제 1 강연

Phytochemical 생리활성 물질의 임상적 적용

조 여 원 교수

경희대학교 동서의학전문대학원 임상영양학교실

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Phytonutrients in Medical Nutrition

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Since the beginning of recorded history, plants have been used in the treatment of specific diseases. Plant foods contain many phytonutrients which are nutritionally significant health-promoting components that benefit humans. Many dietary phytonutrients play unique roles in human metabolism, cell division, and molecular regulation, thereby affecting one's health. A new health paradigm may be evolving that emphasizes the positive aspects of diet, as well as identifies the components that are physiologically active and contribute to prevent the onset of disease.

Phytonutrients are generally classified by structure or unique molecular content, such as carotenoids, polyphenols, sulfides, and thiols. Plant-based phenols, flavonoids, isoflavones, terpenes, glucosinolates, and other compounds that are present in the everyday diet are reported to elicit a variety of biological activities, acting as antioxidants, phytoestrogens, or enzyme inducers. Research on the mechanisms of chemoprotection has focused on the biological activity of compounds found in cruciferous and green leafy vegetables, soybeans, citrus, fruits, green tea, and red wine.

Phytonutrient dietary supplementation has long been claimed to exert beneficial effects on a wide variety of human diseases. Recent technological developments have resulted in the identification and commercial development of an ever-increasing number of bioactive phytochemicals, with the potential for application in the prevention and/or treatment of diseases. In addition, regulatory bodies stipulate that substantiating claims of efficacy and/or safety for phytochemical products require direct evidence from randomized, controlled studies involving human subjects, in other words clinical trials.

Populations consuming diets rich in vegetables, fruits, and grain products have been highly correlated with significantly lower rates of cancer of the colon, breast, lung, stomach, etc. The strongest support for a protective effect against cancer is through fiber-rich foods. Phytochemicals may also contribute to the observed protective effects of vegetables. In general, following the dietary guideline to "Eat a Variety of Foods" - especially if they are plant-derived foods - may result in a diet rich in phytonutrients which will have a positive impact on health.

Phytonutrients in Medical Nutrition

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Medical Nutrition

◈ Medically necessary nutrition therapy
New health care delivery system

Medicine + Human Nutrition

MN
- Nutrition Diagnosis — Nutrition Assessment
- Nutrition Intervention
  - Nutrition Therapy
    - Therapeutic diet
    - Nutrition support
  - Counseling

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Medical Nutrition Therapy
(MNT, 의학영양치료)

JCAHO, ADA : 입원한지 48시간이내에 모든 환자의 영양검색을 통하여 영양위험도가 높은 환자를 선별하여 의학영양 치료를 하고 의무 기록을 함

- 환자의 영양불량 상태를 문서화함으로써 무형의 영양치료를 객관적으로 입증
- 적극적으로 영양불량 상태를 개선시킴으로써 의료비 절감
- 합병증으로 인한 비용지출 감소 (조기영양치료, 영양지원으로 영양불량 개선)
- 환자의 상태를 **monitoring** 하여 추후관리 유도

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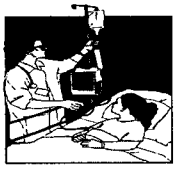
Medical Nutrition Therapy
(MNT, 의학영양치료)



환자의 빠른 회복

환자의 삶의 질 향상

의학영양치료(MNT) : 우리나라 현황

'영양사는 의사가 영양치료를 의뢰한 환자의 영양상태를 평가하고, 영양 상담 및 지도를 실시하며, 그 내용을 기록함'

예방차원에서 교육, 상담을 실시 : 비급여(건강보험법령)

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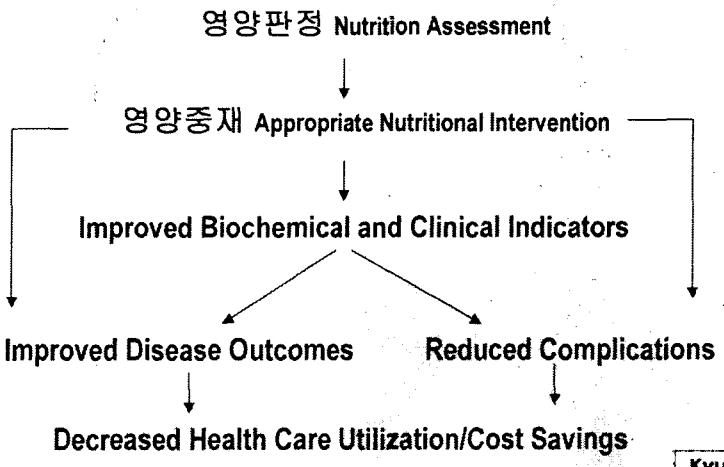
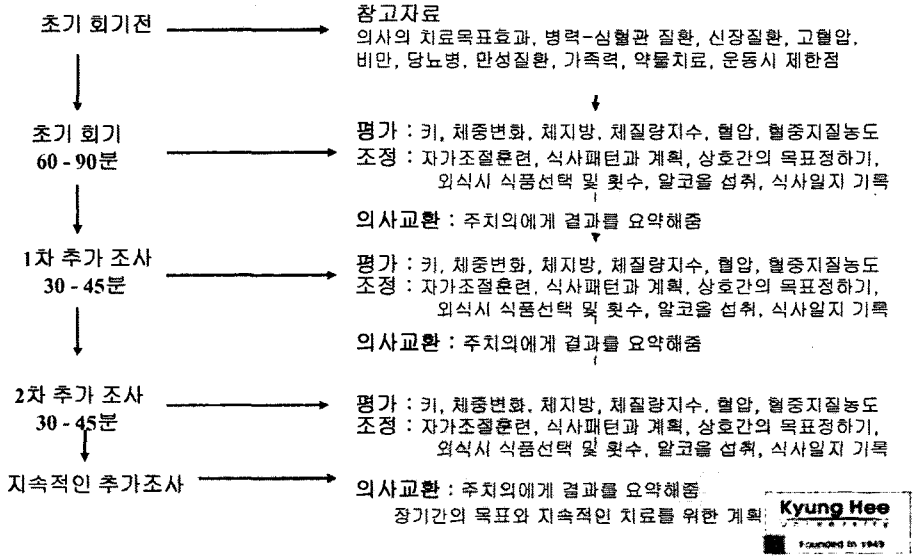
의학영양치료(MNT)의 Flow



Nutrition Assessment For Nutrition Diagnosis

- Anthropometric measurement (wt. ht, SFT, etc)
- Biochemical determinations (lab analysis of blood or urine)
- Clinical examinations (detect the major signs)
- Dietary assessment : 24-hr recall, food record, food frequency, food preference, diet history (determines the sources and amounts of nutrients in the diet) → nutrients intake → compare w/ RDA

MNT Protocol

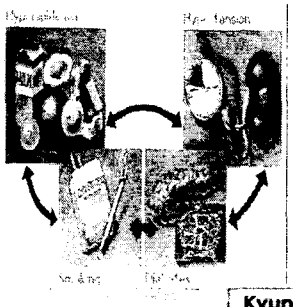


Contents of MNT

효과 판정 요소	기초	조정효과 조정 1	2	3	4	기대효과	이상적인 목표치
임상적인 효과							
생화학적 지표							
혈압, 지질량(콜레스테롤)	✓	✓	✓	✓		LDL-C↓ TC/HDL↓	LDL-C< 130 mg/dl, TC/HDL< 4.5
신체계측							
체중, 체지방, BMI	✓	✓	✓	✓		0.5 kg/week 체중감소	이상체중 이내
임상증상							
의학영양치료의 목표							
영양처방에 따른 저열량, 저염식 식사 패턴							
정상체중							
행동적 효과							
식사계획	✓	✓	✓	✓		규칙적인 식사, 열량제한	적절한 식습관 형성
식사 중 열량 인식	✓	✓	✓	✓		열량, 영양소, 식습관 영양교육	체중 감소를 위한 운동
식사준비	✓	✓	✓	✓		저지방 조리법, 저염 조리법	이상체중 유지
외식	✓	✓	✓	✓		외식시 적절한 메뉴 선택	
운동	✓	✓	✓	✓		유산소 운동 참여(3회/주, 45분)	

Nutritionally High Risk Diseases

- Obesity
- Diabetes Mellitus
- Hypertension
- Hyperlipidemia
- Gastrointestine Disease
- Liver Disease
- Renal Disease
- Cancer



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Medical Nutrition Therapy

- General :

  Regular Diet : Calorie : 2,000-2,500 (Harris-Benedict : BEE x AF x IF)
  CHO : P : F = 60-70% : 15-20% : 15-20%
  protein : 1-1.2g protein/kg BW
  vitamin, mineral : RDA

- Therapeutic :

  Diabetic Diet : Calorie for IBW
  CHO : P : F = 55-60% :15-20% : 20-25%
  dietary fiber : 20-35 g
  Na : < 2,400-3,000mg
  vitamin, mineral : RDA

- Nutrition Support : Calorie : 1kcal/ml
  protein : 12.-1.5g
  vitamin, mineral : > RDA

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Hypertension

◈ 식사처방 기준 : 고혈압의 식사관리는 체중조절과 나트륨 제한에 중점

◈ 영양 기준량 : 일반 환자식 기준에 준함

◈ 저염식 : 2,000 mg Na(소금 5g/d)
한국인의 1일 소금 섭취량이 평균 20-25g

◈ 열량 : 체중조절을 위하여 저열량, 저지방 및 고혈압에 영향을 줄 수 있는 전해질(K, Ca)과 섬유소 등의 영양 권장량을 충족시킬 수 있도록 충분한 섭취 고려

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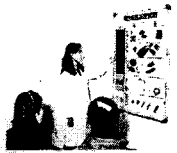
Non Drug Therapy for Hypertension

- 염분섭취 조절
- 동물성지방, 당분 섭취조절
- 콜레스테롤 섭취 조절
- 정상체중 유지, 열량섭취조절
- 고 단백, 고 섬유소식
- 술, 담배의 절제, 향신료 제한
- 규칙적인 운동



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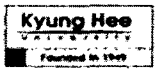
Medical Nutrition for Hyperlipidemia

Nutrients	Recommended Intake	
	American	Korean
Saturated fat	< 7%	6%
Monounsaturated fat	Up to 20%	10%
Polyunsaturated fat	Up to 10%	6%
Total fat	25–35%	15-20%
Carbohydrate	50–60%	60-65%
Fiber	20–30 g/day	20-35 g/day
Protein	15%	15-20%
Cholesterol	< 200mg	200 mg/day
Total calories	to maintain desirable body weight	



Components of Foods

- Macronutrients (provide calories, provide building blocks)
- Micronutrients (enzyme co-factors, antioxidants, functions)
- Additives
- Agricultural chemical contaminants
- Inorganic contaminants
- Chemicals formed in cooking or processing
- Natural and microbial toxin
- Other natural compounds (phytochemicals, etc.)

Natural Compounds in Foods

- Phytochemicals : Any naturally occurring substance present in plants
- Nutraceuticals : Bioactives eliciting medical and health benefits including prevention and treatment of diseases (produced from foods but sold in medical forms
- Functional foods : Modified natural foods or food ingredients which may provide health benefits, beyond the nutrients it contains
- Phytonutrients : Phyto(plant) + Nutrients, antioxidant, detoxification agents, synergize with vitamins, reduce risk of chronic disease, beneficial substance present in plants

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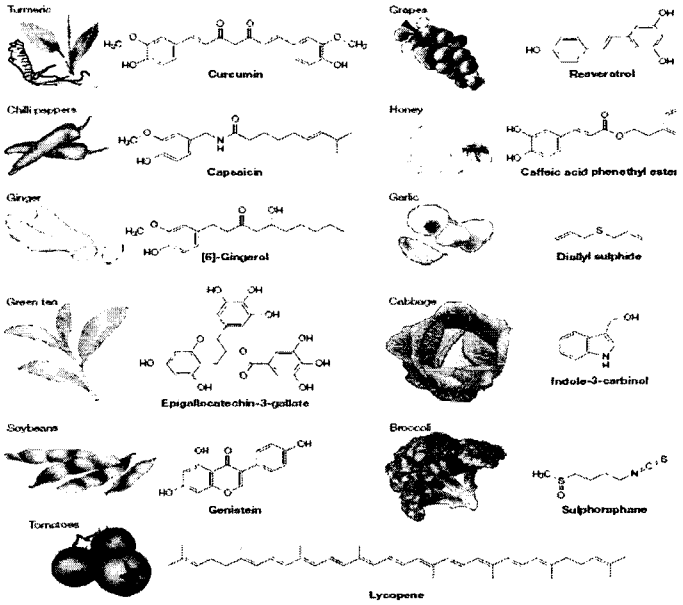

Pytonutrients and their Dietary Sources

Surh. Y.J (2003) Nature Reviews

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Phytonutrients Associated with Health Promotion

Food Sources	Phytonutrients	Biological Activities
Fruits, vegetables	Carotenoids ; α-carotene, β-carotene, β-cryptoxanthin, lutein, lycopene	Source of vitamin A (some) Quench singlet oxygen ↑ Cell-cell communication
Cruciferous vegetables (broccoli), horse radish	Glucosinolates, isothiocyanates, indoles : glucobrassicin, sulphorophane, indole-3-carbinol)	↑ Phase II enzyme activity Alter estrogen metabolism through shift in hydroxylation ↓ DNA methylation
Cereals, soybeans, soy-based foods	Inositol phosphates : phytate, inositol pentaphosphate, inositol tetraphosphate, etc.	Bind divalent cations-especially copper and iron, which may generate hydroxyl radicals through the Fenton reaction

Beecher GR et al. Nutrition Review, 57(9):s3-6, 1999

Phytonutrients Associated with Health Promotion

Food Sources	Phytonutrients	Biological Activities
Citrus, fruits, vegetables	Phenolics, cyclic compounds : chlorogenic acid, ellagic acid, coumarins, limonene	↑ Phase II enzyme activity Inhibit N-nitrosation reactions Antioxidant
Soybeans, soy-based foods flax, rye, vegetables	Phytoestrogens : Isoflavones – daidzein, genistein, glycitein, lignans- matairesinol, secoisolariresinol	Metabolized in GI tract to estrogen-like compounds ↓ Tyrosine kinase activity Induce apoptosis
Vegetable oils, nuts, seeds, cereals, legumes	Phytosterols : Campesterol, β-sitosterol, stigmasterol	Bind bile acids and cholesterol ↓ Colonic cell proliferation

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Phytonutrients Associated with Health Promotion

Food Sources	Phytonutrients	Biological Activities
Fruits, veg, tea, red wine exclusively in black and oolong tea	Polyphenols : flavonoids (~15-20 in foods : quercetin, apigenin, catechin, etc.), theaflavins, thearubigens	Antioxidant ↓ Capillary fragility and permeability Alter tyrosine kinase activity
Soybeans, soy-foods, other legumes, cereals, vegetables	Protease inhibitors	Bind to trypsin and chymotrypsin ↓ Growth of transformed cells ↓ Tumors in animals
Soybeans, soy-based foods, other legumes, nuts	Saponins : soyasaponins, soyasapogenols	Bind bile acids and cholesterol Cytotoxic toward tumor cells Antioxidant
Onions, Cruciferous vegetables(broccoli)	Sulfides and thiols : diallyl sulfides, allyl methyl trisulfides, dithiolthiones	↑ Phase II enzyme activity ↓ Bacterial activity – nitrate to nitrite conversion

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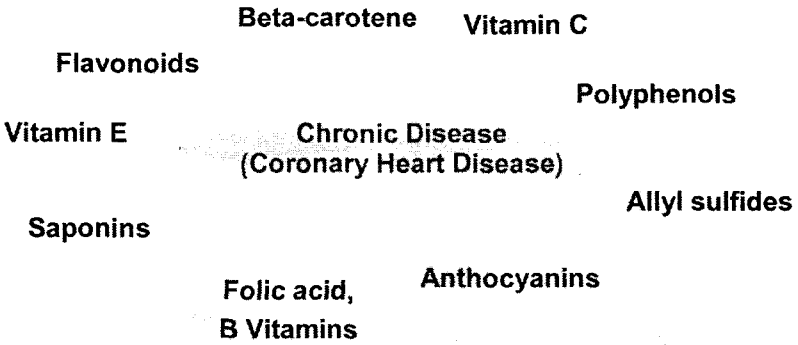
Multiple Phytonutrients are Associated with Risk Reduction for Chronic Disease



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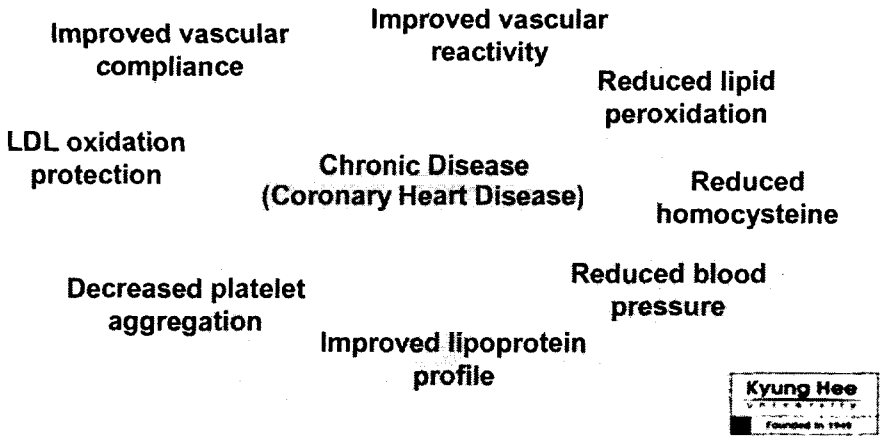
Phytonutrients Impact Chronic Disease via Multiple Mechanisms



Antioxidant Phytonutrients

- Many phytonutrients are antioxidants
- Antioxidants inactivate free radicals
- Antioxidants help to reduce damage to cells, lipids, DNA
- A mixture of antioxidants is thought to offer the most health benefit
- Fruits and vegetables are excellent sources of antioxidants

Phytonutrients

Lycopene : high tomato intake ⇩ risk of prostate cancer 35%
protective effect against stomach & lung cancer

Lutein : ⇩ risk of colon cancer 17%

Flavonoids : ⇩ risk of dying from heart disease by 50%

Resveratrol : ⇩ LDL oxidation, platelet agg. regulate heart rhythm

Catechins : protects against heart disease, atherosclerosis

Hesperidin : improve lipid levels, ⇩ cancer cell proliferation

Isoflavones : ⇩ breast cancer, protect against bone loss

Benefits of Fruits & Vegetables

Spinach	lutein	eyes
Tomatoes	lycopene	heart, prostate
Oranges	hesperidin	cardiovascular
Grapes/wine	resveratrol	cardiovascular
Green tea	catechins	heart, cancer
Soy	isoflavones	breast, bone
Brocoli etc	sulforophanes	detoxification
Berries(blu)	anthocyanins	cardiovascular
Berries(red)	elagic acid	DNA structure

Distribution of Phytochemicals

	sulfides	phytates	flavonoids	carotenoids	coumarins	terpenes	lignans	phenolic acids	indles	isothiocyanates
Garlic	+					+				
Green Tea			+		+			+		
Soybeans		+	+	+	+	+	+	+		
Cereal grains		+	+	+	+	+		+		
Cruciferous	+		+	+	+	+		+	+	+
Umbelliferous			+	+	+	+		+		
Citrus			+	+	+	+		+		
Solanaceous			+	+	+	+		+		
Licorice root			+		+	+		+		
Flaxseed			+		+		+	+		

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Epidemiological
Observational
Experimental
in Vitro Study

Soy Foods have positive effects on prevention of chronic disease & conditions of menopausal women

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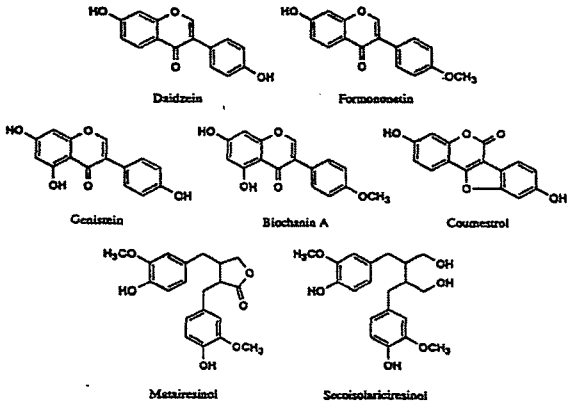
Structures of Phytoestrogens

Figure 2. Structures of Phytoestrogens



Source: Mazur et al

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The Effects of Phytoestrogens(I)

Diseases /conditions	Proposed Mechanisms of Action	Strength of Evidence
Cancers	• Genistein inhibits tyrosine kinase involved in signal transduction in both normal & tumor cell proliferation	+
	• Genistein inhibits angiogenesis required for tumor growth	+
	• Isoflavones act as an antioxidant, potentially protecting against oxidative DNA damage and delay onset of cancer	+
	• Daidzein competes with estradiol for uterine estrogen binding sites	++

0 no effect/unclear, + observation in vitro, ++ animal models in vivo, +++ human studies

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The Effects of Phytoestrogens(II)

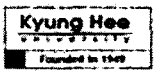
Disease/ conditions	Proposed Mechanisms of Action	Strength of Evidence
CVD	• Genistein : ⇩ tyrosine activity, action of certain growth factors, ⇩ growth of atherosclerotic lesions	+
	• Genistein : ⇩ thrombosis associated w/ atherosclerosis by interfering with platelets and thrombin action	+
	• Soy protein ⇧ fecal excretion of bile acids, ⇩ chol biosyn, ⇧ LDL receptor activity, ⇩ LDL-C	++
	• Soy protein has cholesterol lowering effects when substituted for animal protein	+++

0 no effect/unclear, + observation in vitro, ++ animal models in vivo, +++ human studies
* Soy protein refers to protein & related constituents. such as iosflavonoids

The Effects of Phytoestrogens(III)

Disease/ conditions	Proposed Mechanisms of Action	Strength of evidence
Osteoporosis	• Ipriflavone, a synthetic isoflavone, prevents bone loss	+
	• Isoflavones : estrogen like activity in bone metabolism	+
	• Isoflavonoids : inhibit bone resorption and stimulate bone mineralization	++
	• High doses of soy protein constituents ⇧ bone mineral contents and bone mineral density	+++
Menopausal Relief	Weak estrogenic activity of isoflavones compensate for lack of estrogen production, relieving symptoms of hot flashes, atrophic vaginitis, vaginal dryness	0

0 no effect/unclear, + observation in vitro, ++ animal models in vivo, +++ human studies
* Soy protein refers to protein & related constituents, such as iosflavonoids



Phytoestrogen in Obesity

	Diet	Amount & duration	Effects
Obese [1]	VLCD, soy protein compared with casein	375-425 kcal/day for 10 wk	↓ BW greater ↓ in TG, cholesterol
Obese woman [2]	LCD with soy protein Compared with lean meat	Low-calorie diets for 16 wk	Similar decrease(9%) in BW with both diets
Obese woman [3]	Soy-based liquid formula compared w/ milk-based formula	1,000 kcal/day for 4 wk	No significant difference in BW reduction
Mildly obese[4]	Soy protein compared with animal protein	28~29% of energy as protein for 4 days	Decreased 24-h energy expenditure

1. Bosello O et al. Ann Nutr Metab 1998;32:206-14
2. Yamashita T et al. Metabolism 1998;47;1308-14
3. Jenkins DJA et al. Atherosclerosis 1989;78;99-107
4. Mikkelsen PB et al. Am J Clin Nutr 2000;72:1135-41

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Phytoestrogens in Diatetes

	Diet	Amount and duration	Effects
Type 2[1]	Soy protein & fiber compared w/ casein & cellulose	50g protein, 20g fiber, 150mg isoflavone, 6 wk	↓ LDL-C, TG, apoB100 no change in HDL-C, Hgb A_{1c}
Obese Type 2 hypertesion[2]	Soy protein diet compared with animal-protein diet	1g protein/kg BW, 8 wk	↓ total-chol, TG
Obese Type 2[3]	Soy polysaccharide compared with low fiber	10g fiber as single meal	↓ postprandial hyperglycemia, TG no effect on serum insulin
Type 2[4]	Soy hull	26-52g fiber, 2-4 wk	Improved glucose intolerance, ↓ VLDL-C, TG, hemoglobin A1c

1. Hermansen et al. Diabetes Care 2001;24;228-33
2. Anderson et al. Am J Clin Nutr 1998;68:1347S-53S
3. Tasi AC et al. Am J Clin Nutr 1987;45:596-601
4. Mahalko JR et al. Am J Clin Nutr 1984;39;25-34

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Phamacokinetics of isoflavone in plasma after Ingestion of Soy Products in Korean Women

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Phamacokinetics of isoflavone in plasma (n=26)

65mg isoflavone of ingestion	AUC (μg hr/L)	Cmax (ng/ml)	T max (hr)	$t_{1/2}$ (hr)
Iogen (%of aglycone)				
Daidzein (100%)	2628.9±573.1[a]	230.4±44.2	3.78±1.2	9.75±3.8[a]
Genistein(100%)	2355.7±672.8	160.1±32.4[y]	4.67±2.5	8.53±2.2[x]
Fermented soybean				
Daidzein(60%)	2593.8±465.2[a]	214.0±52.9	2.68±1.5	9.54±1.9[a]
Genistein(52%)	2279.0±724.6	195.7±35.4[xy]	3.50±0.8	8.22±2.1[x]
Soymilk				
Daidzein(1.8%)	2101.3±352.4[b]	211.2±58.3	3.71±2.1	5.92±1.7[b]
Genistein(1.8%)	2325.8±332.4	231.1±44.3[x]	4.86±1.9	5.64±0.7[y]

1) Values are mean ± SD
2) Values within the same row with different superscripts are significantly different ($p<0.05$)
AUC : Area under the curve, C max : Maximum concentration, Tmax : Time of maximum concentration, $t_{1/2}$: Half-life

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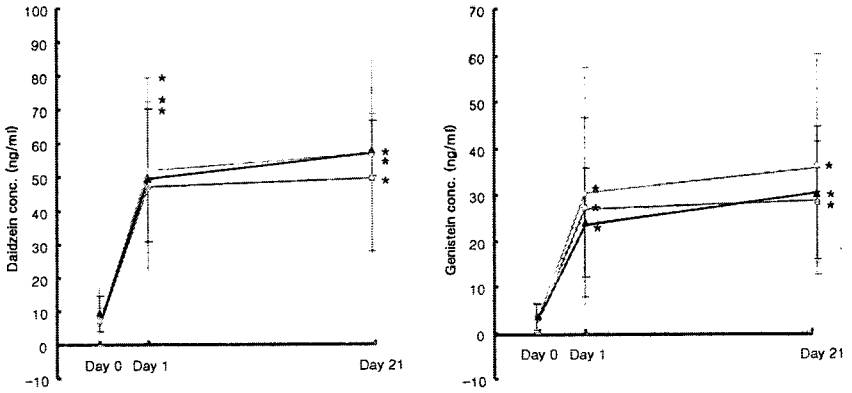
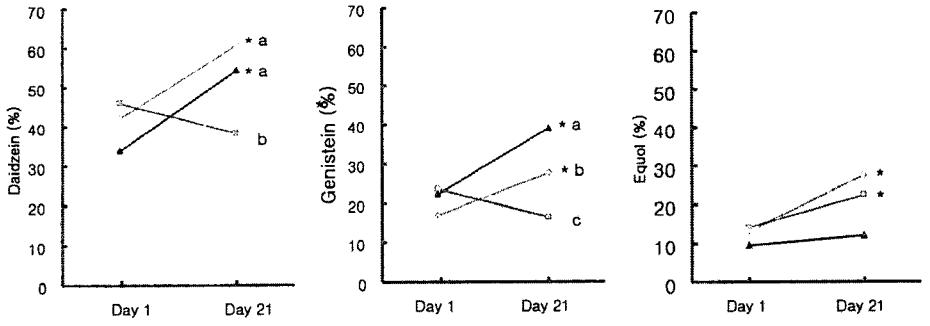


Plasma concentration of isoflavone after ingestion soy products



Urinary recovery of isoflavone after ingestion of soy products

Plasma Concentration and Urinary Excretion of Isoflavone after Feeding of Breast milk, Soy-based Formula and Casein-based Formula

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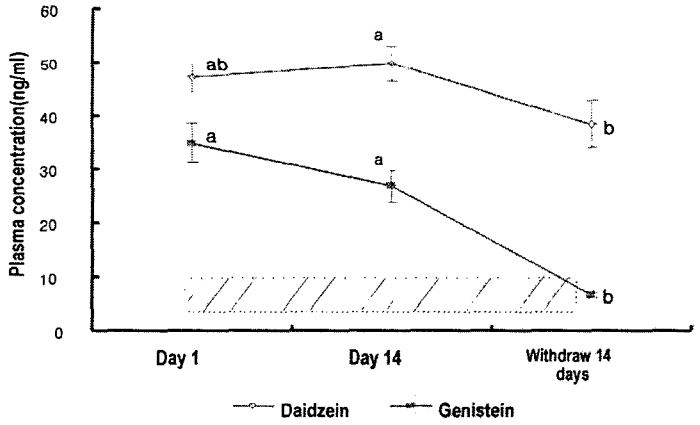

Plasma levels of isoflavone after supplementation of 500ml of soy milk for 2 weeks and 2 weeks after withdrawal in breast-feeding mother

The shade represents a reference concentration of daidzein and genistein in adult women

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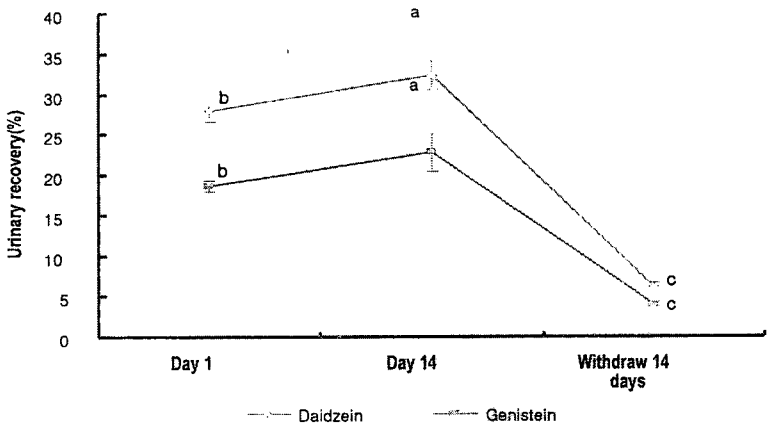

Urinary isoflavone excretion after supplementation of 500ml of soy milk for 2 weeks and 2 weeks after withdrawal in breast-feeding mother

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Isoflavone concentration of breast milk, casein-based formula, and soy-based formula (mg/L)

	Breast Milk	Casein-based Formula	Soy-base Formula
Daidzein	0.63 ± 0.3^{B}	0.028 ± 0.002^{C}	[illegible]^{A}
Genistein	0.89 ± 0.3^{b}	0.022 ± 0.003^{c}	[illegible]^{a}

Values are means ± SD.
Means with different alphabets are significantly different at $p<0.001$ by Duncan's Multiple Range test.

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Plasma isoflavone concentration of 4 months old infants (ng/ml)

	Breast milk-fed infants	Casein-based Formula fed infants	Soy-based Formula fed infants
Daidzein	3.4 ± 1.6[b]	8.1 ± 2.8[b]	264.1±97.1[a]
Genistein	4.8 ± 1.4[b]	9.3 ± 3.7[b]	392.1±160.6[a]

Values are means ± SD.
Means with different alphabets are significantly different at p<0.001 by Duncan's Multiple Range test.

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Isoflavone concentration of urine in 4 months old infants (μg/ml)

	Breast milk fed infants	Casein-based formula fed infants	Soy-based Formula fed infants
Daidzein	0.28 ± 0.09[b]	0.45 ± 0.12[b]	19.62 ± 14.60[a]
Genistein	0.22 ± 0.10[b]	0.33 ± 0.11[b]	17.69 ± 14.51[a]

Values are means ± SD.
Means with the different alphabets are significantly different at p<0.001 by Duncan's Multiple Range test.

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What is Found

The pharmacokinetic study showed that different soy products have different effects on the level of isoflavone in plasma.

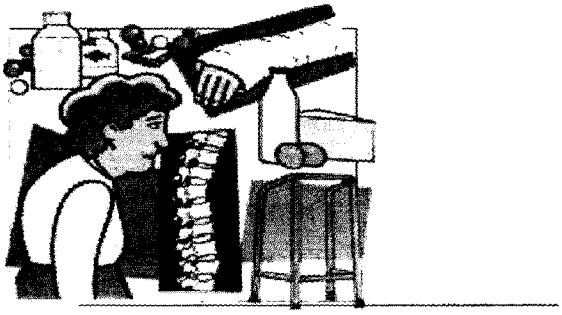
Long term ingestion of any types of soy foods significantly increased plasma concentration of isoflavone.

Human breast milk was not a useful source of isoflavone.

Plasma isoflavone levels in soy-based formula fed infants were significantly higher than those of breast milk and casein-based formula fed infants.

Kyung Hee

Effects of Inulin on Bone Metabolism in Korean Postmenopausal Women



Kyung Hee University
Graduate School of East-West Medical Science
Dept. Medical Nutrition

Kyung Hee

Background

Osteoporosis

- A major public threat for more than 2 million (80 % are women) Koreans.
- One in 2 women and one in 8 men over 50 years of age will have an osteoporosis related fracture in USA.

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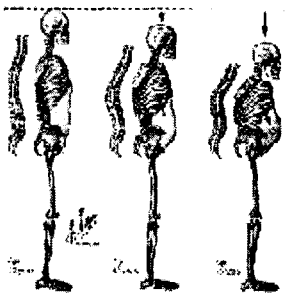
What is it?

Normal bone

Osteoporosis



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Risk Factors

Low intake of dietary calcium

Excessive use of alcohol

Limited bone-related nutrients (protein, Vit D, K etc.)

Use of certain medications

An inactive lifestyle

Smoking

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Korean RDA for Ca (2000)

Recommendation : 700 mg/day

Calcium intake in Korea ('98)
Female : 470gm/day (> 65y : 378.8 mg/day)

USA RDA for > 65y : 1,200mg/day

Upper limit : 2,500mg/day (NRC, 1997)

Ca^{++} absorption : ~30%

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Dietary Fibers

Recommendation : 25g/day

식이섬유 : Lignin(채소), Cellulose (밀, 현미, 보리), Pectin (감, 귤, 사과), Hemicelluose (곡류, 채소), Gum (두류, 귀리, 보리), 해조다당류, glucomannan (Konjac나무), Psyllium (질경이 씨앗 껍질), Beta glucan(귀리, 버섯)

기능성섬유 : Pectin의 일부, gum의 일부, Resistant starch, 생물공학적 제조 (inlin, dextrin, polydextrose), 동물성 탄수화물 (키틴, 기토산, 콜라겐)

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Potential Effects of Soluble Fiber

⇧ Fecal bulk	(⇩)Cholesterol
⇧ Lactic acid bacteria	⇩ TG
⇧ SCFA production (acetate, propionic acid)	⇧ Mineral absorption (Ca, Mg, Fe, Zn)

* David J.A. et al., *J Nutr* 129 : 1431S-1433S, 1999
** Lactic acid producing bacteria

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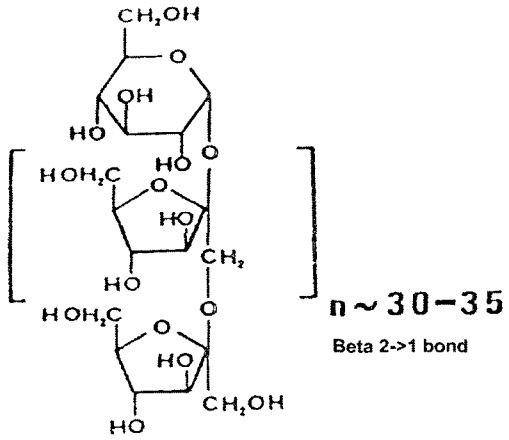
Structure of Inulin



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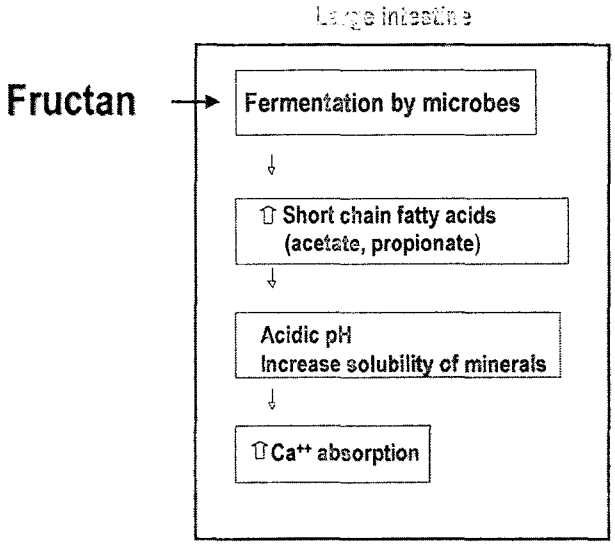
Effect of Fructan on Ca^{++} Absorption



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Purpose of Study

To study the effects of supplements of inulin (Chicory Fructan Fiber) on the absorption of minerals, metabolism of bone, bone mineral density and condition of osteoporosis in postmenopausal women

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Experimental design

0 wk ←---------- Chicory Fructan Fiber supplement ----------→ 12 wks

0 wk	12 wks
AA	AA
BMD	BMD
BA	BA
UA	UA
FA	FA
DA - weekly	
Questionnaire - weekly	

AA : Anthropometric assessment
BMD : Bone Mineral Density
BA : Blood analysis
UA : Urine analysis
FA : Feces analysis
DA : Dietary assess

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Subjects

Control group : Placebo of 8g maltodextrins/sucrose

Inulin group : 8g/day chicory fructan fiber

Inulin + Ca group : 8g/day chicory fructan fiber + 1000mg Ca

Calcium group : Placebo of 8g/day maltodextrins/sucrose + 1000mg Ca

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임상data: Fructan의 허용량

Form	Dosage/day	Reference
Short-chain (DP 3-10)	20g/day	Briet et al. 1995
Long-chain (> DP 30)	30g/day	Rumessen et al. 1998
Inulin (DP 60)	8.0g/day	in this study

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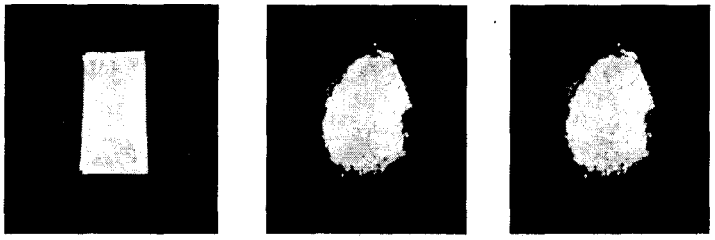
Form of Placebo and Treatment



Maltodextrin sucrose mixture Inulin

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Methods (1)

- Anthropometric assessment – Ht, Wt, BMI (kg/m^2)
- Bone Mineral Density
- Blood Analysis
  - alkaline phosphatase, osteocalcin : biomaker of bone formation
  - TG, total-chol, HDL-chol, LDL-chol
- Urine Analysis
  - deoxypyridinoline : biomaker of osteoclast
  - pyridinium
- Ca absorption = [Ca] in diet* - ([Ca] in feces)
- Dietary Assess : 24-h recall, dietary habits, food records
- Questionnaire: side-effects

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Characteristics of Subjects

		Placebo (n=12)	Inulin (n=11)	Inulin+Ca (n=12)	Ca (n=12)
Age (yrs)		60.6±6.7	60.2±7.0	58.2±6.4	60.6±6.3
Height (cm)	B	155.0±4.7	153.1 ±6.1	157.3±3.5	150.5±5.1
	A	154.6±4.6	153.7±6.3	157.6±3.5	151.0±4.2
Weight (kg)	B	59.6±7.2	55.8±6.6	58.2±5.5	57.1±5.5
	A	59.2±6.5	57.8±7.0	57.8±5.4	57.2±6.1
YSM (yrs)		11.4±7.7	12.5±9.0	10.1±4.7	12.2±8.0
No. child		3.0±1.1	3.1±1.5	2.7±1.0	3.0±1.5

B : Before, A : After
YSM: years since menopause

Characteristics of Subjects

		Placebo (n=12)	Inulin (n=11)	Inulin+Ca (n=12)	Ca (n=12)
BMI (kg/m^2)	B	24.8±2.7	23.8±2.7	23.5±1.8	25.2±1.9
	A	24.0±2.4	24.4±1.9	23.3±1.7	25.2±1.9
W/H ratio	B	0.86±0.05	0.86±0.06	0.87±0.05	0.86±0.04
	A	0.86±0.05	0.86±0.05	0.84±0.05	0.86±0.04
Triceps	B	26.6±8.2	23.2±6.4	23.9±3.5	27.8±4.6
	A	26.3±5.7	23.7±5.2	23.2±4.3	27.1±3.8
Body fat (%)	B	30.9±5.7	31.4±5.8	28.5±4.8	32.4±4.0
	A	30.9±4.9	30.6±5.7	28.7±5.7	32.0±4.5

B : Before, A : After

Gastrointestinal Symptoms

score(n)

	Placebo (n=12)	Inulin (n=11)	Inulin+Ca (n=12)	Ca (n=12)
Pain	0	0	0	0
Diarrhea	0	3	2	0
Borborygmia	1	6	5	0
Distension	4	2	3	2
Flatulence	2	7	6	1
Nausea	0	0	0	0
Total	7	18	16	3

All symptoms were rated every half hour
Scale: 0(none) to 3(severe)

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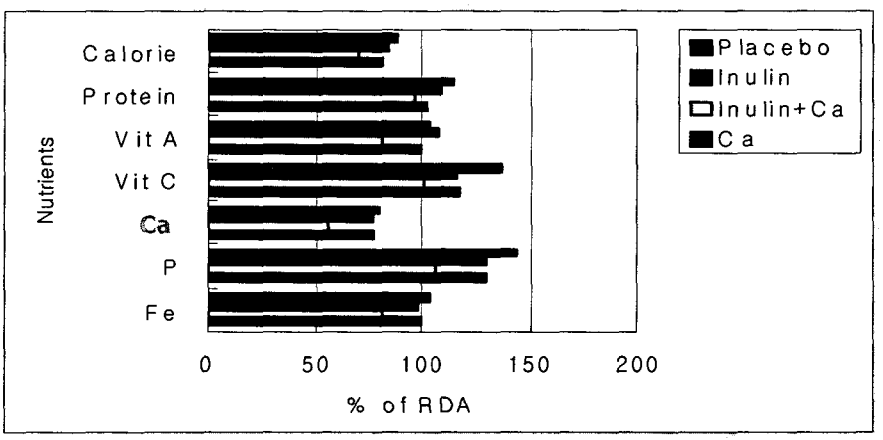
Comparison of Daily Nutrients Intake w/ RDA



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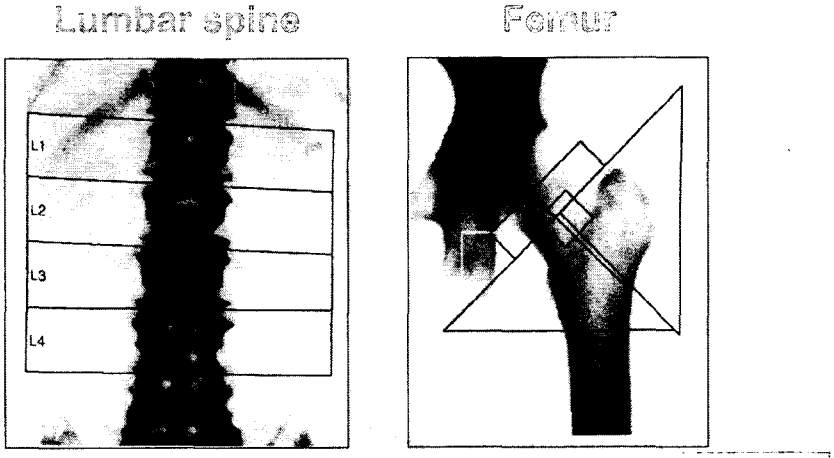
Dual X-ray Absorptiometry



Bone Mineral Density (BMD)

		Placebo (n=12)	Inulin (n=11)	Inulin+Ca (n=12)	Ca (n=12)
Lumbar spine	B	0.82±0.17	0.79±0.11	0.83±0.17	0.73±0.14
(g/cm²)	A	0.81±0.18	0.79±0.12	0.83±0.16	0.75±0.16
T-score	B	-2.36±1.47	-2.57±0.87	-2.13±1.46	-2.78±1.25
	A	-2.41±1.53	-2.52±1.01	-2.13±1.43	-2.19±1.29
Femoral neck	B	0.86±0.12	0.80±0.12	0.88±0.12	0.85±0.14
(g/cm²)	A	0.85±0.11	0.80±0.13	0.89±0.15	0.85±0.13
T-score	B	-0.64±0.98	-1.09±1.03	-0.44±1.05	-0.71±1.14
	A	-0.56±0.94	-1.03±1.00	-0.42±1.03	-0.71±1.13

Definition of osteoporosis and osteopenia for white women
T-score; above -1.0 (Normal) : -1.0~2.5 (Osteopenia); below -2.5 (Osteoporosis)

Correlation of BMD with Age, Ht, Wt, YSM, No. Child

Variables	Lumbar spine (g/cm²)	N = 47
	r	p
Age (yrs)	- 0.477	0.000
Height (cm)	**0.122**	**0.423**
Weight (kg)	**0.166**	**0.275**
YSM (yrs)	- 0.535	0.000
No.children	- 0.364	0.014

r : Pearson's correlation coefficient
YSM : number of years since menopause

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Correlation of BMD with Age, Ht, Wt, YSM, No. Child

Variables	Femoral neck (g/cm²)	N = 47
	r	p
Age (yrs)	- 0.485	0.000
Height (cm)	**0.002**	**0.981**
Weight (kg)	**0.110**	**0.471**
YSM (yrs)	- 0.544	0.000
No.children	**- 0.270**	**0.063**

r : Pearson's correlation coefficient
YSM : number of years since menopause

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Serum Ca and Phosphorus Levels

		Placebo	Inulin	Inulin + Ca	Ca
Calcium	B	8.66±1.59	8.97±0.92	8.43±1.12	8.22±1.43
(mg/dl)	A	9.18±0.94	8.83±0.77	8.98±0.59	8.66±0.87
Phosphorus	B	2.20±0.36	2.41±0.51	2.29±0.55	2.48±0.62
(mg/dl)	A	3.17±0.35[a]	2.31±0.44[b]	2.89±0.37[ab]	2.81±0.33[ab]

B : Before, A : After

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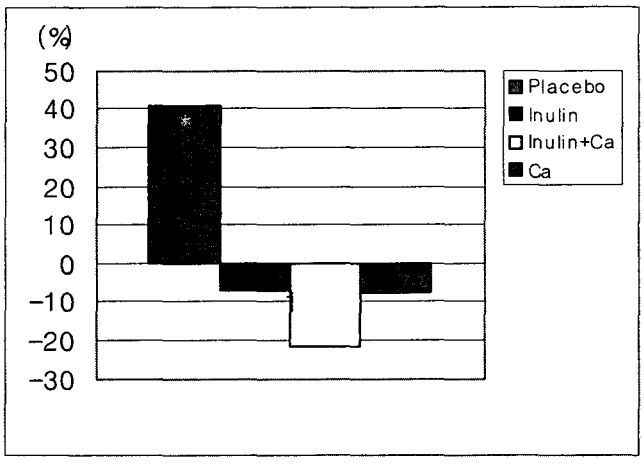
Changes of Urinary Ca Excretion
(before & after supplement)



[(A-B)/A] X 100

A : After
B : Before

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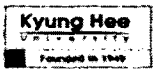
Concentration of Minerals in Feces

mg/day

		Placebo	Inulin	Inulin + Ca	Ca
Calcium	B	318.1±133.7	315.6±134.0	368.5±113.5[1]	343.4±131.4[1]
	A	388.2±159.3[a]	231.8±63.1[a]	877.7±153.4[b,2]	793.8±135.2[b,2]
Phosphorus	B	254.9±91.9[1]	234.3±87.9	284.0±83.7[1]	280.9±123.8[1]
	A	352.2±113.7[ab,2]	258.5±103.8[a]	450.4±122.3[b,2]	381.4±98.6[b,2]

B : Before, A : After



Bone Turnover Biomarkers

		Placebo	Inulin	Inulin + Ca	Ca
ALP	B	9.2±2.52	7.7±1.70	7.4±2.97	7.2±1.72
(K-A)	A	9.2±3.85	6.3±2.90	5.9±3.54	8.6±5.67
Osteocalcin	B	11.2±2.62	13.5±5.61	12.4±3.04[1]	12.5±4.13[1]
(ng/ml)	A	10.3±4.01	11.7±6.13	10.3±3.63[2]	9.4±4.21[2]
u-DPD	B	6.7±1.39	7.1±1.40	6.8±1.52	6.9±1.63
(nm/mM.creat)	A	6.8±1.51	6.5±2.07	6.2±1.31	7.1±2.11

B : Before, A : After
ALP : alkaline phosphatase, u-DPD : urinary deoxypyridinolin

Plasma Levels of TG, Total-C, LDL-C

	Control (n=12)		Inulin Group (n=11)	
	Before	After	Before	After
TG	181.2±92.5	[illegible]	155.4±70.5	127.2±98.2
T-Chol	228.0±50.1	[illegible]	215.8±28.3	[illegible]
LDL-C	141.7±57.1	105.9±43.9	136.6±26.6	[illegible]
HDL-C	50.1±12.0	51.0 ±7.5	48.2 ±11.8	51.6 ±8.3

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What is Found

Korean postmenopausal women daily calcium intake was about 70% of RDA.

A tendency of calcium absorption to be higher with inulin supplement than with placebo treatment was observed.

Intake of inulin may not influence bone turnover markers. (ALP, osteocalcin, urinary deoxypyridinoline)

Inulin supplement significantly decreased plasma total- and LDL-cholesterol levels.

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Participants

Kyung Hee University

Prof. Ryowon Choue, Ph.D
Soon-Ah Kang, Ph.D
Ki-Hyo Jang, Ph.D
Yun-Young Kim, Ph.D student
Eun-Young Lee, MS student
Young-Eun Chang, Ph.D student
Hyun-Joo Lee, MS student

COSUCRA S. A.

Heidi Jacob, Health & Nutrition Manager

Dr. Chung's Food

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Can Long-term Daily Administration of Phytonutrient Supplements Prevent the Immediate Adverse Impact of a High-fat Meal

Gary D. Plotnick et.al.
J ACC 41(10):1744-1749, 2003

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Subjects & Supplementation

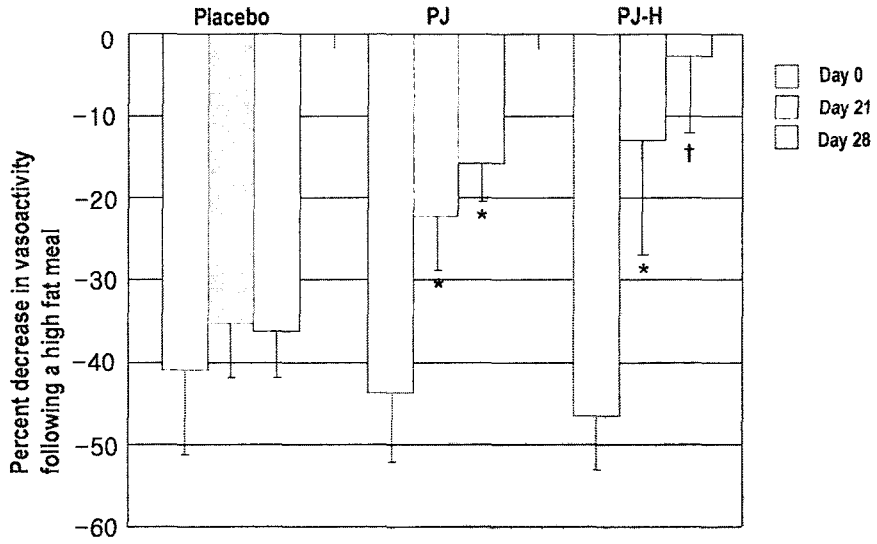
38 healthy volunteers
(age 36.4 ± 10.1 years)

Placebo (N=10)	**JP** (N=14)	**JP + V** (N=12)
High fat meal (900 calorie 50 g fat meal)	High fat meal + powdered fruit vegetable juice concentrate	High fat meal + powdered fruit vegetable juice concentrate + Herbal extract

0 Wk — 3 Wk — 4 Wk

Preprandial diameter
BART(brachial artery reactivity test)

Lipid profiles (T-C,LDL-C, HDL-C, TG)
Homocysteine
NO (Serum nitrate/nitrite concentrations)



Postprandial decreases on brachial artery vasoactivity after a single high-fat meal in randomized to placebo, PJ, or PJ-H supplementation.

*p < 0.05, † p < 0.02 compared with baseline (day 0)

Plasma lipid, homocysteine, NO levels after supplement

	Placebo (n=10)		PJ (n=14)		PJ-H (n=12)	
	Baseline	4 wks	Baseline	4 wks	Baseline	4 wks
Total-C (mg/dl)	195 ±36	191 ±31	184 ±30	172 ±22*	185 ±31	182 ±24
LDL-C (mg/dl)	123 ±36	123 ±25	110 ±25	100 ±26*	113 ±27	113 ±22
HDL-C (mg/dl)	56 ±13	53 ±14	53 ±16	51 ±14	54 ±16	52 ±13
TG (mg/dl)	77 ±32	77 ±36	104 ±45	101 ±73	85 ±29	84 ±34
Homocysteine (μmol/l)	6.2 ±1.1	5.9 ±0.7	6.8 ±0.9	6.8 ±1.3	8.1 ±2.1	7.8 ±2.3
NO (μmol/l)	63 ±39	68 ±31	77 ±43	110 ±64†	84 ±45	115 ±59†

* $p < 0.05$ versus baseline.
† $p < 0.1$ versus baseline. All values are mean ± SD.

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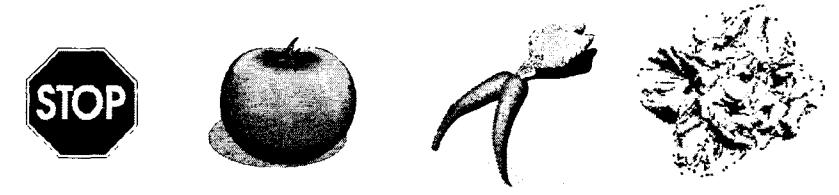
Study Design

23 male, non smoking healthy volunteers
27- 40 years, BMI 20 - 28 (Pool-Zobel et al., Carcinogenesis, 1997)

	330 ml juice	330 ml juice	10 g powder
depletion	40 mg lycopene	21.5 mg beta-carotene 15.7 mg beta-carotene	11.3 mg lutein 3.1 mg beta-carotene



2 weeks | 2 weeks | 2 weeks | 2 weeks

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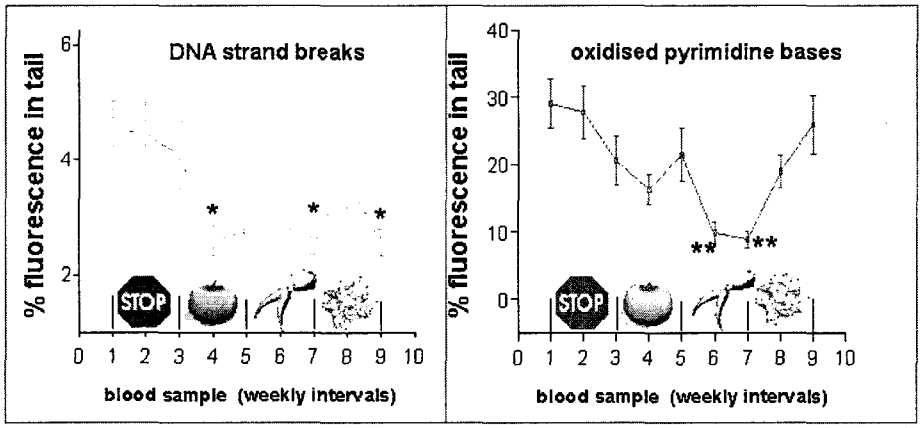
Vegetable consumption reduces genetic damage in blood lymphocytes of healthy human subjects

*(means ± SEM, n=21-23, *p< 0.05, **p< 0.001different from 3)*



(Pool-Zobel et al., Carcinogenesis, 1997)

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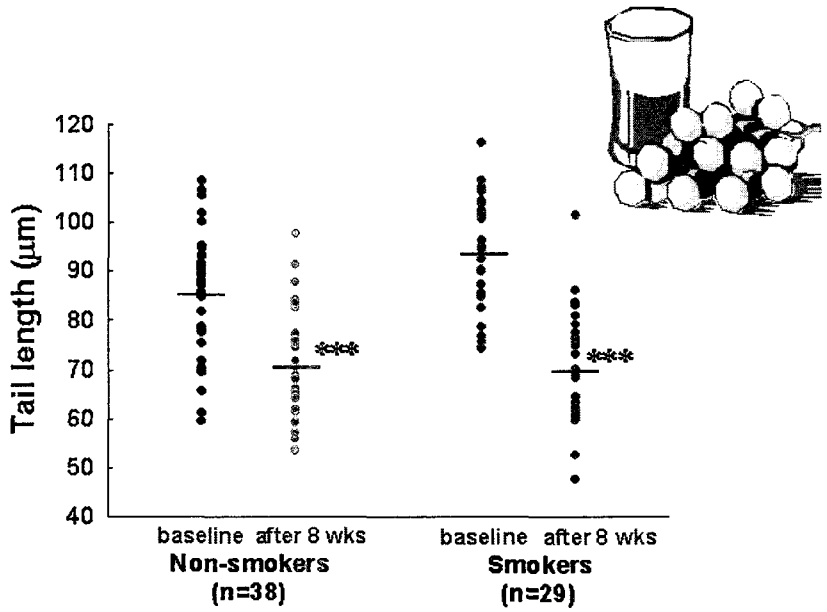

Effect of grape juice supplementation on DNA damages divided by smoking status

*** p<0.001

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Conclusion

Phytonutrients in Medical Nutrition

- Recent technological developments have resulted in the identification and commercial development of an ever-increasing number of bioactive phytochemicals, with the potential for application in the prevention and/or treatment of diseases.
- Following the dietary guideline to 'Eat a Variety of Foods'- especially if they are plant-derived foods- may result in a diet rich in phyonutrients that will have a positive impact on health.
- A new health paradigm may be evolving that emphasizes the positive aspects of diet, as well as identifies the components that are physiologically active and contribute to prevent the onset of disease.

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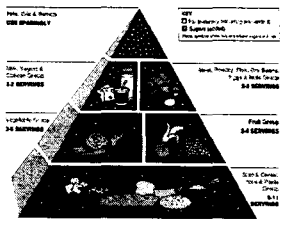
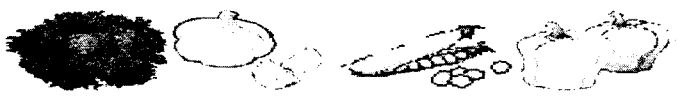
Application of Dietary Phytonutrients

- Do not self-prescribe
- Supplement may interfere with medicine
- Stick to daily value
- Store in safe place
- Read the label
- See your doctor
- Do not waste money





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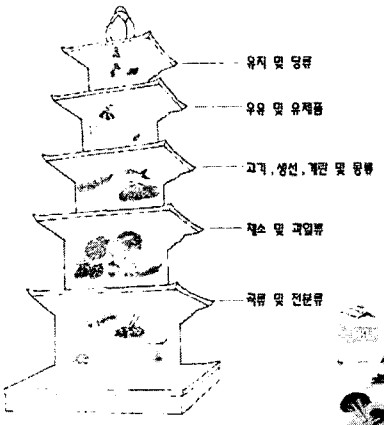

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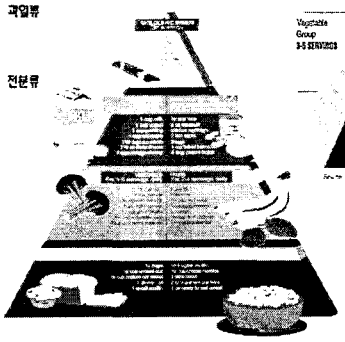

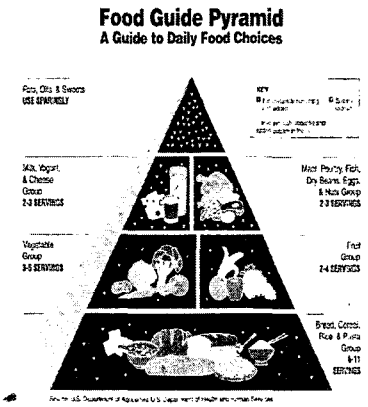

Food Guide Pyramid

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