorption and bioavailability of calcium in OVX and OVX-OS rats fed with fortified milk powders.

REFERENCES

Aggett, P.J. (2010). Population reference intakes and micronutrient bioavailability: A European perspective. *The American Journal of Clinical Nutrition,* 91(5): 1433S-1437S.

Akahoshi, R., Mizobuchi, T., Takahashi, Y. & Saita, T. (2000). United States Patent No. 6025008.

Aloia, J.F., Vaswani, A., Yeh, J.K., Ross, P.L., Flaster, E. & Dilmanian, F.A. (1994). Calcium supplementation with and without hormone replacement therapy to prevent post-menopausal bone loss. *Annals of Internal Medicine,* 120(2): 97-103.

American Academy of Orthopaedic Surgeons. Burden of Musculoskeletal Diseases in the United States: Prevalence, Societal and Economic Cost. Rosemont, IL, 2008.

Amin, M. & Reusch, J. (1987). High-performance liquid chromatography of water-soluble vitamins. part 3. simultaneous determination of vitamins B1, B2, B6, B12 and C, nicotinamide and folic acid in capsule preparations by ion-pair reversed-phase high-performance liquid chromatography. *Analyst,* 112(7): 989-991.

Arnaud, C. & Sanchez, S. (1990). The role of calcium in osteoporosis. *Annual Review of Nutrition,* 10(1): 397-414.

Arun, K., Babu, C.J., Laksmaiah, P., Rao, C.B., Ravi, B. & Harshavardhan, P. (2012). Teqniques to improve the absorption of poorly soluble drugs. *International Journal of Research in Pharmacy and Chemistry*, 2(2): 2231-2781.

Ayed, M.A. & Thannoun, A.M. (2006). Calcium bioavailability of calcium carbonate based diets formale growing rats. *Mesopotamia Journal of Agriculture*, 34(2): 1-14.

Badarud, D. & Hundal, M.K. (2009). Comparison of anthropometric characteristics and blood pressure phenotypes between pre-and post-menopausal punjabi women. *Anthropologist,* 11(4): 271-275.

Baş, D. & Boyacı, İ.H. (2007). Modeling and optimization II: Comparison of estimation capabilities of response surface methodology with artificial neural networks in a biochemical reaction. *Journal of Food Engineering,* 78(3): 846-854.

Behera, A., Sahoo, S. & Patil, S. (2010). Enhancement of solubility: A pharmaceutical overview. *Der Pharmacia Letter Journal,* 2: 310-318.

Bischoff-Ferrari, H., Willett, W.C., Wong, J.B., Giovannucci, E., Dietrich, T. & Dawson-Hughes, B. (2005). Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. *Journal of the American Medical Association*, 293: 2257-64.

Bolscher, M.T., Coennetelenbos, J., Barto, R., Van Buuren, L.M. & Van der vijgh, W.J.F. (1999). Estrogen Regulation of Intestinal Calcium Absorption in the Intact and Ovariectomized Adult Rat. *Journal of Bone and Mineral Research,* 14(7): 1197-1202.

Bolt, M.J., Cao, L.P., Kong, J., Sitrin, M.D. & Li, Y.C. (2005). Vitamin D receptor is required for dietary calcium-induced repression of calbindin-D9k expression in mice. *Journal of Nutritional Biochemistry*, 16(5): 286-90.

Bonjour, J.P. & Rizzoli, R. (2001). Bone acquisition in adolescence Osteoporosis. ed. R. Marcus, D. Feldman, & J. Kelsey, pp. 621–38. San Diego, CA: Academic.

Booth, S.L. & Broe, K.E. (2003). Vitamin K intake and bone mineral density in women and men. *American Journal of Clinical Nutrition*, 77(2): 512-516.

Breitman, P.L., Fonseca, D., Cheung, A.M. & Ward, W.E. (2003). Isoflavones with supplemental calcium provide greater protection against the loss of bone mass and strength after ovariectomy compared to isoflavones alone. *Journal of Bone*, 33(4): 597-605.

Bronner, F. (2003). Mechanisms and functional aspects of intestinal calcium absorption. *Journal of Experimental Zoology Part A: Comparative Experimental Biology,* 300(1): 47-52.

Brown, E. & Hebert, S. (1997). Calcium-receptor-regulated parathyroid and renal function. *Bone,* 20(4): 303-309.

Bügel, S. (2008). Vitamin K and bone health in adult humans. *Vitamins & Hormones,* 78: 393-416.

Cámara-Martos, F. & Amaro-López, M.A. (2000). Influence of dietary factors on calcium bioavailability: a brief review. *Biological Trace Element Research*, 89(1): 43-52.

Campbell, W.W., Trappe, T.A., Wolfe, R.R. & Evans, W.J. (2001). The recommended dietary allowance for protein may not be adequate for older people to maintain skeletal muscle. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences,* 56(6): M373-M380.

Carabin, I.G. & Flamm, W.G. (1999). Evaluation of safety of inulin and oligofructose as dietary fiber. *Regulatory Toxicology and Pharmacology,* 30(3): 268-282.

Caroli, A., Poli, A., Ricotta, D., Banfi, G. & Cocchi, D. (2011). Dairy intake and bone health: A viewpoint from the state of the art. *Journal of Dairy Science*, 94 (11): 5249-5262.

Carr, B.R. & Bradshaw, K.D. (1998). Disorders of the ovary and female reproductive tract. In *Harrison's Principles of Internal Medicine*, eds. A. Fauci, E. Braunwald, K.J. Isselbacher, pp. 2102-2106. New York: McGraw Hill.

Cashman, K. (2002). Calcium intake, calcium bioavailability and bone health. *British Journal of Nutrition,* 87(2): 169-178.

Castillejo, G., Bulló, M., Anguera, A., Escribano, J. & Salas-Salvadó, J. (2006). A controlled, randomized, double-blind trial to evaluate the effect of a supplement of cocoa husk that is rich in dietary fiber on colonic transit in constipated pediatric patients. *Pediatrics,* 118(3): e641-e648.

Chapuy, M.C., Pamphile, R., Paris, E., Kempf, C., Schlichting, M. & Arnaud, S. (2002). Combined calcium and vitamin D3 supplementation in elderly women: confirmation of reversal of secondary hyperparathyroidism and hip fracture risk: the Decalyos II study. *Osteoporosis International*, 13: 257–264.

Chaudhary, A., Nagaich, U., Gulati, N., Sharma, V.K. & Khosa R.L. (2012). Enhancement of solubilization and bioavailability of poorly soluble drugs by physical and chemical modifications: A recent review. *Journal of Advanced Pharmacy Education & Research*, 2 (1): 32-67.

Chaudhry, Q., Scotter, M., Blackburn, J., Ross, B., Boxall, A. & Castle, L. (2008). Applications and implications of nanotechnologies for the food sector. *Food Additives and Contaminants*, 25 (3): 241-58.

Chen, H., Hayakawa, D. & Emura, S. (2002). Effect of low or high dietary calcium on the morphology of the rat femur. *Histology Histopathology,* 17: 1129–1135.

Chen, Y.C. & Chen, T.C. (2004). Mineral utilization in layers as influenced by dietary oligofructose and inulin. *International Journal of Poultry Sciences,* 3: 442–445.

Chiong, M.R. & Abaya, L.M.M. (2012). *Atomic Absorption Spectroscopy: Chemical Interferences in Calcium Analysis*, Institute of Chemistry, University of the Philippines, Diliman, Quezon City.

Cho, W.S., Kang, B.C., Lee, J.K., Jeong, J., Che, J.H. & Seok, S.H. (2013). Comparative absorption, distribution, and excretion of titanium dioxide and zinc oxide nanoparticles after repeated oral administration. *Particle and Fibre Toxicology*, 10: 9-19.

Christie, W.W. (1993). Preparation of ester derivatives of fatty acids for chromatographic analysis. *Advances in Lipid Methodology*, 2: 69-111.

Cocato, M.L. (2007). Avaliaçãopormétodos in vitro e in vivo da biodisponibilidade de sulfato ferroso micro encapsulado. *Review Nutrition PUCCAMP*, 20(3): 239-247.

Codex Alimentarius Commission. General principles for the addition of essential nutrients to foods. CAC/GL 09-1987 (amended 1989, 1991). Codex Alimentarius volume 4.Foods for special dietary uses (including foods for infants and children). 2nd ed. Joint FAO/WHO Food Standards Programme. Rome, Italy: Codex Alimentarius Commission, 1994: 9–12.

Coudray, C., Rambeau, M., Feillet-Coudray, C., Tressol, J.C., Demigne, C., Gueux, E., Mazur A. & Rayssiguier, Y. (2005). Dietary inulin intake and age can significantly affect intestinal absorption of calcium and magnesium in rats: a stable isotope approach*.* *Journa of Nutrition*, 4: 29-40.

Coudray, C., Tressol, J.C., Gueux, E. & Rayssiguier, Y. (2003). Effects of inulin-type fructans of different chain length and type of branching on intestinal absorption and balance of calcium and magnesium in rats. *European Journal of Nutrition,* 42 (2): 91-98.

Creedon, A. & Cashman, K.D. (2001). Nutritional Sciences. *British Journal of Nutrition*. 186(4):453-459.

Cummings, S.R., Rubin, S.M. & Black, D. (1990). The future of hip fractures in the united states: Numbers, costs, and potential effects of post-menopausal oestrogen. *Clinical Orthopaedics and Related Research,* 252*:* 163-166.

Curhan, G.C., Willett, W.C., Speizer, F.E., Spiegelman, D. & Stampfer, M.J. (1997). Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. *Annals of Internal Medicine,* 126 (7): 497-504.

Dall'Amico, R., Montini, G., Pisanello, L., Piovesan, G., Bottaro, S., Cracco, A. & Zacchello, F. (1995). Determination of inulin in plasma and urine by reversed-phase high-performance liquid chromatography. *Journal of Chromatography B: Biomedical Sciences and Applications,* 672(1): 155-159.

Dawson-Hughes, B. (1996). Calcium and vitamin D nutritional needs of elderly women. *Journal of Nutrition*, 126: 1165S-1167S.

Dawson-Hughes, B., Dallal, G.E., Krall, E.A., Sadowski, L., Sahyoun, N. & Tannenbaum, S. (1990). A controlled trial of the effect of calcium supplementation on bone density in post-menopausal women. *New England Journal of Medicine,* 323 (13): 878-883.

Dawson-Hughes, B., Harris, S. & Finneran, S. (1995). Calcium absorption on high and low calcium intakes in relation to vitamin D receptor genotype. *Journal of Clinical Endocrinology & Metabolism,* 80 (12): 3657-3661.

Delaney, M.F. (2006). Strategies for the prevention and treatment of osteoporosis during early post-menopause. *American Journal of Obstetrics and Gynecology,* 194(2): S12-S23.

Denis,M., Aaron, P., Dianne, J. & Barbara, S. (2002). Bone morphology, strength and density are compromised in iron-deficient rats and exacerbated by calcium restriction. *Journal of Nutrition*, 132 (10): 3135-3141.

Deroisy, R., Zartarian, M., Meurmans, L., Nelissenne, N., Micheletti, M., Albert, A. & Reginster, J. (1997). Acute changes in plasma calcium and parathyroid hormone circulating levels induced by the oral intake of five currently available calcium salts in healthy male volunteers. *Clinical Rheumatology,* 16(3): 249-253.

Des Rieux, A., Fievez, V., Garinot, M., Schneider, Y.J. & Preat, V. (2006). Nanoparticles as potential oral delivery systems of proteins and vaccines: a mechanistic approach. *Journal of Control Release,* 116(1): 1-27.

Devine, A, Dhaliwal, S.S., Dick, I.M., Bollerslev, J. & Prince, R.L. (2004). Physical activity and calcium consumption are important determinants of lower limb bone mass in older women. *Journal of Bone and Mineral Research,* 19 (10): 1634-1639.

Dickinson, A. (2002). Benefits of calcium and vitamin D: building and maintaining healthy bones. *Council for Responsible Nutrition,* 285: 785–795.

Din, J.N. & Newby, D.E. (2004). Omega 3 fatty acids and cardiovascular disease - fishing for a natural treatment. *British Medical Journal*, 328 (7430): 30-35.

Dionex. Application Note 221. *Rapid Determination of Melamine in Liquid Milk and Milk Powder by HPLC on the Acclaim Mixed-Mode WCX-1 Column with UV Detection.*

Dionex. Application Note 251. *Determination of Water- and Fat-Soluble Vitamins in Nutritional Supplements by HPLC with UV Detection*.

Dirschl, D., Henderson, R. & Oakley, W. (1997). Accelerated bone mineral loss following a hip fracture: A prospective longitudinal study. *Bone,* 21(1): 79-82.

Doetsch, A., Faber, J., Lynnerup, N., Wätjen, I., Bliddal, H. & Danneskiold–Samsøe, B. (2004). The effect of calcium and vitamin D3 supplementation on the healing of the proximal humerus fracture: A randomized placebo-controlled study. *Calcified Tissue International,* 75(3): 183-188.

Dowd, R. (2001). Role of calcium, vitamin D, and other essential nutrients in the prevention and treatment of osteoporosis. *The Nursing Clinics of North America,* 36(3): 417-431.

Ebeling, P., Yergey, A., Vieira, N., Burritt, M., O'Fallon, W., Kumar, R. & Riggs, B. (1994). Influence of age on effects of endogenous 1, 25-dihydroxyvitamin D on calcium absorption in normal women. *Calcified Tissue International,* 55(5): 330-334.

Eltokhey, H.M. & Zahran, D.H. (2011). Evaluation of the effect of omega 3 fatty acid (N-3) on socket healing in orchiectomized rats. *Journal of American Science*, *7*(9): 263–271.

Ensminger, A. H., Ensminger, M. E., Konlande, J. E. & Robson, J. R. K. (1995). Calcium. In: *The Concise Encyclopedia of Foods and Nutrition*, pp. 137-143.CRC Press.

Ensrud, K. E., Duong, T., Cauley, J. A., Heaney, R. P., Wolf, R. L., Harris, E. & Cummings, S. R. (2000). Low fractional calcium absorption increases the risk for hip fracture in women with low calcium intake. *Annals of Internal Medicine,* 132(5): 345-353.

Erlebacher, A., Filvaroff, E.H., Ye, J. & Derynck, R. (1998). Osteoblastic responses to TGF-β during bone remodeling. *Molecular Biology of the Cell*, 9(7): 1903-1918.

Fardellone, P., Brazier, M., Kamel, S., Gueris, J., Graulet, A., Lienard, J. & Sebert, J. (1998). Biochemical effects of calcium supplementation in post-menopausal women: Influence of dietary calcium intake. *American Journal of Clinical Nutrition,* 67: 1273-1278.

Farrin, N., Ostadrahimi, A. R., Mahboob, S. A., Kolahi, S. & Ghavami, M. (2008). Dietary intake and plasma bone related chemistry and their correlations in post-menopausal Iranian women. *Saudi Medical Journal,* 29(11): 1643-1648.

Feldman, D., Malloy, P.J. & Gross, C. (1996). Vitamin D: Metabolism and action. In: *Osteoporosis*, eds. R. Marcus, D. Feldman, & J. Kelsey, pp. 205-235. San Diego, Academia Press.

Feskanich, D., Weber, P., Willett, W.C., Rockett, H., Booth, S.L. & Colditz, G.A. Finkelstein, E.A., Corso, P.S. & Miller, T.R. (2006). *The incidence and economic burden of injuries in the united states.* Oxford University Press.

Finstad, H., Myhrstad, M., Heimli, H., Lømo, J., Blomhoff, H.K., Kolset, S. & Drevon, C. (1998). Multiplication and death-type of leukemia cell lines exposed to very long-chain polyunsaturated fatty acids. *Leukemia,* 12(6): 921-929.

Fischer, M. & Raue, F. (1999).Measurements of bone mineral density.mineral density in metabolic bone disease. *The Quarterly Journal of Nuclear Medicine: Official Publication of the Italian Association of Nuclear Medicine (AIMN) [and] the International Association of Radiopharmacology (IAR),* 43(3): 233-240.

Food and Agriculture Organization of the United Nations (FAO) and World Health Organization (WHO). *Application of Nanotechnologies in the Food and Agriculture Sectors: Potential Food Safety Implications;* Report of Joint FAO/WHO Expert Meeting: Italy, 2009.

Gadomska-Nowak, M., Szulc, B. & Ryszka, F. (2003). Comparison of intestinal absorption of selected calcium organic salts through the rat jejunum in vitro. *Bollettino Chimico Farmaceutico,* 142(3): 109-111.

Gallagher, J.C., Satpathy, R., Rafferty, K. & Haynatzka, V. (2004). The effect of soy protein isolate on bone metabolism. *Menopause,* 11(3): 290-298.

Garnero, P., Sornay-Rendu, E., Chapuy, M.C. & Delmas, P.D. (1996). Increased bone turnover in late post-menopausal women is a major determinant of osteoporosis. *Journal of Bone and Minereral Research*, 11: 337-49.

Garti, N. (2005). Food goes nano. *Journal of Information*, 6: 588–589.

Gennari, C., Agnusdei, D., Nardi, P. & Civitelli, R. (1990). Estrogen preserves a normal intestinal responsiveness to 1, 25-dihydroxyvitamin D3 in oophorectomized women. *The Journal of Clinical Endocrinology and Metabolism*, 71:1288-1293.

Grados, F., Brazier, M., Kamel, S., Mathieu, M., Hurtebize, N., Maamer, M. & Fardellone, P. (2003). Prediction of bone mass density variation by bone remodeling markers in post-menopausal women with vitamin D insufficiency treated with calcium and vitamin D supplementation. *Journal of Clinical Endocrinology & Metabolism,* 88 (11): 5175-5179.

Grashoff, K. (2002). Osteoporose padiatris cheerkrankung. *Ernahrungsumschau,* 49 (9): 367-371.

Grau, M. J., Kayser, O. & Mu¨ ller, R. H. (2000). Nanosuspensions of poorly soluble drugs – reproducibility of small-scale production. *International Journal of Pharmaceutics*, 196: 155-157.

Guéguen, L. & Pointillart, A. (2000). The bioavailability of dietary calcium. *Journal of the American College of Nutrition,* 19 (2): 119S-136S.

Hasnah, H., Amin, I. & Suzana, S. (2012). Bone Health Status and Lipid Profile among Post-menopausal Malay Women in Cheras, Kuala Lumpur. *Malaysian Journal of Nutrition,* 18 (2): 161-171.

Hasnah, H., Suzana, SH., Kimberly, O'brien., Amin, I., Norazmi, K. & Suriah, A. R. (2010). Absorption of calcium from milk and tempeh consumed by postmenopausal Malay women using the dual stable isotope technique. *International Journal of Food Sciences and Nutrition,* 61 (2): 125–137.

Heaney, R. (1991). Calcium supplements: Practical considerations. *Osteoporosis International*, 1(2): 65-71.

Heaney, R. P., Dowell, M. S., Bierman, J., Hale, C. A. & Bendich, A. (2001). Absorbability and cost effectiveness in calcium supplementation. *Journal of the American College of Nutrition,* 20 (3): 239-246.

Heaney, R., Dowell, M. & Barger-Lux, M. (1999). Absorption of calcium as the carbonate and citrate salts, with some observations on method. *Osteoporosis International,* 9(1): 19-23.

Heaney, R.P. (2000) Dietary Protein and Phosphorus Do Not Affect Calcium Absorption. *American Journal of Clinical Nutrition*, 72: 675-676.

Heaney, R.P., Bilezikian, J.P., Holick, M.F., Nieves, J.W. & Weaver, C.M. (2006). The role of calcium in peri- and post-menopausal women: 2006 position statement of The North American Menopause Society. *Journal of the North American Menopause Society*, 13 (6): 862-877.

Heaney, R.P., Dawson-Hughes, B., Gallagher, J., Marcus, R. & Nieves, J. (2001). The role of calcium in peri-and post-menopausal women: Consensus opinion of the North American menopause society. *Menopause-the Journal of the North American Menopause Society*, 8 (2): 84-95.

Heaney, R.P., Dowell, M.S., Hale, C.A. & Bendich, A. (2003). Calcium absorption varies within the reference range for plasma 25-hydroxyvitamin D. *Journal of the American College of Nutrition,* 22 (2): 142-146.

Heller, H.J., Greer, L.G., Haynes, S.D., Poindexter, J.R, & Pak, C.Y. (2000). Pharmacokinetic and pharmacodynamic comparison of two calcium supplements in post-menopausal women. *Journal of Clinical Pharmacology,* 40 (11): 1237-1244.

Hetal, T., Bindesh, P. & Sneha, T. (2010). Techniques for oral bioavailability enhancement of drugs. *International Journal of Pharmaceutical Sciences*, 4 (3): 203-223.

Hill, G.M., Cromwell, G.L., Chrenshaw, T.D., Ewan, R.C., Knabe, D.A., Lewis, A.J., Mahan, D.C., Shurson, G.C., Southern, L.L. & Veum, T.L., (1996). NCR-42 and S-145 Regional Swine Nutrition Committees, Impact of pharmacological intakes of zinc and (or) copper on performance of weanling pigs. *Journal of Animal Science*, 74 (1): 181-189.

Hillyer, J.F. & Albrecht, R.M. (2001). Gastrointestinal persorption and tissue distribution of differently sized colloidal gold nanoparticles. *Journal of Pharmaceutical Science,* 90 (12): 1927-1936.

Hirasawa, T., Omi, N. & Ezawa, I. (2001). Effect of 1α-hydroxyvitamin D3 and egg-shell calcium on bone metabolism in ovariectomized osteoporotic model rats. *Journal of Bone and Mineral Metabolism,* 19 (2): 84-88.

Hock, J., Krishnan, V., Onyia, J., Bidwell, J., Milas, J. & Stanislaus, D. (2001). Osteoblast apoptosis and bone turnover. *Journal of Bone and Mineral Research,* 16 (6): 975-984.

Holick, M., Matsuoka, L. & Wortsman, J. (1989). Age, vitamin D, and solar ultraviolet. *The Lancet,* 334 (8671): 1104-1105.

Holick, M.F. & Chen, T.C. (2008). Vitamin D deficiency: a worldwide problem with health consequences. *The American Journal of Clinical Nutrition*, 87: 1080S-1086S.

Holloway, L., Moynihan, S., Abrams, S. A., Kent, K., Hsu, A. R. & Friedlander, A. L. (2007). Effects of oligofructose-enriched inulin on intestinal absorption of calcium and magnesium and bone turnover markers in post-menopausal women. *British Journal of Nutrition,* 97 (2): 365-372.

Horn, D. & Rieger, J. (2001).Organic nanoparticles in the aqueous phase—theory, experiment, and use. *Angewandte Chemie International Edition,* 40 (23): 4330-4361.

Huang, S., Chen, J.C., Hsu, C.W. & Chang, W.H. (2009). Effects of nano calcium carbonate and nano calcium citrate on toxicity in ICR mice and on bone mineral density in an ovariectomized mice model. *Nanotechnology,* 20 (37): 375102.

Hunt, C.D. & Johnson, L.K. (2007). Calcium requirements: New estimations for men and women by cross-sectional statistical analyses of calcium balance data from metabolic studies. *The American Journal of Clinical Nutrition,* 86 (4): 1054-1063.

Hunt, J.R., Hunt, C.D., Zito, C.A., Idso, J.P. & Johnson, L.K. (2008). Calcium requirements of growing rats based on bone mass, structure, or biomechanical strength are similar. *The Journal of Nutrition,* 138 (8): 1462-1468.

Hurrell, R. & Egli, I. (2010). Iron bioavailability and dietary reference values. *The American Journal of Clinical Nutrition,* 91(5): 1461S-1467S.

Hussain, N., Jaitley, V. & Florence, A.T. (2001). Recent advances in the understanding of uptake of microparticulates across the gastrointestinal lymphatics. *Advance Drug Delivery Reviews*, 50:107–42.

Ian, B. H. & Randolph, E. R. (2007). Calcium and vitamin D in the prevention and treatment of osteoporosis: Shedding Light on New Developments, *Continuing Education Credit*, 32 (9): 502-511.

Ilich, J.Z., Brownbill, R.A., Tamborini, L. & Crncevic-Orlic, Z. (2002). To drink or not to drink: How are alcohol, caffeine and past smoking related to bone mineral density in elderly women? *Journal of the American College of Nutrition*, 21(6): 536-544.

International Osteoporosis Foundation. (2006). Invest in your bones. Bone Appétit − The role of food and nutrition in building and maintaining strong bones. http://www.iofbonehealth. org/publications/bone-appetit.html.

Ishida, H., Uesugi, T., Hirai, K., Toda, T., Nukaya, H., Yokotsuka, K. & Tsuji, K. (1998). Preventive effects of the plant isoflavones, daidzin and genistin on bone mineral density in oestrogenand/or dietary calcium-deficient rats. *Bone*, 16: 149-156.

Jackson, C., Gaugris, S., Sen, S. & Hosking, D. (2007). The effect of cholecalciferol (vitamin D3) on the risk of fall and fracture: A meta-analysis. *Oxford Journals Medicine,* 100 (4): 185-192.

Jinno, J., Kamada, N., Miyake, M., Yamada, K., Mukai, T., Odomi, M. & Kimura, T. (2006).Effect of particle size reduction on dissolution and oral absorption of a poorly water-soluble drug, cilostazol, in beagle dogs. *Journal of Controlled Release,* 111 (1): 56-64.

Joglekar, A. & May, A. (1987). Product excellence through design of experiments. *Cereal Foods World,* 32 (12): 857-868.

Johnell, O. & Kanis, J.A. (2006). An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporosis International*, 17: 1726-1733.

Kanis, J., Geusens, P. & Christiansen, C. (1991). Guidelines for clinical trials in osteoporosis. *Osteoporosis International,* 1(3): 182-188.

Karkkainen, M.U., Lamberg-Allardt, C.J., Ahonen, S. & Välimäki, M. (2001). Does it make a difference how and when you take your calcium? The acute effects of calcium on calcium and bone metabolism. *The American Journal of Clinical Nutrition,* 74 (3): 335-342.

Kaur, N. & Gupta, A. K. (2002). Applications of inulin and oligofructose in health and nutrition. *Journal of Biosciences,* 27 (7): 703-714.

Kaushik, R., Sachdeva, B. & Arora, S. (2014). Bioavailability of vitamin D2 and calcium from fortified milk. *Food Chemistry,* 147: 307–311.

Keck, C.M. & Müller, R.H. (2006). Drug nanocrystals of poorly soluble drugs produced by high pressure homogenisation. *European Journal of Pharmaceutics and Biopharmaceutics,* 62 (1): 3-16.

Kelly, O., Cusack, S. & Jewell, C. (2003). The effect of polyunsaturated fatty acids, including conjugated linoleic acid, on calcium absorption and bone metabolism and composition in young growing rats. *British Journal of Nutrition,* 90: 743–750.

Ken, K., Yasuhiro, T., Hiroaki, M., Jun-Ichi, Y., Yasuhiro, M., Hiroshi, K., Akira, I., Masayoshi, K., Seiichiro, A. & Yukihiro, T. (2000). Milk basic protein enhances the bone strength in ovariectomized rats. *Journal of Food Biochemistry*, 24: 467–476.

Kenny, A.M., Prestwood, K.M., Biskup, B., Robbins, B., Zayas, E. & Kleppinger, A. (2004). Comparison of the effects of calcium loading with calcium citrate or calcium carbonate on bone turnover in post-menopausal women. *Osteoporosis International,* 15 (4): 290-294.

Klibanski, A. (2001). Osteoporosis prevention, diagnosis, and therapy. *Journal of American Medical Association*, 285:785–95.

Kreyling, W.G., Semmler, M., Erbe, F., Mayer, P., Takenaka, S. & Schulz, H. (2002). Translocation of ultrafine insoluble iridium particles from lung epithelium to extra pulmonary organs is size dependent but very low. *Journal of Toxicology and Environmental Health Part A,* 65: 1513-30.

Kris-Etherton, P.M. & Harris, W.S. (2002). Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Journal of Circulation*, 106 (21): 2747-2757.

Kruger, M.C., Brown, K.E., Collett, G., Layton, L. & Schollum, L.M. (2003). The effect of fructooligosaccharides with various degrees of polymerization on calcium bioavailability in the growing rat. *Experimental Biology and Medicine,* 228: 683-688.

Kruger, M.C., Gallaher, B.W. & Schollum, L.M. (2003). Bioavailability of calcium is equivalent from milk fortified with either calcium carbonate or milk calcium in growing male rats. *Nutrition Research,* 23 (9): 1229-1237.

Kruger, M.C., Schollum, L.M., Kuhn-Sherlock, B., Hestiantoro, A., Wijanto, P., Li-Yu, J. & Eastell, R. (2010). The effect of a fortified milk drink on vitamin D status and bone turnover in post-menopausal women from south East Asia. *Bone,* 46(3): 759-767.

Kwaka, H.S., Leeb, W.J. & Leeb, M.R. (2012). Revisiting lactose as an enhancer of calcium absorption. *International Dairy Journal*, 22 (2): 147-51.

LaMora, K. (2011). Soluble fiber's enhancement of calcium absorption in the intestine, in partial fulfillment for the requirements of NUTR340 Advanced Nutrition I, pp. 1-10.

Lau, E.M., Lee, J.K., Suriwongpaisal, P., Saw, S.M. & Das De, S. (2001). The incidence of hip fracture in four Asian countries: the Asian Osteoporosis Study (AOS). *Osteoporosis International*, 12: 239-243.

Lee, J.K. & Khir, A.S.M. (2007). Incidence of hip fracture in Malaysian above 50 years of age: variation in different ethnic groups. *International Journal of Rheumatic Diseases*, 10 (4): 300-305.

Lee, J.K. (1998). Hip fractures in Peninsular Malaysia. 2nd Annual Scientific Meeting of the Malaysian Osteoporosis Society, pp. 21–22. Kuala Lumpur.

Lee, J.K., Khir, A.S.M. (1997). Incidence of hip fracture in Malaysian above 50 years of age – variation in different ethnic groups. *Journal of Rheumatology*, 10 (4): 300 - 305.

Lee, W. (1993). Requirements of calcium: Are there ethnic differences. *Asian Pacific Journal of Clinical Nutrition*, 2: 183-190.

Lee, Y., Lim, Y., Ling, P., Tan, Y., Cheong, M. & Lam, K. (2007). Inadequate dietary calcium intake in elderly patients with hip fractures. *Singapore Medical Journal,* 48 (12): 1117-1121.

Leuner, C. & Dressman, J. (2000). Improving drug solubility for oral delivery using solid dispersions. *European Journal of Pharmaceutics and Biopharmaceutics*, 50: 47-60.

Lilliu, H. & Pamphile, R. (2003). Calcium-vitamin D3 supplementation is cost-effective in hip fractures prevention. *Journal of Maturitas*, 44 (4): 299-305.

Lipinski, C.A., Lombardo, F., Dominy, B.W. & Feeney, P.J. (2001). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Advanced Drug Delivery Reviews*, 46(1-3): 3-26.

Lips, P. (2006). Vitamin D physiology. *Progress in Biophysics and Molecular Biology*, 92: 4-8.

Lobo, A.R., Filho, J.M., Alvares, E.P., Cocato, M.L. & Colli, C. (2009). Effects of dietary lipid composition and inulin-type fructans on mineral bioavailability in growing rats. *Journal of Nutrition*, 25 (2): 216-225.

Looker, A.C., Melton, L.J. & Harris, T.B. (2006). Osteoporosis and Bone Health, *Journal of Medicine*, 119: 25S-31S.

Looker, A.C., Orwoll, E.S., Johnston, C.C., Lindsay, R.L., Wahner, H.W., Dunn, W. L. & Heyse, S.P. (1997). Prevalence of low femoral bone density in older US adults from NHANES III. *Journal of Bone and Mineral Research,* 12 (11): 1761-1768.

Ma, J., Johns, R.A. & Stafford, R.S. (2007). Americans are not meeting current calcium recommendations. *The American Journal of Clinical Nutrition,* 85 (5): 1361-1366.

Macdonald, H.M., McGuigan, F.E., Lanham-New, S.A., Fraser, W.D., Ralston, S.H. & Reid, D.M. (2008). Vitamin K1 intake is associated with higher bone mineral density and reduced bone resorption in early post-menopausal scottish women: No evidence of gene-nutrient interaction with apolipo protein E polymorphisms. *The American Journal of Clinical Nutrition,* 87 (5): 1513-1520.

Madruga, M.S. & Camara, F.S. (2000). The chemical composition of "Multimistura" as a food supplement. *Food Chemistry*, 68: 41-44.

Martin, B.R., Weaver, C.M., Heaney, R. P., Packard, P.T. & Smith, D.L. (2002). Calcium absorption from three salts and CaSO4-fortified bread in premenopausal women. *Journal of Agricultural and Food Chemistry,* 50 (13): 3874-3876.

Masse, P., Vuilleumier, J.P. & Weiser, H. (1988). Is pyridoxine an essential nutrient for bone? *International Journal for Vitamin and Nutrition research. Internationale Zeitschrift Fur Vitamin- Und Ernahrungsforschung. Journal International De Vitaminologie Et De Nutrition,* 58 (3): 295-299.

Masse, P.G., Pritzker, K.P., Mendes, M.G., Boskey, A.L. & Weiser, H. (1994). Vitamin B6 deficiency experimentally-induced bone and joint disorder: Microscopic, radiographic and biochemical evidence. *British Journal of Nutrition,* 71 (6): 919-932.

Matkovic, V. & Heaney, R.P. (1992). Calcium balance during human growth: Evidence for threshold behavior. *The American Journal of Clinical Nutrition,* 55 (5): 992-996.

Medeiros, D.M., Plattner, A., Jennings, D. & Stoecker, B. (2002). Bone morphology, strength and density are compromised in iron-deficient rats and exacerbated by calcium restriction. *Journal of Nutrition*, 132 (10): 3135-3141.

Mekary, R.A. (2005). Osteoporosis and osteopenia management in women: survey, case referent study, and interventional exercise trial. PhD Dissertation. The School of Human Ecology.

Mellisea, K.T. & Donald, M. (1998). Hypovitaminosis D in medical in patients. *New England Journal of Medicine,* 338: 777–783.

Merisko-Liversidge, E.M. & Liversidge, G.G. (2008). Drug nanoparticles: Formulating poorly water-soluble compounds. *Toxicologic Pathology,* 36 (1): 43-48.

Miller, G.D., Groziak, S.M. & DiRienzo, D. (1996). Age considerations in nutrient needs for bone health. *Journal of the American College of Nutrition*, 15 (6): 553-555.

Miller, G.D., Jarvis, J.K. & McBean, L.D. (2001). The importance of meeting calcium needs with foods. *Journal of the American College of Nutrition,* 20(2): 168S-185S.

Ministry of Health Malaysia. The Malaysian Adult Nutrition Survey (MANS). Putrajaya, Malaysia: Nutrition Section, Family Health Development Division, 2003.

Mirhosseini, H. & Tabatabaee Amid, B. (2012). Influence of chemical extraction conditions on the physicochemical and functional properties of polysaccharide gum from durian (*Duriozibethinus*) seed, *Molecules,* 17: 6465–6480.

Mirhosseini, H., Tan, C. P., Hamid, N. S. A. & Yusof, S. (2007). Modeling the relationship between the main emulsion components and stability, viscosity, fluid behavior, ζ-potential and electrophoretic mobility of orange beverage emulsion using response surface methodology. *Journal of Agricultural and Food Chemistry*, 55: 7659–7666.

Mirhosseini, H., Tan, C. P., Hamid, N. S. A. & Yusof, S. (2008). Effect of Arabic gum, xanthan gum and orange oil on flavour release from diluted orange beverage emulsion. *Food Chemistry*, 107: 1161–1172.

Mirhosseini, H., Tan, C. P., Taherian, A. R. & Boo, H. C. (2009). Modeling the physicochemical properties of orange beverage emulsion as function of main emulsion components using response surface methodology. *Carbohydrate Polymer,* 75: 512–520.

Mohanty, A.K., Dilnawaz, F., Mohanty, C. & Sahoo, S.K. (2010). Etoposide-loaded biodegradable amphiphilicmethoxy (polyethylene glycol) and poly (epsilon caprolactone) copolymericmicelles as drug delivery vehicle for cancer therapy. *Drug Delivery*, 17: 330–342.

Montgomery, D.C. (2001). Design and analysis of experiments. New York: Wiley.

Mortensen, L. & Charles, P. (1996). Bioavailability of calcium supplements and the effect of vitamin D: Comparisons between milk, calcium carbonate, and calcium carbonate plus vitamin D. *The American Journal of Clinical Nutrition,* 63 (3): 354-357.

Müller, R., Jacobs, C. & Kayser, O. (2001). Nanosuspensions as particulate drug formulations in therapy: Rationale for development and what we can expect for the future. *Advanced Drug Delivery Reviews,* 47 (1): 3-19.

Müller, R.H., Runge, S., Ravelli, V., Mehnert, W., Thunemann, A.F. & Souto, E.B. (2006). Oral Bioavailability of Cyclosporine: Solid Lipid Nanoparticles (SLNR) Versus Drug Nanocrystals. *International Journal of Pharmaceutics,* 317: 82-89.

Murray, T. M. (1996). Prevention and management of osteoporosis: Consensus statements from the scientific advisory board of the osteoporosis society of Canada. Calcium nutrition and osteoporosis. *Canadian Medical Association Journal,* 155 (7): 935-942.

Myers, R.H. & Montgomery, D.C. (2002). Response surface methodology. New York: Wiley.

National Academy of Sciences. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washington DC: National Academy Press. 2001.

National Institutes of Health. Vitamin D: Dietary supplement factsheet for health professionals.(2012).Washington, http://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional.

National Institutes of Health. Optimal calcium intake.NIH Consents Statement, (1994).

National Osteoporosis Foundation. America's Bone Health: The State of Osteoporosis and Low Bone Mass in Our Nation. Washington DC: National Osteoporosis Foundation, 2002.

National Osteoporosis Foundation. Boning up on osteoporosis: a guide to prevention and treatment. Washington, D.C. National Osteoporosis Foundation, 2003.

Nicole, M., Hensch, P., Imboden, M., Dietrich, D.F., Barthélemy, J.C., Ackermann-Liebrich, U., Berger, W., Gaspoz, J.M. & Schwartz, J. (2008). Glutathione S-Transferase Polymorphisms, Passive Smoking, Obesity, and Heart Rate Variability in Nonsmokers. *Environmental Health Perspective*, 116: 1494–1499.

Nieves, J. W. (2005). Osteoporosis: the role of micronutrients. *American Journal of Clinical Nutrition,* 81 (suppl): 1232S–1239S.

Nieves, J., Barrett-Connor, E., Siris, E., Zion, M., Barlas, S. & Chen, Y. (2008). Calcium and vitamin D intake influence bone mass, but not short-term fracture risk, in caucasian post-menopausal women from the national osteoporosis risk assessment (NORA) study. *Osteoporosis International,* 19 (5): 673-679.

Nordin, B.E.C. (1976). Nutritional considerations. In: *Calcium, phosphate and magnesium metabolism,* ed. B.E.C. Nordin, pp. 1-35. Edinburgh, UK, Churchill Livingstone.

O'Neill, J.E. & Yeung, S.C. (2011). Do dental implants preserve and maintain alveolar bone?.*Journal of Investigative and Clinical Dentistry*, 2: 229–235.

O'Brien, K., Abrams, S., Liang, L., Ellis, K. & Gagel, R. (1996). Increased efficiency of calcium absorption during short periods of inadequate calcium intake in girls. *The American Journal of Clinical Nutrition,* 63 (4): 579-583.

Ohta, A., Ohtsuki, M., Hosono, A., Adachi, T., Hara, H. & Sakata, T. (1998). Dietary fructooligosaccharides prevent osteopenia after gastrectomy in rats. *The Journal of Nutrition,* 128(1): 106-110.

Ohta, A., Uehara, M., Sakai, K., Takasaki, M., Adlercreutz, H., Morohashi, T. & Ishimi, Y. (2002). A combination of dietary fructooligosaccharides and isoflavone conjugates increases femoral bone mineral density and equolproduction in ovariectomized mice. *The Journal of Nutrition,* 132 (7): 2048-2054.

Park, H., Jeon, B., Ahn, J. & Kwak, H. (2007). Effects of nanocalcium supplemented milk on bone calcium metabolism in ovariectomized rats. *Asian Australasian Journal of Animal Sciences,* 20 (8): 12-66.

Park, H.S., Ahn, J. & Kwak, H.S. (2008). Effect of nano-calcium-enriched milk on calcium metabolism in ovariectomised rats. *Journal of Medicinal Food*, 11 (3): 454-459.

Park, J., Omi, N., Nosaka, T., Kitajima, A. & Ezawa, I. (2008). Estrogen deficiency and low-calcium diet increased bone loss and urinary calcium excretion but did not alter arterial stiffness in young female rats. *Journal of Bone and Mineral Metabolism,* 26 (3): 218-225.

Patravale, V.B., Date A.A. & Kulkarni, R.M. (2004). Nanosuspensions: a promising drug delivery strategy. *Journal of pharmacy and pharmacology*, 56: 827–840.

Persson, P., Gagnemo-Persson, R., & Håkanson, R. (1993). The effect of high or low dietary calcium on bone and calcium homeostasis in young male rats. *Calcified Tissue International,*52: 460–464.

Picherit, C., Coxam, V., Bennetau-Pelissero, C., Kati-Coulibaly, S., Davicco, M., Lebecque, P. & Barlet, J. (2000). Daidzein is more efficient than genistein in preventing ovariectomy-induced bone loss in rats. *The Journal of Nutrition,* 130 (7): 1675-1681.

Porter, C.J.H. & Charman, W.N. (2001). In vitro assessment of oral lipid based formulations. *Advanced Drug Delivery Reviews*, 50: 127–147.

Price, C.T., Langford, J.R. & Liporace, F.A. (2012). Essential Nutrients for Bone Health and a Review of their Availability in the Average North American Diet. *The Open Orthopaedics Journal*, 6: 143-149.

Prince, R. L., Devine, A., Dhaliwal, S.S. & Dick, I.M. (2006). Effects of calcium supplementation on clinical fracture and bone structure: Results of a 5-year, double-blind, placebo-controlled trial in elderly women. *Archives of Internal Medicine,* 166 (8): 869-875.

Ranhotra, G., Gelroth, J., Leinen, S. & Schneller, F. (1997). Bioavailability of calcium in breads fortified with different calcium sources. *Cereal Chemistry,* 74 (4): 361-363.

Ranhotra, G.S., Gelroth, J.A. & Leinen, S.D. (2000). Utilization of calcium in breads highly fortified with calcium as calcium carbonate or as dairy calcium. *Cereal Chemistry*, 77 (3): 293–296.

Raschka, L. & Daniel, H. (2005). Mechanisms underlying the effects of inulin-type fructans on calcium absorption in the large intestine of rats. *Bone,* 37 (5): 728-735.

Rasti, B., Jinap, S., Mozafari, M. & Yazid, A. (2012). Comparative study of the oxidative and physical stability of liposomal and nanoliposomal polyunsaturated fatty acids prepared with conventional and mozafari methods. *Food Chemistry,* 135 (4): 2761-2770.

Riggs, B.L. & Melton, L.J. (1992). The prevention and treatment of osteoporosis. *New England Journal of Medicine*, 327: 620-627.

Rizzoli, R. (2008). Nutrition: Its role in bone health. *Best Practice & Research Clinical Endocrinology & Metabolism,* 22 (5): 813-829.

Roberfroid, M. (1993). Dietary fiber, inulin, and oligofructose: A review comparing their physiological effects. *Critical Reviews in Food Science & Nutrition,* 33 (2): 103-148.

Roberfroid, M. (2007). Prebiotics: The concept revisited. *The Journal of Nutrition,* 137 (3): 830S-837S.

Robert, P. (2000). The role of calcium in peri- and post-menopausal women: consensus opinion of The North American Menopause Society. *Journal of the North American Menopause Society*, 8 (2): 84–95.

Rossi, L. (2001). Reduced growth and skeletal changes in zinc-deficient growing rats are due to impaired growth plate activity and inanition. *Journal of Nutrition*, 131: 1142-1146.

Ruml, L.A., Sakhaee, K.. & Peterson, R. (1999). The effect of calcium citrate on bone density in the early and mid-post-menopausal period: a randomized placebo controlled study. *American Journal of Therapeutics,* 6: 303-311.

Ryan, P. & Robert, T.D. (2007). Department of Nutrition Dietetics and Food Sciences.

Sakaguchi, K., Morita, I. & Murota, S. (1994). Eicosapentaenoic acid inhibits bone loss due to ovariectomy in rats. *Prostaglandins, Leukotrienes and Essential Fatty Acids,* 50 (2): 81-84.

Sakhaee, K., Bhuket, T., Adams-Huet, B. & Rao, D. S. (1999). Meta-analysis of calcium bioavailability: A comparison of calcium citrate with calcium carbonate. *American Journal of Therapeutics*, 6 (6): 313-322.

Sanguansri, P. & Augustin, M.A. (2006). Nanoscale materials development — a food industry perspective. *Trends in Food Science and Technology*, 17: 547–556.

Sato, Y., Kaji, M.,Tsuru, T., Satoh, K. & Kondo, I. (2002). Vitamin K deficiency and osteopenia invitamin D-deficient elderly women with Parkinson's disease. *Journal of Archives of Physical medicine and Rehabilitation,* 83 (1): 86-91.

Scholz-Ahrens, K.E. & Schrezenmeir, J. (2002). Inulin, oligofructose and mineral metabolism-experimental data and mechanism. *British Journal of Nutrition,* 87 (S2): S179-S186.

Scholz-Ahrens, K.E. & Schrezenmeir, J. (2004).Ernährung und Osteoporoseprävention. *Ernährungs-Umschau*, 51: 22-26.

Scholz-Ahrens, K.E., Ade, P., Marten, B., Weber, P., Timm, W., Açil, Y. & Schrezenmeir, J. (2007). Prebiotics, probiotics, and synbiotics affect mineral absorption, bone mineral content, and bone structure. *The Journal of Nutrition,* 137 (3): 838S-846S.

Shahnazari, M., Martin, B.R., Legette, L.L., Lachcik, P.J., Welch, J. & Weaver, C.M. (2009). Diet calcium level but not calcium supplement particle size affects bone density and mechanical properties in ovariectomized rats. *The Journal of Nutrition,* 139 (7): 1308-1314.

Shapiro, R. & Heaney, R. (2003). Co-dependence of calcium and phosphorus for growth and bone development under conditions of varying deficiency. *Bone,* 32 (5): 532-540.

Shchekin, A.K. & Rusanov, A.I. (2008). Generalization of the Gibbs-Kelvin-Köhler and Ostwald-Freundlich equations for a liquid film on a soluble nanoparticle. *Journal of Chemical Physics*, 129: 1-5.

Shen, V., Birchman, R., Xu, R., Lindsay, R. & Dempster, D. (1995). Short-term changes in histomorphometric and biochemical turnover markers and bone mineral density in estrogen-and/or dietary calcium-deficient rats. *Bone,* 16 (1): 149-156.

Shimomura, M. & Sawadaishi, T. (2001). Bottom-up strategy of materials fabrication: a new trend in nanotechnology of soft materials. *Current Opinion in Colloid Interface Science*, 6: 11–16.

Shireen, K.F. (2002). Bioavailability of calcium from sweet potato and soy flour supplemented diets in hamsters. *Journal of Environment Science Health*, 37 (6): 637-645.

Shirke, S.S., Jadhav, S.R. & Jagtap, A.G. (2008). Methanolic extract of cuminum cyminum inhibits ovariectomy-induced bone loss in rats. *Experimental Biology and Medicine,* 233 (11): 1403-1410.

Singh, R.K., Sadhasivam, T., Sheeja, G.I., Singh, P. & Srivastava, O, N. (2013). Effect of different sized CeO2 nano particles on decomposition and hydrogen absorption kinetics of magnesium hydride. *International Journal of Hydrogen Energy*, 1-5.

Stransky, M. & Rysava, L. (2009).Nutrition as Prevention and Treatment of Osteoporosis. *Journal of Phisiological Research*, 58 (1): S7-S11.

Sunyecz, J.A. (2008). The use of calcium and vitamin D in the management of osteoporosis. *Journal of Therapeutics and Clinical Risk Management*, 4: 827–836.

Swaim, R.A., Barner, J.C. & Brown, C.M. (2008). The relationship of calcium intake and exercise to osteoporosis health beliefs in post-menopausal women. *Research in Social and Administrative Pharmacy,* 4 (2): 153-163.

Tabatabaee Amid, B. & Mirhosseini, H. (2012). Optimization of aqueous extraction of gum from Durian (*Duriozibethinus*) seed: A potential, low cost source of hydrocolloid. *Food Chemistry*, 132: 1258–1268.

Tahiri, M., Tressol, J.C. & Arnaud, J. (2003). Effect of short-chain fructooligosaccharides on intestinal calcium absorption and calcium status in post-menopausal women: a stable-isotope study. *American Journal of Clinical Nutrition,* 77: 449–457.

Takahara, S., Morohashi, T., Sano, T., Ohta, A., Yamada, S. & Sasa, R. (2000). Fructooligosaccharide consumption enhances femoral bone volume and mineral concentrations in rats. *Journal of Nutrition*, 130 (7): 1792-1795.

Tamaki, H., Akamine, T., Goshi, N., Kurata, H. & Sakou, T. (1998). Effects of exercise training and etidronate treatment on bone mineral density and trabecular bone in ovariectomized rats. *Bone,* 23 (2): 147-153.

Terano, T. (2001). Effect of omega 3 polyunsaturated fatty acid ingestion on bone metabolism and osteoporosis. *World Review of Nutrition and Dietetics*, 88: 141-147.

Thakkar, K.N., Snehit, S., Mhatre, M.S., Rasesh, Y. & Parikh, M.S. (2010). Biological synthesis of metallic nanoparticles. *Nanomedicine: Nanotechnology, Biology, and Medicine*, 6: 257–262.

Theobald, H.E. (2005). Dietary calcium and health. *British Nutrition Foundation Nutrition Bulletin,* 30: 237–277.

Tucci, J.R. (2006). Importance of early diagnosis and treatment of osteoporosis to prevent fracture. *American Journal of Managed Care*, 12 (Suppl 7): S181-S190.

Tucker, K.L., Chen, H., Hannan, M.T., Cupples, L.A., Wilson, P.W., Felson, D. & Kiel, D.P. (2002). Bone mineral density and dietary patterns in older adults: The framingham osteoporosis study. *The American Journal of Clinical Nutrition,* 76 (1): 245-252.

Turner, C.H. (2002). Biomechanics of bone: determinants of skeletal fragility and bone quality. *Osteoporosis International,* 13: 97-104.

United States Department of Agriculture, US Department of Health and Human Services. Dietary Guidelines for Americans. Washington, DC, 2005.

United States Department of Health and Human Services. Bone Health and Osteoporosis: A Report of the Surgeon General. Rockville, MD: U.S. Department of Health and Human Services, Office of the Surgeon General, 2004.

Van den, H., Regin, E M., Miret, S., Slettenaar, M., Duchateau, G.S., Rietveld, A.G., Wilkinson, J.E. & Teucher, B. (2009). Calcium absorption from fortified ice cream formulations compared with calcium absorption from milk. *Journal of the American Dietetic Association,* 109 (5): 830-835.

Van Eerdenbrugh, B., Vermant, J. & Martens, J.A. (2010). Solubility Increases Associated with Crystalline Drug Nanoparticles: Methodologies and Significance. *Molecular Pharmaceutics*, 7 (5): 1858-1870.

Van Rooyen, J.M., Kruger, H.S. & Huisman, H.W. (2000). An epidemiological study of hypertensionand its determinants in a population in transition: the THUSA study. *Journal of Human Hypertension*, 14 (12): 779-787.

Varnai, V.M., Šariae, M., Mokroviae, G., Piasek, M., Blanusa, M., Culej, J.B., Sariae, M.M. & Kostial, K. (2003). The effect of dietary supplementation with calcium salts on skeletal calcium in suckling rats. *Archives of Industrial Hygiene and Toxicology*, 54: 119-125.

Wang, Y., Zeng, T., Wang, S., Wang, W., Wang, Q. & Yu, H. (2010). Fructo-oligosaccharides enhance the mineral absorption and counteract the adverse effects of phytic acid in mice. *Nutrition,* 26 (3): 305-311.

Waterbeemd, H.V., Lennernäs, H. & Artursson, P. (2009). The importance of gut wall metabolism in determining drug bioavailability. In: *Drug Bioavailability-Estimation of solubility Permeability, Absorption and bioavailability*, eds. H. Waterbeemd, & B. Testa, pp. 321.

Watkins, B.A., Li, Y., Lippman, H. & Seifert, M.F. (2001). Omega-3 olyunsaturated Fatty Acids and Skeletal Health. *Experimental Biology & Medicine*, 226 (6): 485–497.

Watkins, B.A., Li, Y., Lippman, H.E. & Feng, S. (2003). Modulatory effect of omega-3 polyunsaturated fatty acids on osteoblast function and bone metabolism. *Prostaglandins, Leukotrienes and Essential Fatty Acids,* 68: 387–398.

Weaver, C.M., Heaney, R.P. (2006). Food sources, supplements, and bioavailability. In: *Calcium in human health*, eds. C.M. Weaver, R.P. Heaney, pp. 129-42. Totowa, Human Press Inc.

Weber, P. (1999). The role of vitamins in the prevention of osteoporosis–a brief status report. *International Journal for Vitamin and Nutrition Research,* 69 (3): 194-197.

Wegmüller, R., Zimmermann, M.B., Moretti, D., Arnold, M., Langhans, W. & Hurrell, R.F. (2004). Particle size reduction and encapsulation affect the bioavailability of ferric pyrophosphate in rats. *Journal of Nutrition*, 134: 3301–3304.

Whitesides, G.M. & Grzybowski, B. (2002). Self-assembly at all scales. *Science*, 295: 2418–2421.

WHO/FAO. Report of a joint WHO/FAO expert consultation. Diet, nutrition and the prevention of chronic diseases. Geneva, 2003.

World Health Organisation.WHO technical report series 843. Assessment of fracture risk and its application to screening for post-menopausal osteoporosis, Geneva, 1994.

World Health Organization. WHO Scientific Group on the Assessment of Osteoporosis at Primary Health Care Level. Brussels, Belgium: WHO Press, Geneva, Switzerland, 2004.

World Health Organization. WHO Study Group on Assessment of Fracture Risk, & its Application to Screening for Post-menopausal Osteoporosis. Assessment of fracture risk and its application to screening for post-menopausal osteoporosis. Brussels, Belgium: WHO Press, Geneva, Switzerland, 1994.

World Health Organization. Human vitamin and mineral requirements: report of a joint FAO/WHO expert consultation, Bangkok, Thailand, 2001.

World Health Organization/Food Agriculture Organization. Guidelines on food fortification with micronutrients. Geneva, Switzerland, 2006.

Younes, H., Coudray, C., Bellanger, J., Demigné, C., Rayssiguier, Y. & Rémésy, C. (2001). Effects of two fermentable carbohydrates (inulin and resistant starch) and their combination on calcium and magnesium balance in rats. *British Journal of Nutrition,* 86 (4): 479-485.

Yu, L.X., Gatlin, L. & Amidon, G.L. (1999). Predicting oral drug absorption. In *Transport Processes in Pharmaceutical Systems*, eds. G.L. Amidon, P.I. Lee , E.M. Topp, pp. 377-409. New York: Marcel Dekker, Inc.

Zafar, T.A., Weaver, C.M., Zhao, Y., Martin, B.R. & Wastney, M.E. (2004). Non digestible oligosaccharides increase calcium absorption and suppress bone resorption in ovariectomized rats. *The Journal of Nutrition,* 134 (2): 399-402.

Zempleni, J., Rucker, R.B., McCormick, D.B. & Suttie, J.W. (2007). Handbook of vitamins, Fourth edition.

Zeyuan, D., Bingying, T., Xiaolin, L., Jinming, H. & Yifeng, C. (1998). Effect of green tea and black tea on the metabolisms of mineral elements in old rats. *Biological Trace Element Research,* 65 (1): 75-86.

Zhou, J.R. & Erdman J.W. (1995). Phytic acid in health and disease. *Critical Reviews in Food Science & Nutrition,* 35 (6): 495-508.

Zittermann, A. (2007). Osteoporose. *Ernährungs-Umschau*, 54: 33-38.