건강기능식품의 체중, 체지방 감량 효과의 진실

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Conflict of Interest Declaration

- 본 강좌의 내용에 대해서 본 강의의 강사는 직접적 또는 간접적인 어떠한 이해관계도 없음을 밝힙니다.

- 강의록에 제시된 그림과 사진은 이해를 돕기 위해 삽입한 것임을 밝힙니다.

Obesity is chronic, relapsing disease !!

Pharmacotherapy for long-term use

Despite the efficacy of pharmacotherapy in producing weight loss, drugs used for weight loss are often discontinued. Reasons for cessation of therapy include costs, concerns regarding side effects and the perception that the medication is no longer necessary as a sufficient amount of weight is lost.[31] On the contrary, if therapy is well tolerated and effective, it should be continued, similarly to the way antihypertensive and antidiabetic medications are continued even after blood pressure or glycaemic control is at target. This reflects the fact that obesity is a chronic disease that requires sustained treatment, with pharmacotherapy playing an important role in promoting long-term weight maintenance and limiting weight regain.

AFP VOL.46, NO.7, JULY 2017

ECO, Glasgow, Scotland 2019

ICO, Melbourne, Australia, 2022

Mechanism of Appetite Regulation

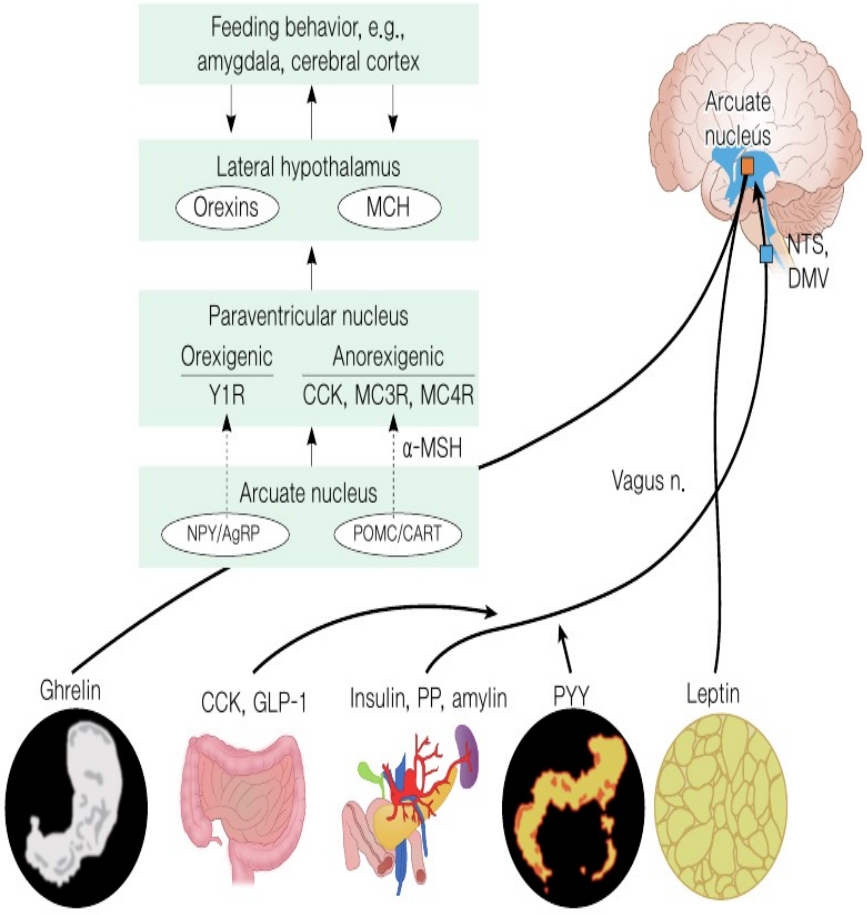


그림 2 식욕 조절에 관여하는 각종 요인

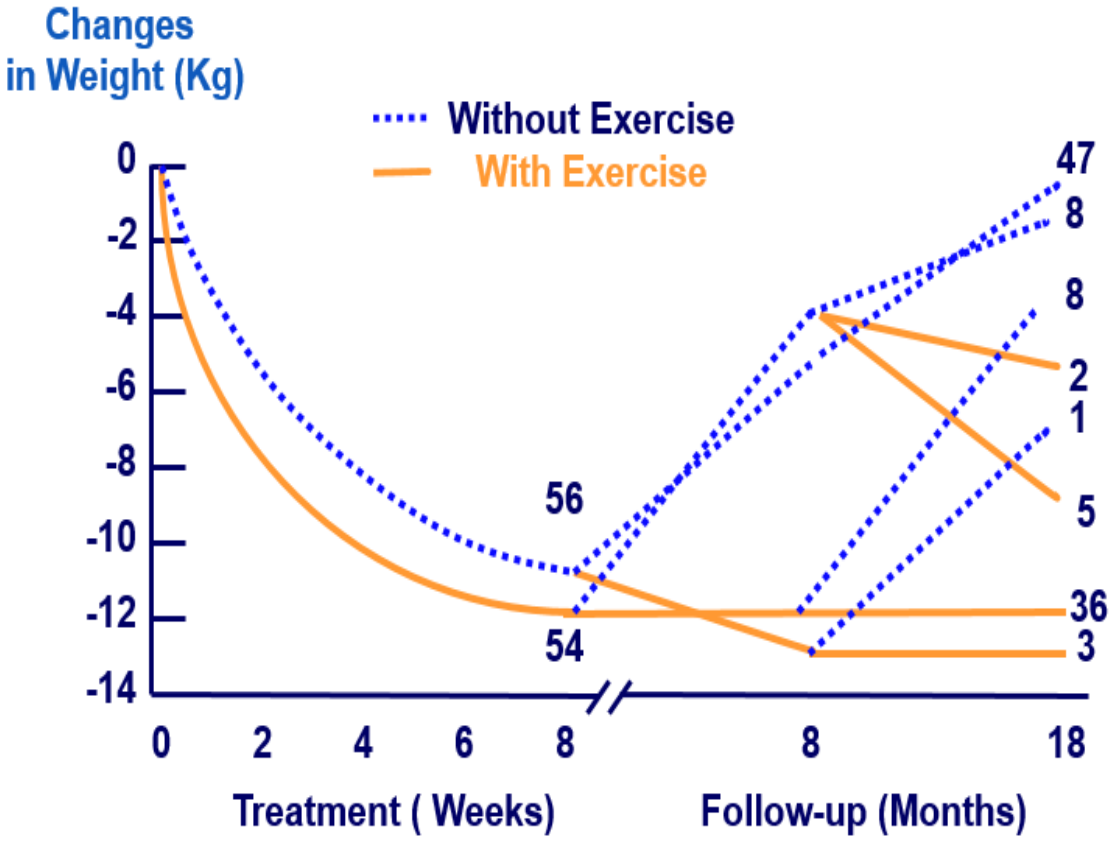
(출처: Gastroenterology 2015;148:1219-1233)

표 3 FDA에서 허가한 비만 치료제

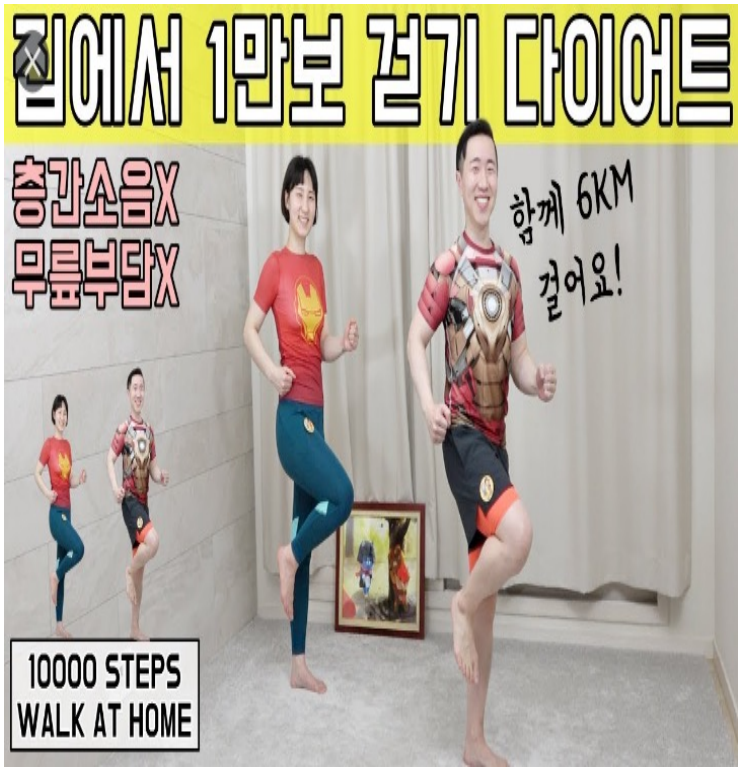
약품	기전	금기사항	병용 금기	부작용
Phentermine	Suppresses appetite	Hyperthyroidism Glaucoma Agitation Pregnancy or bresat feeding (Category X) MAO inhibitor within 14 days Use with caution: cardiovascuar diseases, history of drug abuse	MAO inhibitors	Nervousness Insomnia Dry mouth
Orlistat	Inhibit fat absorption	Pregnancy or bresat feeding (Category X)	Cyclosporine Warfarine Other fat-soluble drugs	Abdominal pain Bowel urgency Steatorrhea Fecal incontinence Hepatotoxicity Oxalate nephropathy
Phentermine-Topiramate (Qsymia®)	Phentermine effect + topiramate: unknown	Hyperthyroidism Glaucoma Agitation Pregnancy or bresat feeding (Category X) MAO inhibitor within 14 days Use with caution: cardiovascuar diseases, history of drug abuse Depression	MAO inhibitors Opioid or other central nervous system depressants CYP3A4 and CYP1A2 inducers	Dry mouth Dizziness Constipation Paresthesia Psychiatric and cognitive adverse events Nephrolithiasis Increased heart rate Angle-closure glaucoma Acute myopia
Naltrexone-Bupropion (Contrave®)	Supress appetite	ESRD Pregnancy or bresat feeding (Category X) MAO inhibitor within 14 days Uncontrolled hypertension Seizure disorder Eating disorder	Bupropion Chronic opioid use or acute opiate withdrawal Linezolid CYP2B6 inhibitores	Nausea, vomiting Constipation or diarrhea Headache Dizziness Insomnia Dry mouth
Liraglutide (Xansenda®)	Slows gastric empthying Increase satiety	Personal or family history of medullary thyroid cancer Pregnancy or bresat feeding (Category X) Moderate to severe renal impairment Use with caution: History of pancreatitis, severe renal insufficiency	Other hypoglycemci agents	Nausea, vomiting Diarrhea Constipation Hypoglycemia Pancreatitis Gallbladder disease Renal impairment Suicidal thoughts

(출처: Bersoux S, et al. Cleve Clin J Med 2017;84(12):951-958)

Effects of Exercise on Weight change



(Blair, 1993)



Moderate Physical Activity (KNHANES 08-15)

중등도신체활동실천여부[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	14689	68.9	68.9	68.9
	1	3370	15.8	15.8	84.7
	2	3268	15.3	15.3	100.0
	Total	21327	100.0	100.0	

a. 성별 = 1

중등도신체활동실천여부[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	19944	70.2	70.2	70.2
	1	3636	12.8	12.8	82.9
	2	4848	17.1	17.1	100.0
	Total	28428	100.0	100.0	

a. 성별 = 2

Current Strategies for Obesity Management

Dietary advice

Physical activity

Behavioral/ lifestyle change

Medical care (Pharmacotherapy, surgery)

+

??

비만 보조제 써야 하나?

- **대학/학회**
  - **Evidence-based medicine!!**
  - **전통적인 치료로 충분**
  - **근거 수준**

- **개원가**
  - Evidence-based medicine
  - 생존
  - 도움?이 된다면…

"I'm part of a double-blind study to see how weight loss supplements help people lose weight. I'm guessing I received the sugar pill placebos."

- **대게 효과 없거나, 부분적인 효과만 보임 ▶ 단독 치료는…??**

건강기능식품 시장

• 국내 건강기능식품 시장 규모 •

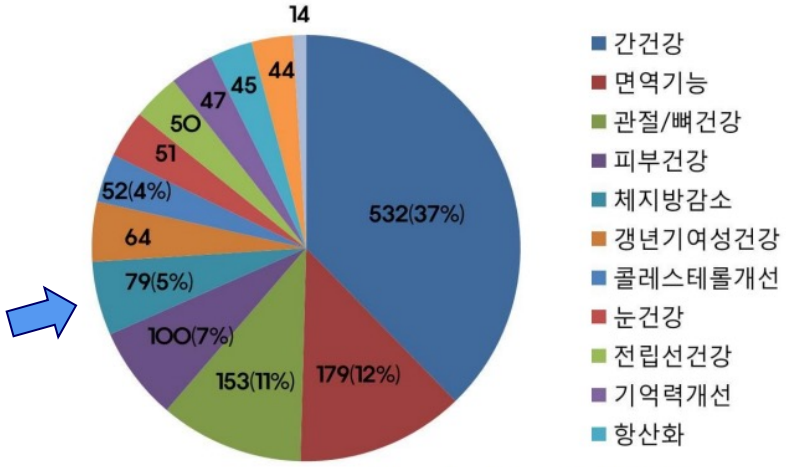
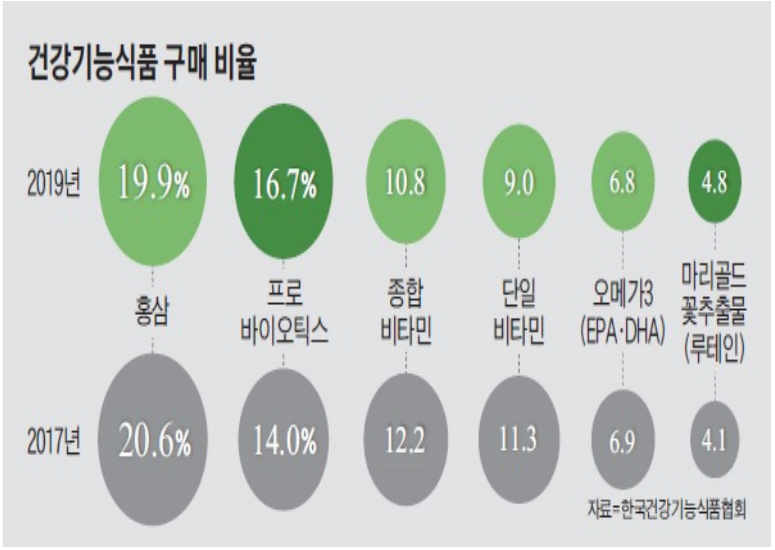


그림 2. 개별인정형 세부품목별 생산현황

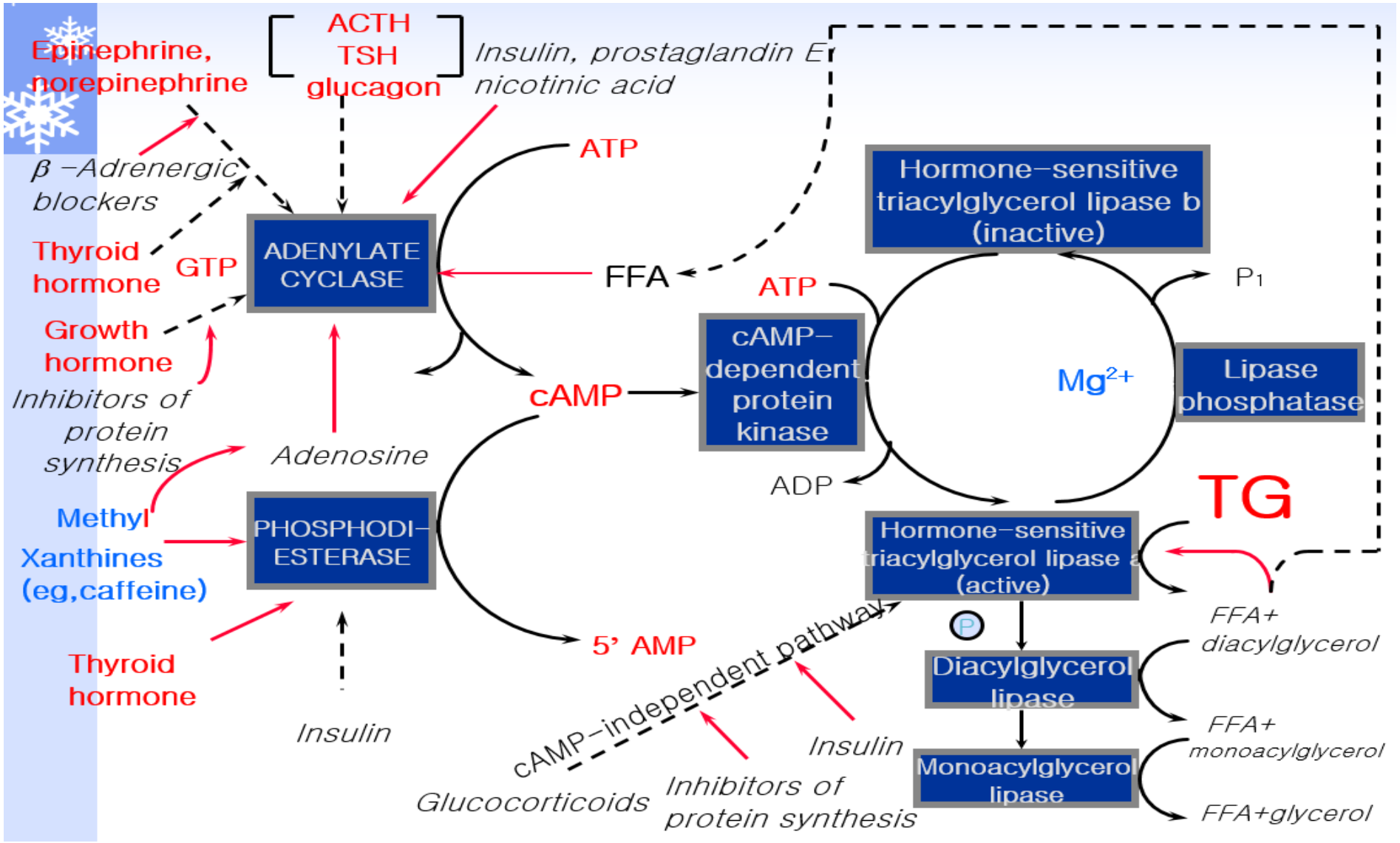
식품산업과 영양 2014;19:19-23



건기식협회, 240개사 마케팅 담당자 대상 설문 결과

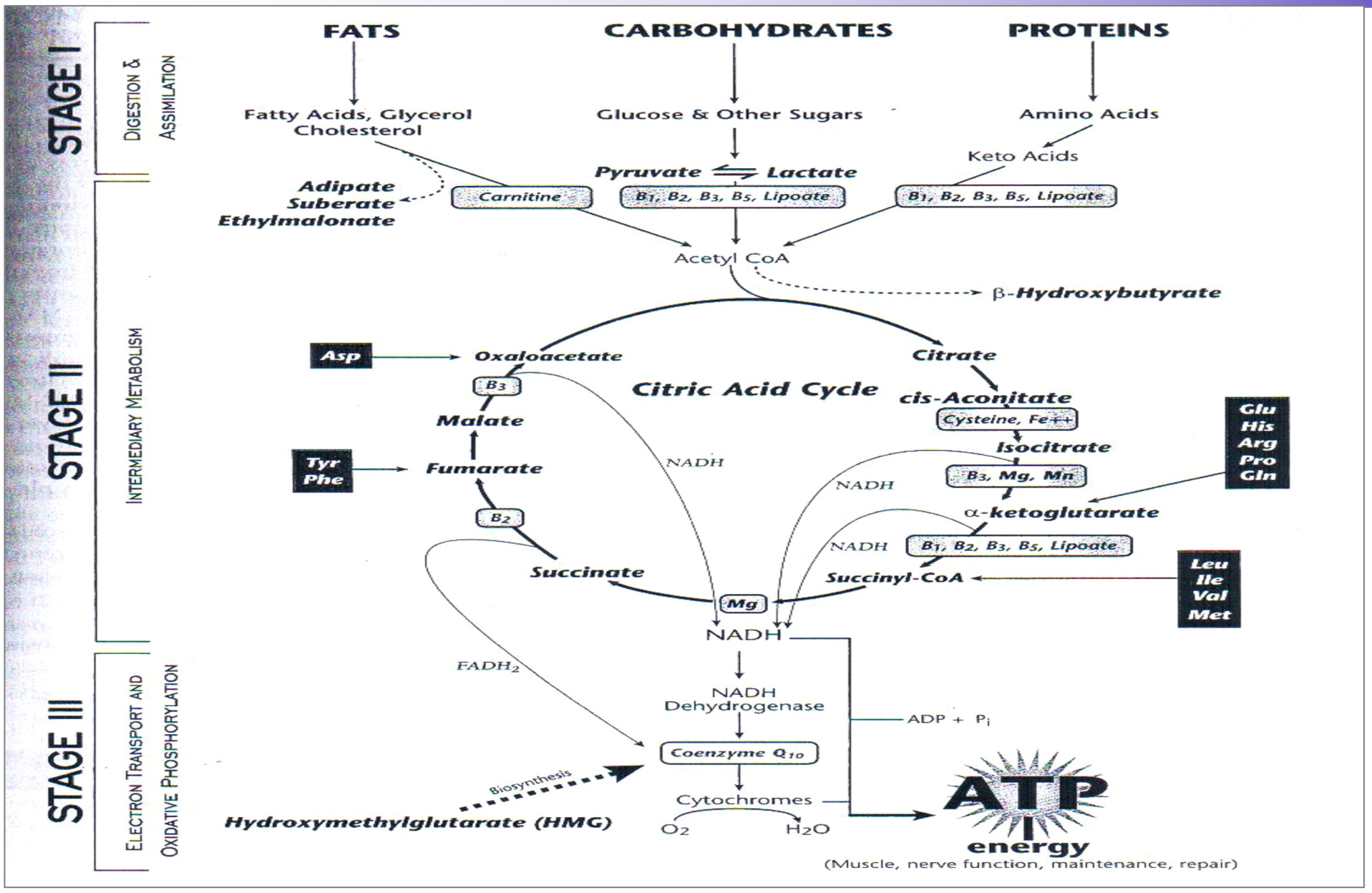
▲ 자료: 한국건강기능식품협회

Mechanism of Lipolysis



Physiology & Behavior 94 (2008) 219–230

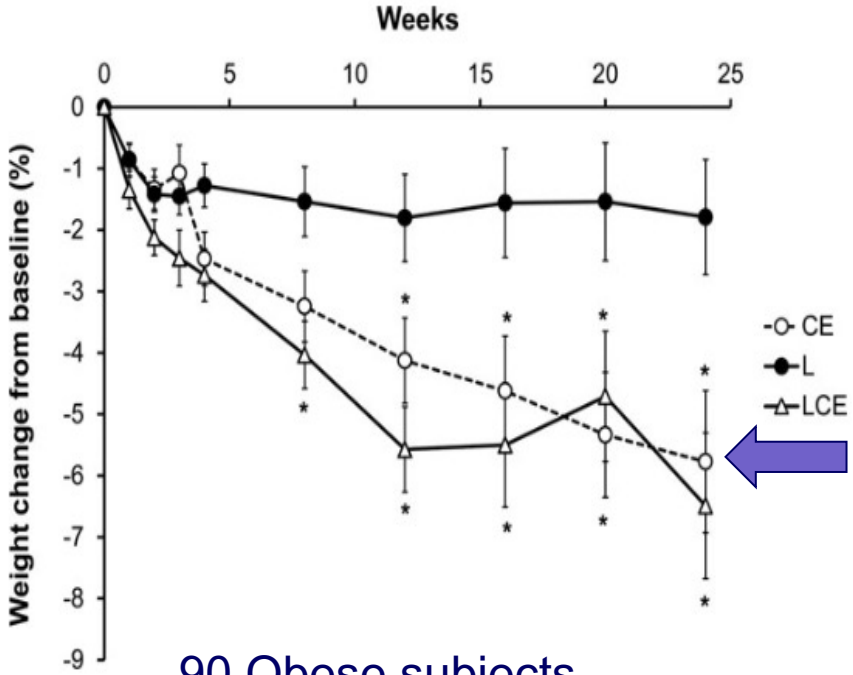
Roles of Vitamins & Minerals



비만 보조제

- Conjugated Linoleic acid (CLA); NA
- 가르시아 캄보지아; NA
- 키토산; NA
- L-carnitine; 부분적 효과
- Xanthigen (Fucoxanthin); 이론적 가능, 장기간 연구 결과 없음
- Caffeine; 일부 효과
- Green tea; 일부 효과
- Protein Supplement; 일부 효과
- Probiotics
- Arginine
- Vitamins & minerals; vitamin D, Cr
- Omega 3 fatty acid
- Tryptophan

Caffeine/ephedrine, Leptin



-90 Obese subjects
-24 weeks
-200mg caffeine/20mg ephedrine, leptin A-200
-RCT

Obesity (Silver Spring) 2013;21:1991-6

[표 1] 시중판매 고카페인 음료 유형별 카페인 함량 현황

구 분		에너지드링크				인스턴트 커피	원두 캔커피
		식품			의약외품		
제품명		핫식스	레드불	몬스터	박카스F	조지아 오리지날	TOP 마스터 블렌드
제품 이미지							
용량/용기		250ml캔	250ml캔	355ml캔	120ml병	240ml캔	275ml캔
카페인 함량	캔당	60mg	62.5mg	100mg	30mg	104mg	94mg
	ml당	0.24mg	0.25mg	0.28mg	0.25mg	0.43mg	0.34mg

시중판매 고카페인 음료 유형별 카페인 함량 현황
[보건복지위원회 장정숙 의원실 제공]

유명 커피전문점 '아메리카노' 카페인 함량

브랜드명	기본 사이즈	평균 용량(g)	카페인 (mg/1잔)	에스프레소 shot 수
파스쿠찌	Regular	293	196	
커피빈	Small	300	168	
카페베네	Regular	299	168	
투썸플레이스	Regular	311	159	
할리스커피	Regular	310	152	
스타벅스커피	Tall	309	114	
엔젤리너스커피	Small	283	95	
이디야커피	One size	279	91	
탐앤탐스커피	Tall	267	91	

Caffeine + glucosyl hesperidin

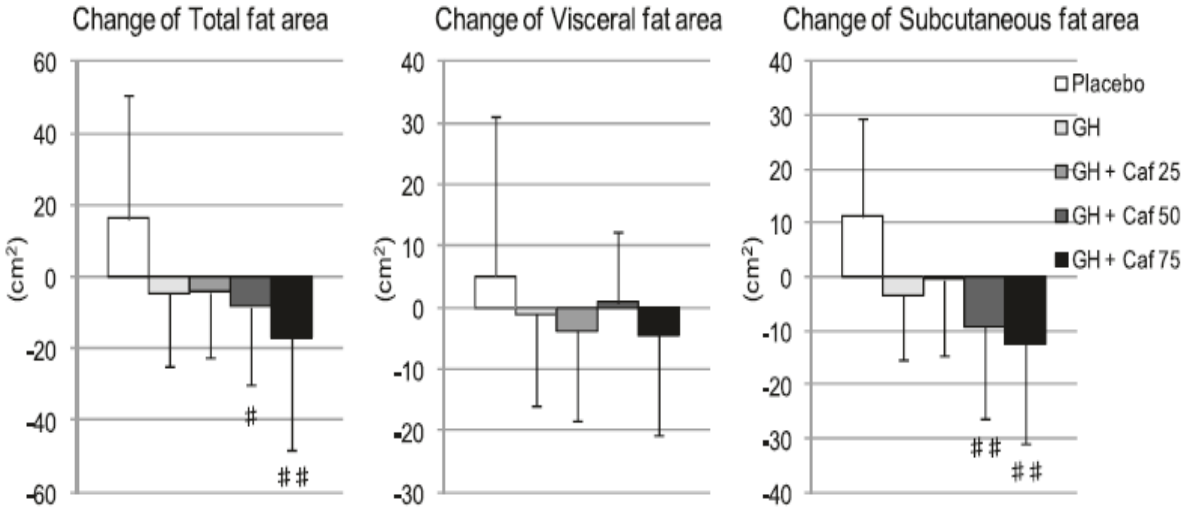


Fig. 2 Change in abdominal fat area after 12 weeks of intervention. Data are expressed as Mean ± SD. #:$p < 0.05$, ##:$p < 0.01$ v.s. Placebo. $n = 15$ in each of groups except for Placebo ($n = 14$). *GH* glucosyl hesperidin 500 mg, *Caf 25, 50, 75* caffeine 25 mg, 50 mg, 75 mg

-75 healthy subjects with BMI; 24~30
-12 week intervention
-daily intake of 500mg of G-hesperidin ± 25, 50, 75mg of caffeine vs. placebo
-Double blined RCT

- **Adenylate cyclase activation**
- **β adrenergic receptor activation?**

Nutr J 2016;15:6

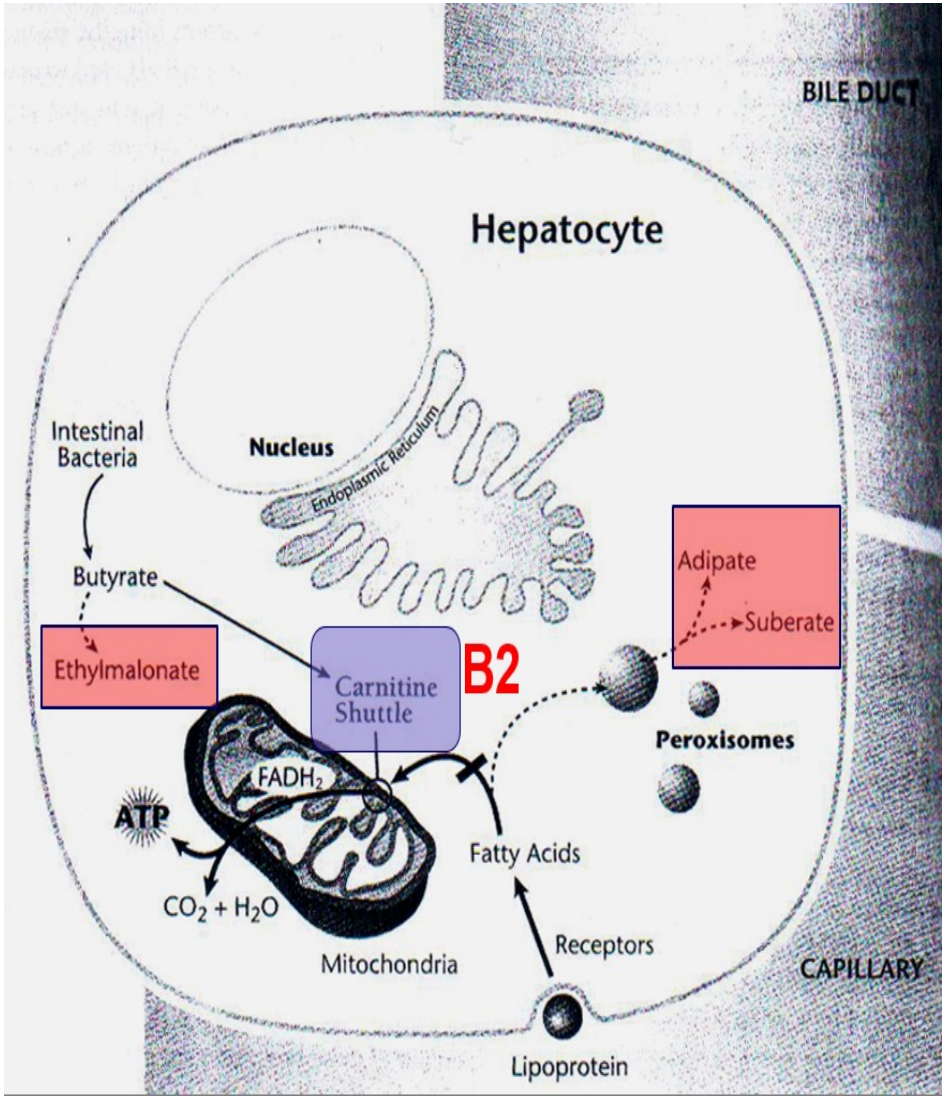
Role of Carnitine in Fatty acid metabolism

- **Play role in mitochondrial energy production & functions as a neurotransmitter**

- **Acetyl-L-carnitine**
  - precursor to the molecule acetyl coenzyme A, important in TCA cycle

- **N-acetyl-carnitine**
  - assists in the transportation of long-chain fatty acids into mitochondria for ß-oxidation

Nutritional Medicine. A. Gaby



Laboratory Evaluation for Integrative and Functional Medicine

L-Carnitine on weight change

1000mg L-carnitine

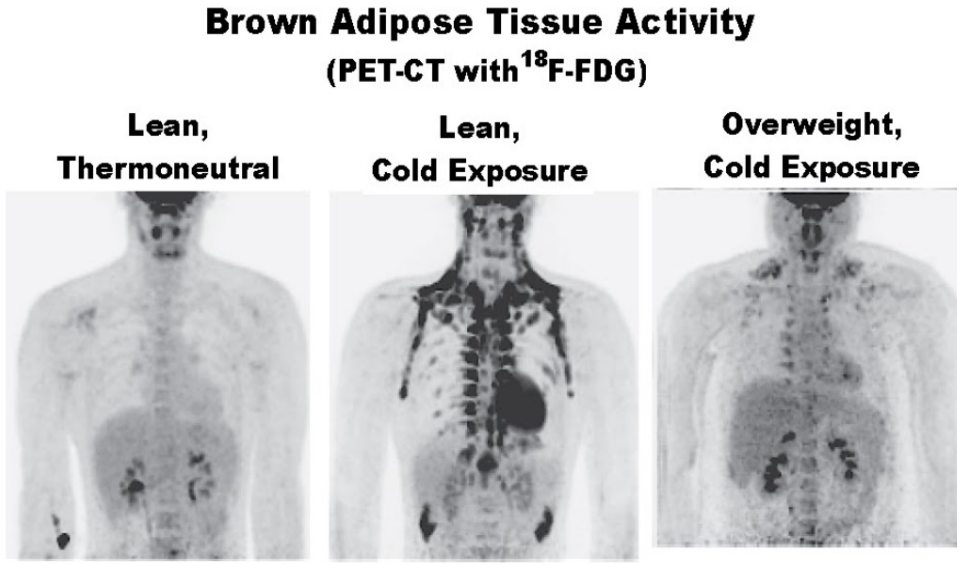
Table 3 Anthropometry changes in patients treated with placebo and L-carnitine before and after 12 weeks of treatment

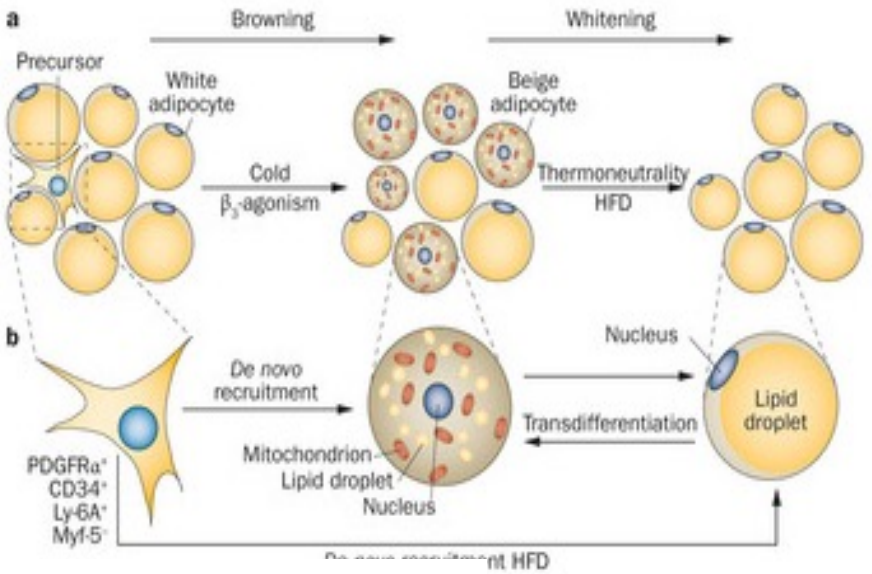
		L-carnitine group ($n = 34$)	P^a	Placebo group ($n = 36$)	P^b	P^c
Weight (Kg)	before	78.7 ± 10.86	0.001	78.91 ± 12.18	0.001	0.937
	after	75.19 ± 10.84		76.99 ± 12.70		0.527
	chnge	−2.76 ± 1.69		−1.95 ± 1.73		0.052
BMI (kg/m2)	before	33.04 ± 6.67	0.001	32.10 ± 4.30	0.001	0.471
	after	31.87 ± 6.56		31.29 ± 4.56		0.669
	change	−1.21 ± 0.84		−0.79 ± 0.70		0.027
Waist circumference (Cm)	before	105.13 ± 9.04	0.001	105.92 ± 10.57	0.001	0.728
	after	99.45 ± 11.72		102.39 ± 10.1		0.262
	change	−5.65 ± 5.85		−3.64 ± 3.37		0.081
Hip circumference (Cm)	before	115.63 ± 9.37	0.001	117.87 ± 10.56	0.001	0.332
	after	108.44 ± 9.67		112.19 ± 10.58		0.127
	change	−6.82 ± 3.56		−5.64 ± 4.07		0.201
Free fat mass (%)	before	24.00 ± 1.74	0.8	24.59 ± 2.64	0.531	0.253
	after	24.11 ± 1.75		23.99 ± 3.78		0.865
	change	0.04 ± 0.09		−0.71 ± 3.47		0.384
Fat mass (%)	before	45.19 ± 4.85	0.03	43.63 ± 6.77	0.915	0.251
	after	44.07 ± 4.33		43.95 ± 5.66		0.921
	change	−0.71 ± 1.83		−0.3 ± 1.93		0.360
Visceral fat (%)	before	10.71 ± 1.95	0.001	10.47 ± 1.82	0.644	0.587
	after	10.24 ± 2.104		10.50 ± 1.89		0.581
	change	−0.41 ± 0.49		−0.55 ± 0.752		0.320

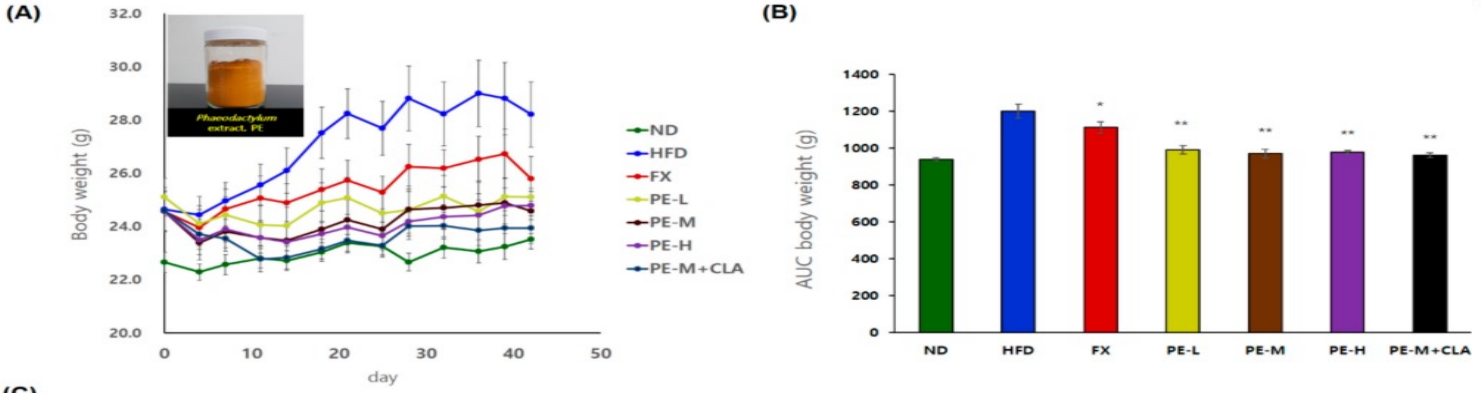
Mean ± SD (all such values)
[a]Determined with the use of paired Student's t tests for differences between baseline and follow-up in the L-carnitine group
[b]Determined with the use of paired Student's t tests for differences between baseline and follow-up in the placebo group
[c]Determined with the use of independent samples t tests between L-carnitine and placebo groups

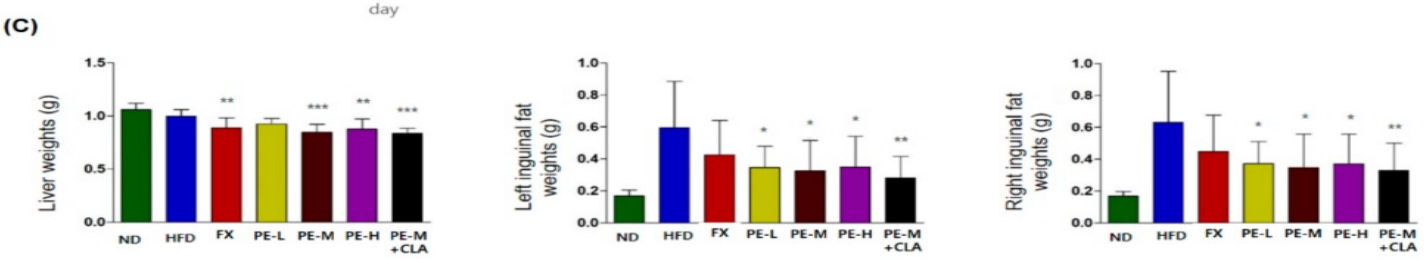
BMC Musculoskelet Disord 2021;22:195

Cold Exposure on Fat Browning









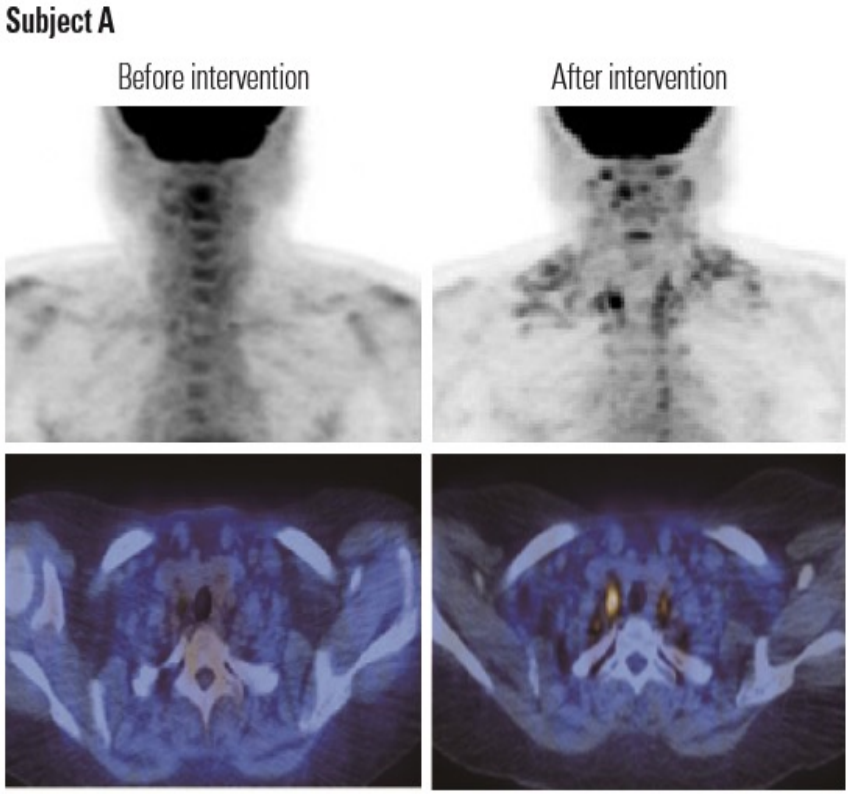
Mar Drugs 2019;17:311

Case Report
Yonsei Med J 2016 Jul;57(4):1038-1041
http://dx.doi.org/10.3349/ymj.2016.57.4.1038
Yonsei Medical Journal
YMJ
pISSN: 0513-5796 · eISSN: 1976-2437

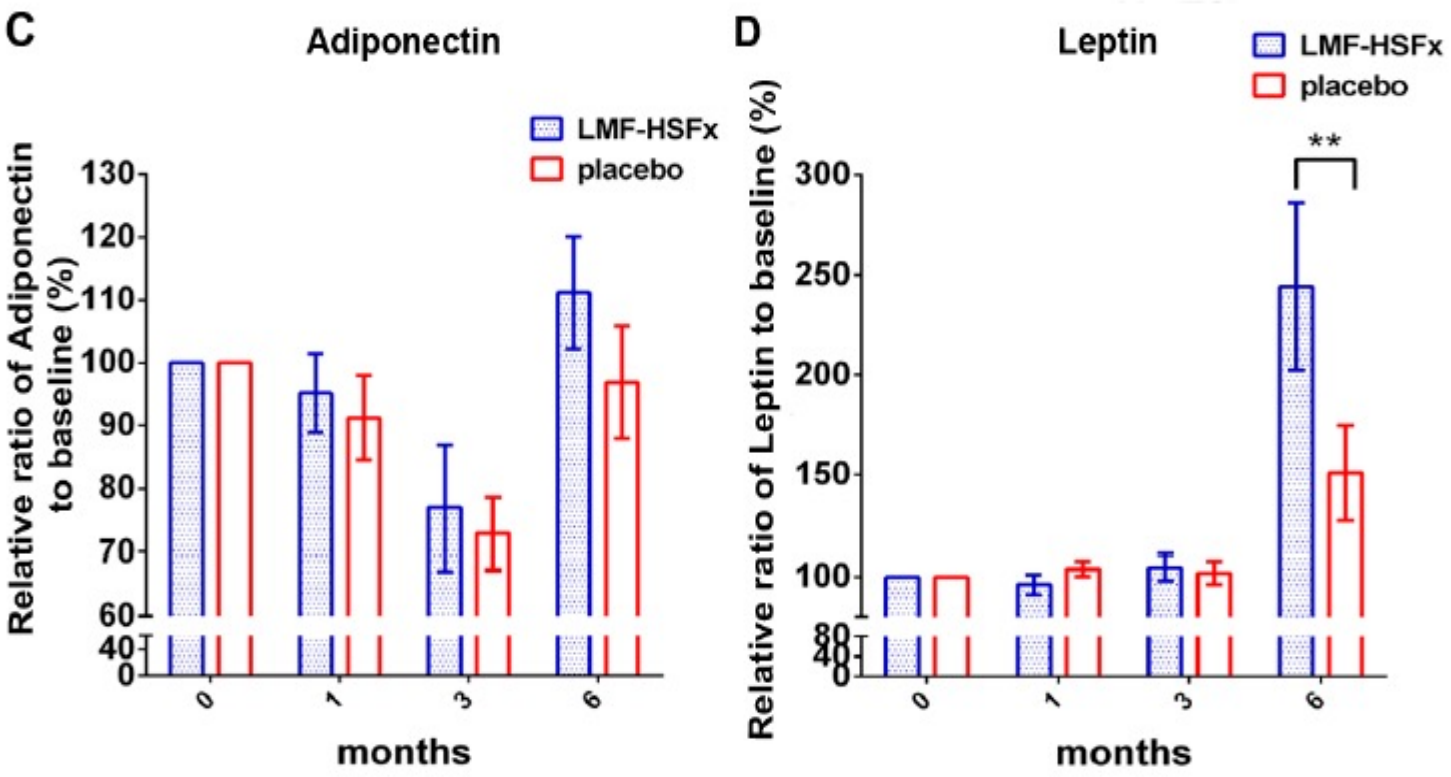
The Effect of Xanthigen on the Expression of Brown Adipose Tissue Assessed by ^{18}F-FDG PET

Kwang-Min Kim[1], Sang-Man Kim[2], Doo-Yeon Cho[1], Soo-Jung Park[1], and Nam-Seok Joo[1]

[1]Department of Family Practice and Community Health, Ajou University School of Medicine, Suwon;
[2]Green Cross Reference Lab, Seoul, Korea.



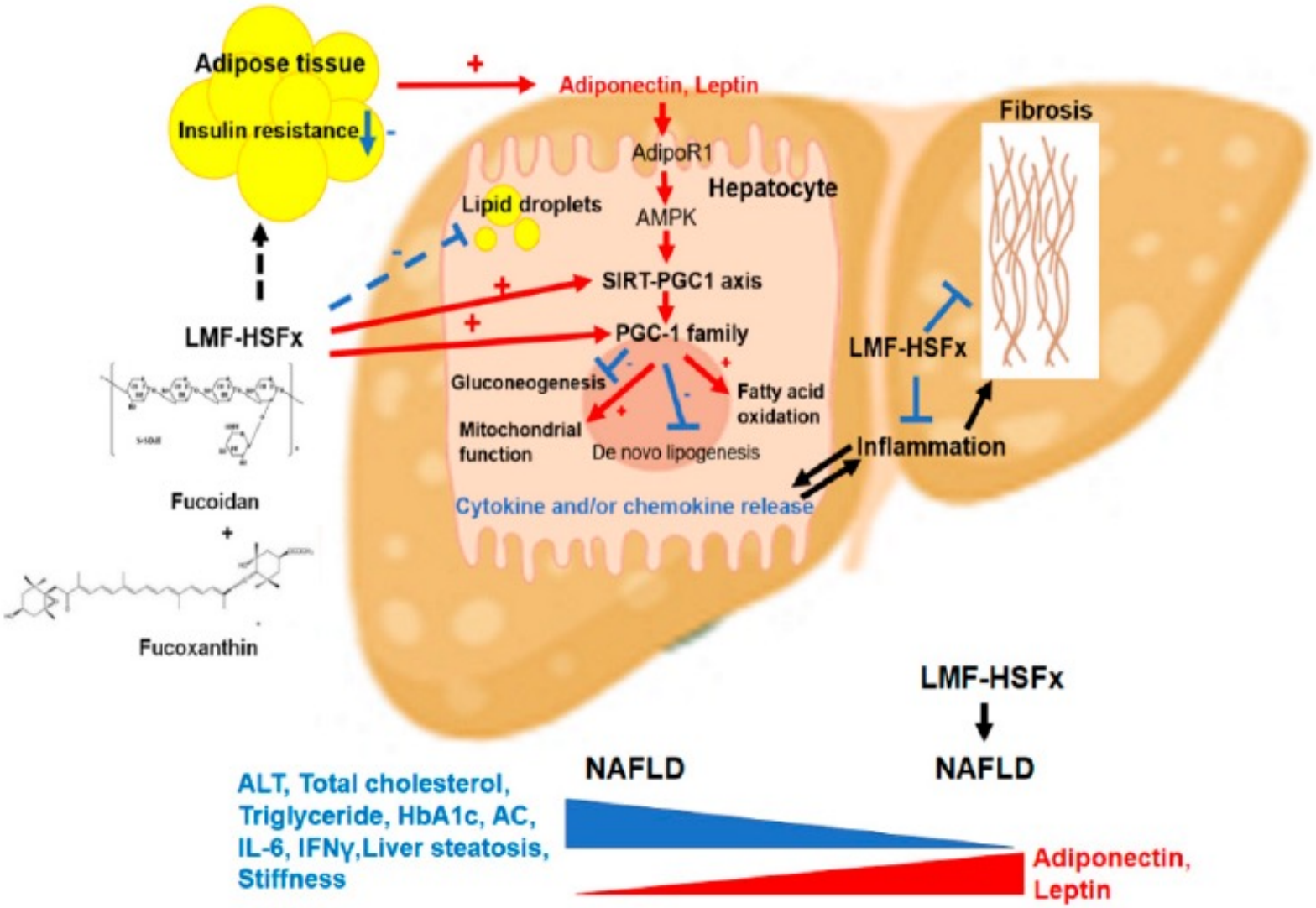
Fucoxanthin on Adiponectin, Leptin in NAFLD patients



-42 NAFLD patients
-Low molecular weight fucoidan and high stability **fucoxanthin** vs. placebo
-For 24 weeks

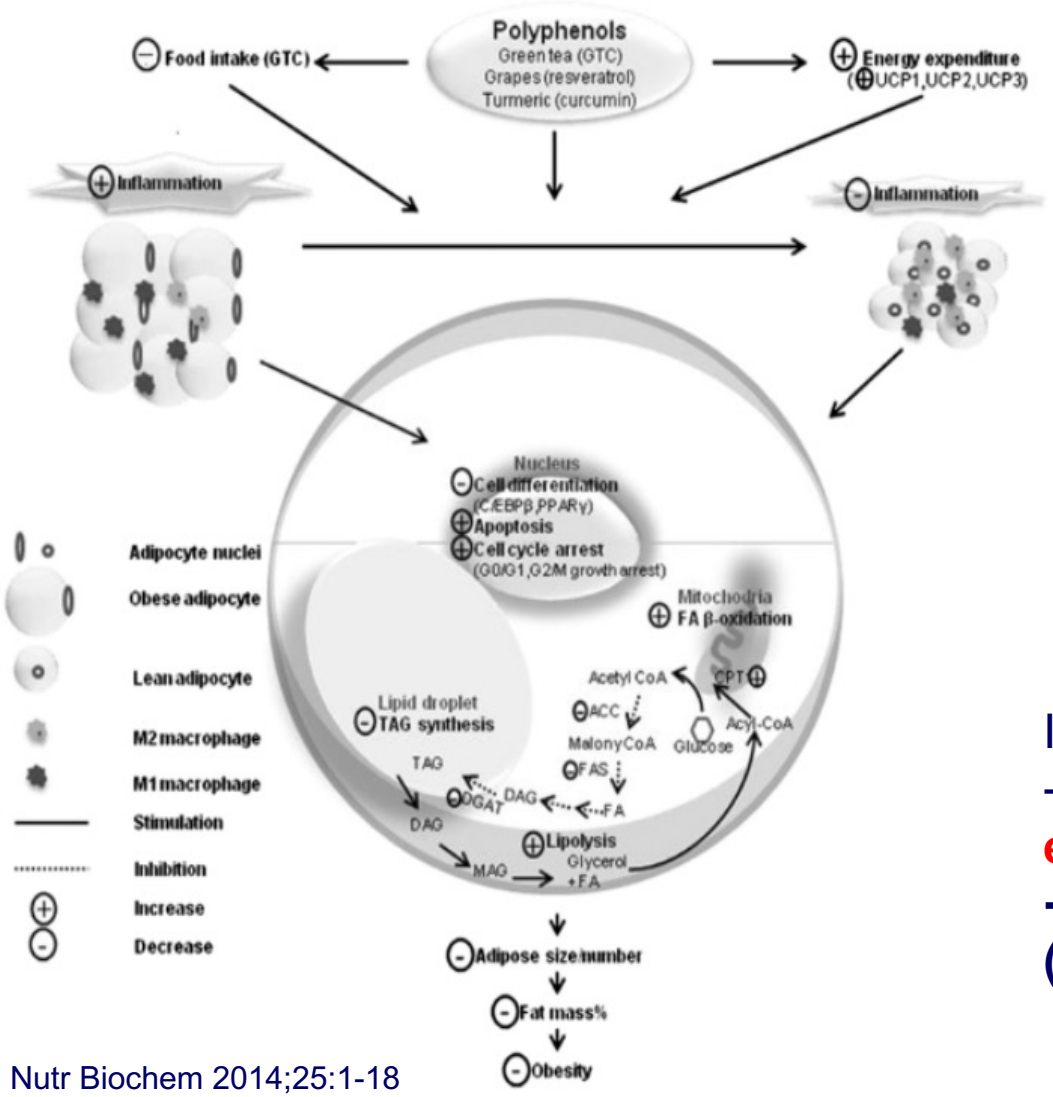
Mar Drugs 2021;19:148

Mechanism of Fucoxanthin in NAFLD



Mar Drugs 2021;19:148

Potential Actions of Dietary Polyphenol



J Nutr Biochem 2014;25:1-18

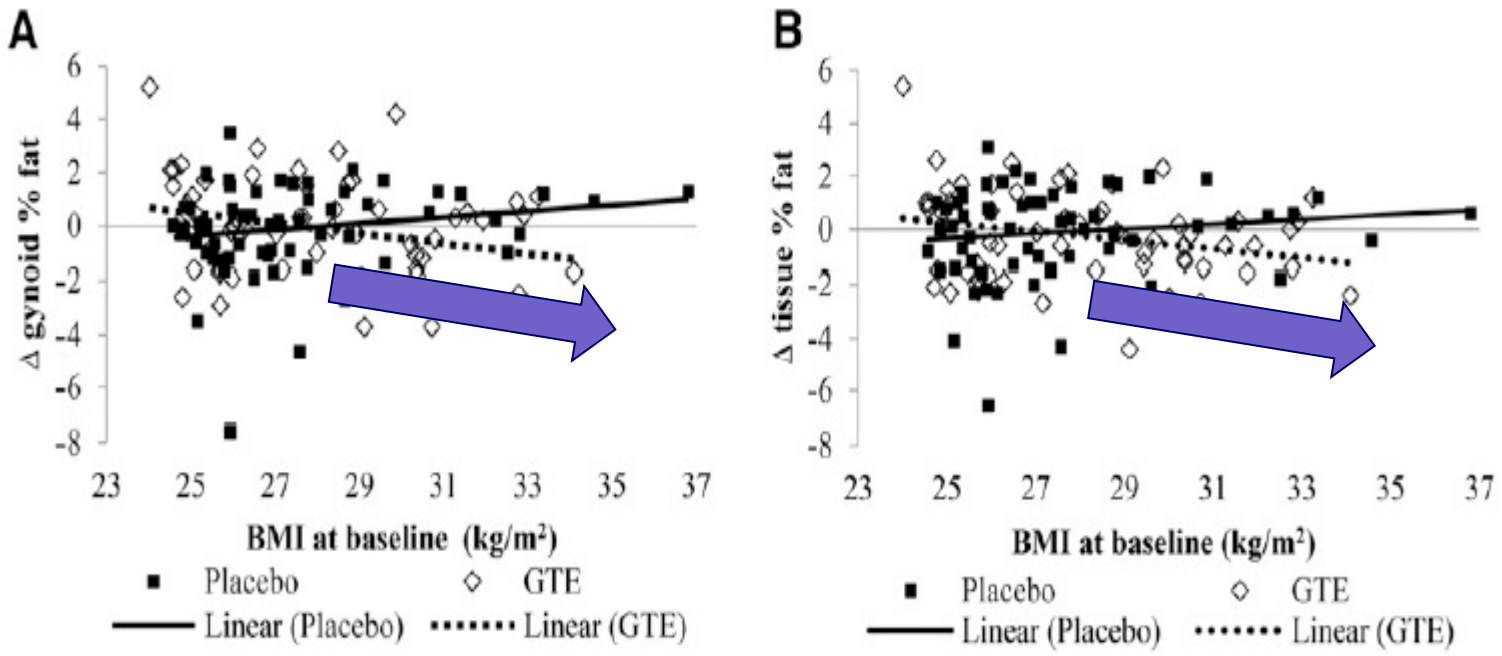
In addition,

-Regulation of leptin level or expression

-NKB/NK3R signaling pathway (signaling in the onset of puberty)

J Nutr Biochem 2022;108:109085

Long-term Green Tea on Adiposity



-The Minnesota Green Tea Trial
-12 month, RCT
-937 postmenopausal women, 50~70 years old
-843mg EGCG vs. placebo
-No effect, however, **may be beneficial in higher BMI**

J Nutr 2016;146:256-64

Decaffeinated Green Tea Polyphenols on body fat in obese girls; RCT

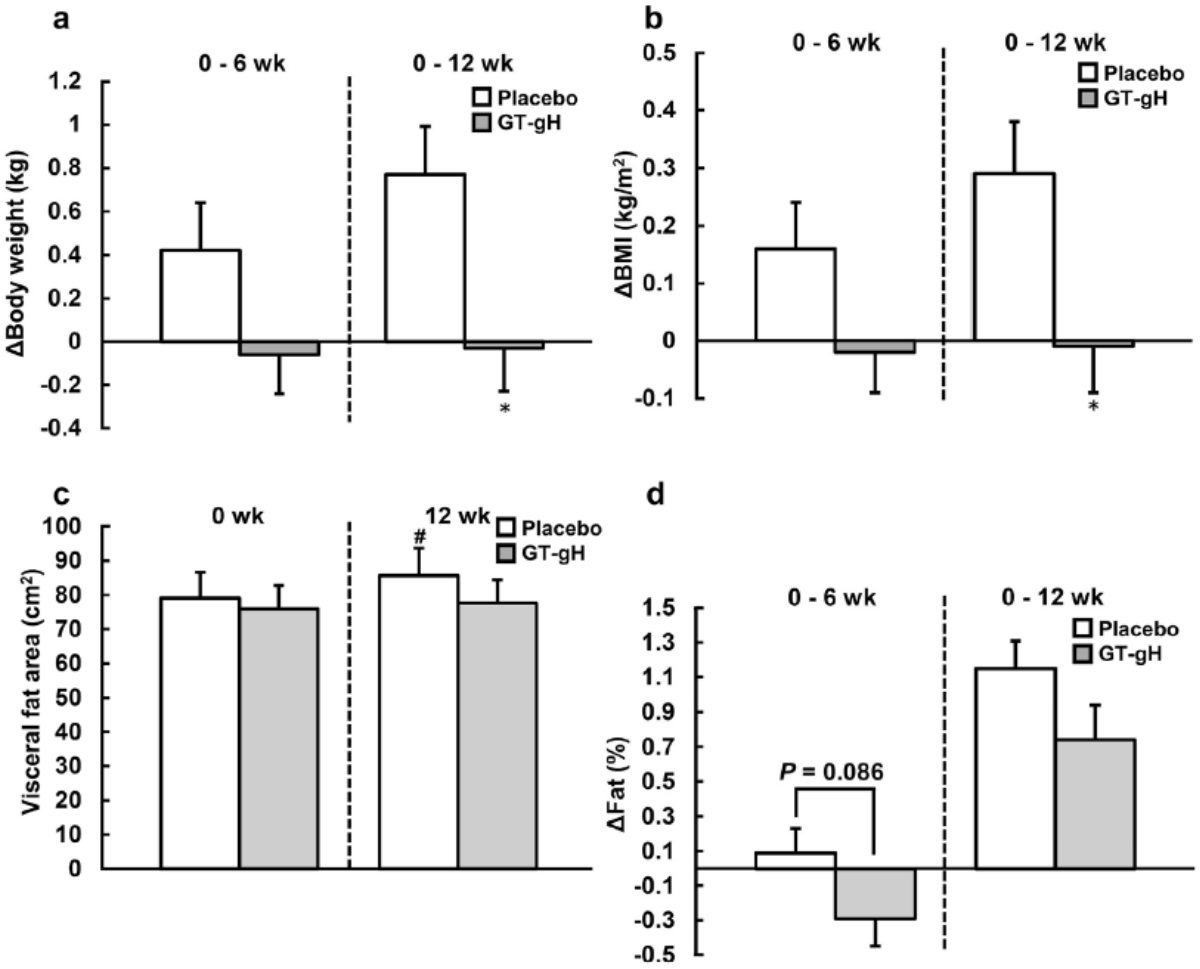
TABLE 3 | Changes in anthropometrics and body composition after daily DGTP intervention for 12 weeks[1].

	DGTP group (n = 31)			Control group (n = 31)		
	Baseline	**After intervention**	**Change at week 12**	**Baseline**	**After intervention**	**Change at week 12**
Anthropometrics						
Height, cm	136.6 (7.5)	138.8 (7.6)†	2.3 (0.9)	139.3 (8.4)	141.7 (8.2)‡	2.4 (0.9)
Weight, kg	42.5 (7.5)	43.7 (9.4)	1.2 (7.0)	46.0 (10.3)	46.3 (9.9)	0.3 (1.7)
BMI, kg/m^2	22.6 (2.9)	21.9 (2.7)†	−0.8 (1.4)	23.5 (3.3)	22.8 (2.9)‡	−0.7 (1.4)
WC, cm	76.2 (7.4)	73.4 (8.2)†	−2.8 (5.4)	78.4 (8.6)	75.9 (7.5)‡	−2.5 (4.9)
HC, cm	83.4 (6.1)	83.3 (5.6)	−0.2 (4.8)	85.8 (7.6)	86.3 (7.6)	0.5 (3.5)
WHR	0.91 (0.06)	0.88 (0.06)†	−0.03 (0.05)	0.91 (0.05)	0.88 (0.06)‡	−0.03 (0.06)
WHtR	0.56 (0.04)	0.53 (0.05)†	−0.03 (0.04)	0.56 (0.05)	0.54 (0.04)‡	−0.03 (0.04)
Systolic blood pressure, mmHg	106.1 (12.7)	106.1 (11.0)	0.00 (11.7)	105.8 (13.8)	107.0 (16.0)	1.2 (15.8)
Diastolic blood pressure, mmHg	72.2 (20.3)	71 (12.4)	−1.2 (21.2)	66.8 (10.8)	70.2 (14.1)	3.4 (13.3)
Body composition						
Fat mass, kg	15.6 (4.6)	14.9 (4.5)†	−0.7 (2.4)	16.17 (5.0)	16.4 (5.5)	0.3 (4.2)
Skeletal muscles, kg	13.9 (2.5)	14.3 (2.6)	0.4 (1.0)	15.4 (2.8)*	15.8 (3.2)	0.2 (1.7)
FFM, kg	27.0 (4.1)	27.7 (4.4)†	0.7 (1.6)	29.3 (4.9)	29.9 (5.6)	0.6 (2.3)
PBF, %	36.0 (5.3)	34.2 (4.9)†	−1.8 (4.3)	35.0 (6.1)	35.1 (5.4)	0.1 (5.0)
Basal metabolic rate, kcal	950.3 (91.2)	968.3 (94.1)†	18.0 (39.9)	1,008.3 (104.4)*	1,013.3 (122.5)‡	5.0 (62.0)

[1]*Data are expressed as mean (SD) for all continuous variables. *Statistical significance when comparing DGTP and control groups at baseline. †Change statistical significance after 12 weeks within the DGTP group. ‡Change statistical significance after 12 weeks within the control group. BMI, body mass index; DGTP, decaffeinated green tea polyphenols; FFM, fat-free mass; HC, hip circumference; PBF, percentage of body fat; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio.*

Front Endocrinol 2021;12:736724

Green tea + citrus polypenols



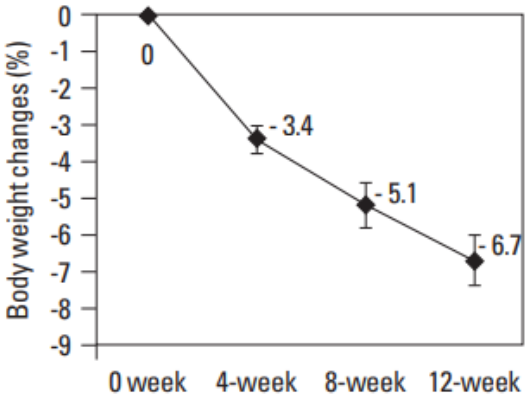
- 60 healthy Japanese male and females
- 30~70 years
- 146mg EGCG + 178mg citrus polyphenol
- 12 weeks, RCT

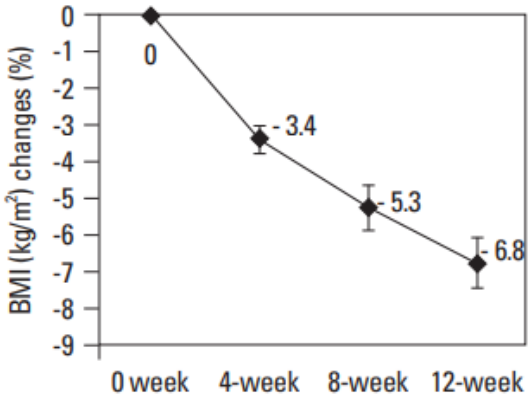
Sci Rep 2021;11:19067

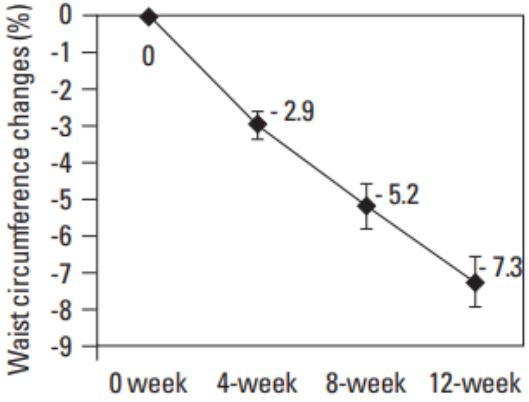
Protein-Rich Oriental Diet

Table 2. Comparison of Anthropometry and Calorie Changes between the Conventional Diet Program and PRO Diet Application in Per Protocol Group

Variables	Conventional (PP, n = 78)	PRO Diet (PP, n = 177)	PRO Diet (ITT, n = 302)
Age (yrs)	44.7 ± 6.2	44.2 ± 9.3	42.3 ± 10.1
ΔBwt (kg)	- 2.3 ± 0.7	- 4.7 ± 2.5*	- 3.9 ± 1.3
ΔBMI (kg/m^2)	- 1.1 ± 0.3	- 1.9 ± 0.1*	- 1.6 ± 0.5
ΔWc (cm)	- 3.3 ± 1.1	- 6.7 ± 0.3*	- 5.4 ± 1.7
ΔFM (kg)	- 2.0 ± 0.1	- 4.2 ± 0.2*	- 3.6 ± 0.8
ΔF%M (%)	- 1.8 ± 0.9	- 3.9 ± 0.5*	- 3.2 ± 1.1
ΔCalories$_{total}$ (kcal)	53.2 ± 98.5	- 235.7 ± 619.3*	- 231.6 ± 675.7
ΔCarbohydrate (g)(Δ%)	- 1.5 ± 13.4 (- 2.4)	- 58.8 ± 123.1 (- 7.9)*	- 56.2 ± 137.2
ΔFat (g)(Δ%)	3.0 ± 29.4 (0.1)	1.11 ± 24.8 (4.0)*	0.41 ± 27.1
ΔProtein (g)(Δ%)	6.1 ± 10.5 (2.2)	0.63 ± 22.90 (3.9)*	- 1.15 ± 25.19







N-S Joo et al. Yonsei Med J 2011;52:249-56

Leucine-Enriched Protein, RCT

Table 5. Muscle health during the 12-week study period in participants aged 50–64 years (n = 90).

	Mean (S.E)		Time	Group	Time × Group
	Control	Intervention			
ASM (kg)			0.007	0.380	0.654
Baseline	16.74 (0.50)	17.37 (0.56)			
12 weeks	16.88 (0.49)	17.56 (0.55)			
ASMI (kg/m^2)					
Baseline	6.43 (0.13)	6.59 (0.14)	0.094	0.424	0.543
12 weeks	6.48 (0.13)	6.66 (0.14)			
ASM/Wt (kg/kg, %)					
Baseline	27.57 (0.47)	27.88 (0.53)	0.602	0.553	0.177
12 weeks	27.50 (0.47)	28.03 (0.53)			
ASM/BMI [kg/(kg/m^2)]					
Baseline	0.71 (0.01)	0.73 (0.02)	0.539	0.524	0.214
12 weeks	0.71 (0.01)	0.73 (0.02)			
LBM (kg)			0.047	0.444	0.049 *
Baseline	38.83 (0.96)	39.70 (1.08)			
12 weeks	38.83 (0.94)	40.15 (1.05)			
LBM/Ht (kg/m^2)					
Baseline	14.94 (0.22)	15.09 (0.25)	0.031	0.473	0.033 *
12 weeks	14.94 (0.22)	15.27 (0.24)			
LBM/Wt (kg/kg, %)					
Baseline	64.09 (0.90)	64.03 (1.01)	0.313	0.749	<0.001 *
12 weeks	63.45 (0.88)	64.37 (0.98)			
LBM/BMI [kg/(kg/m^2)]					
Baseline	1.66 (0.03)	1.68 (0.04)	0.333	0.630	0.001 *
12 weeks	1.65 (0.03)	1.69 (0.04)			
Femoral muscle strength (N)					
Baseline	171.79 (7.64)	182.41 (8.55)	0.820	0.357	0.864
12 weeks	170.18 (6.15)	182.61 (6.88)			
Femoral muscle strength/Wt (N/kg)					
Baseline	2.83 (0.12)	2.97 (0.13)	0.832	0.438	0.952
12 weeks	2.81 (0.10)	2.94 (0.11)			

Note: Mixed effect Model Repeated Measurement (MMRM) analysis was adjusted for age.* Significant main effect or interaction, $p < 0.05$. ASMI: appendicular skeletal muscle mass index; ASM: appendicular skeletal muscle mass; LBM: lean body mass; Wt: weight; Ht: weight.

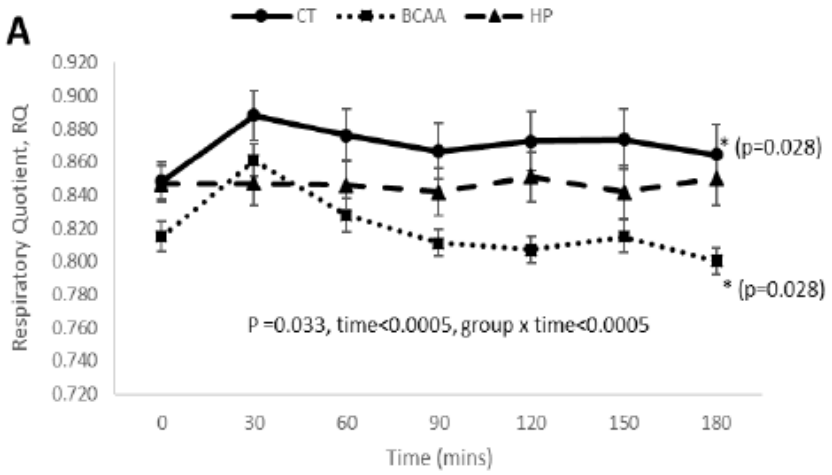
-120 healthy Koreans
-Leucine-enriched supplement (protein 20g, total leucine 3000mg)

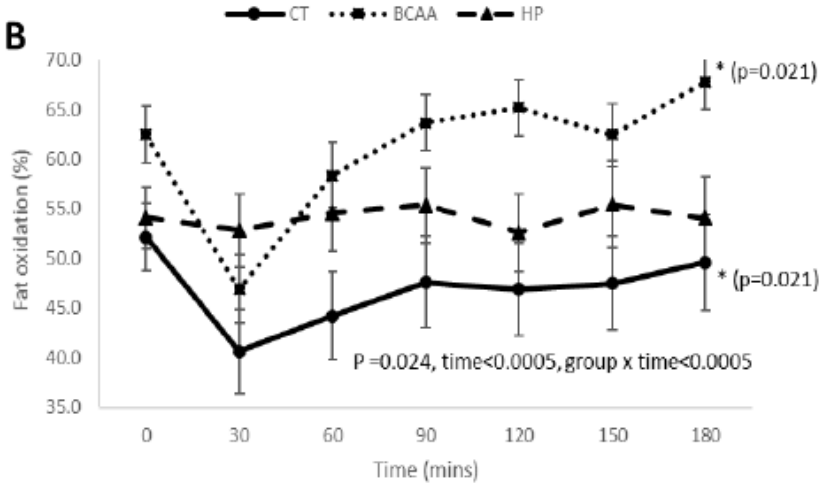
- Muscle preserving effect

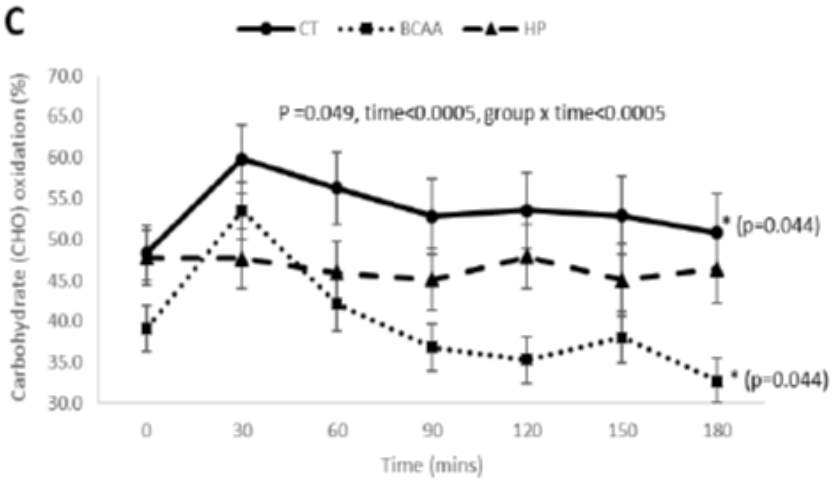
Nutrients 2020;12:1816

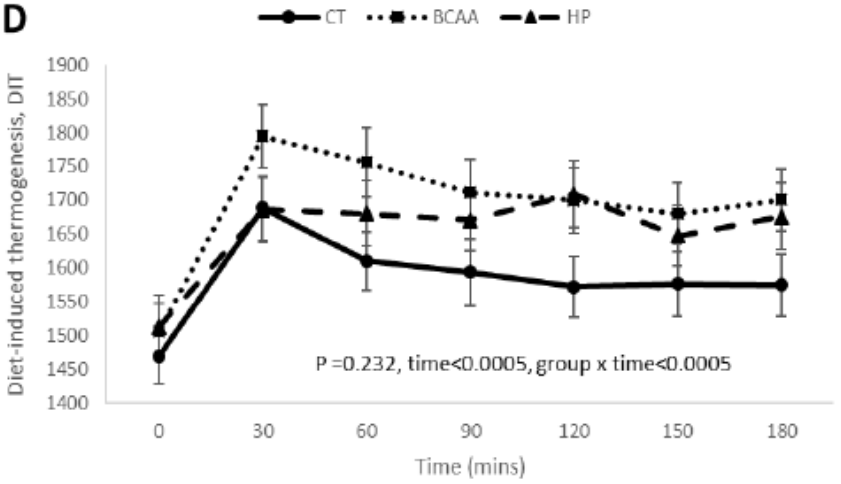
Branched Chain Amino Acid, RCT

RQ; Respiratory Quotient
탄수화물=1　지방=0.7　단백질=0.8



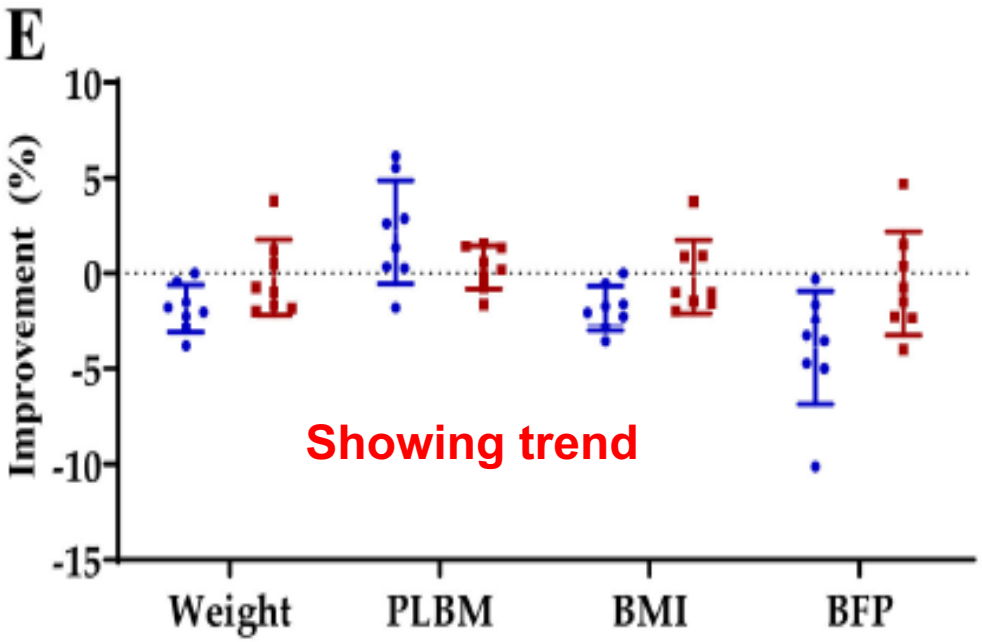






Nutrients 2021;13:4245

Soy protein + Exercise



60mins,
twice/wk,
40~65% HRR

- AET group
- AET + ISP group

40g/day
5 days/wk
for 8 weeks

Int J Environ Res Public Health 2021;18:11798

Regulation by Gut Microbiomes

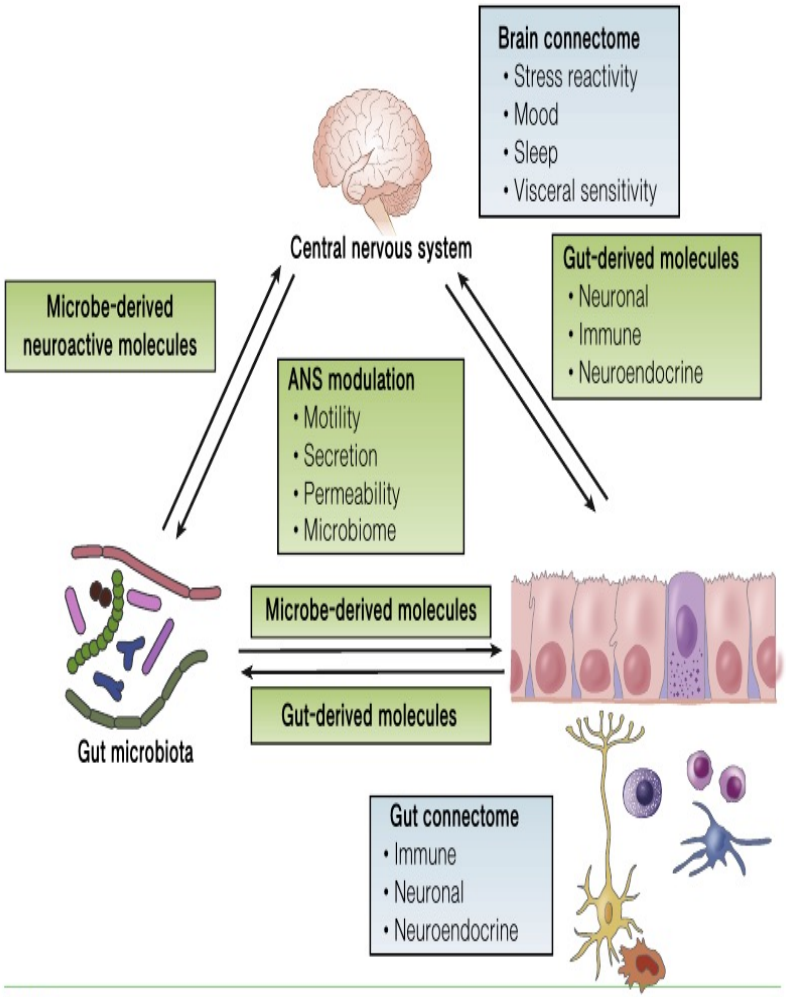
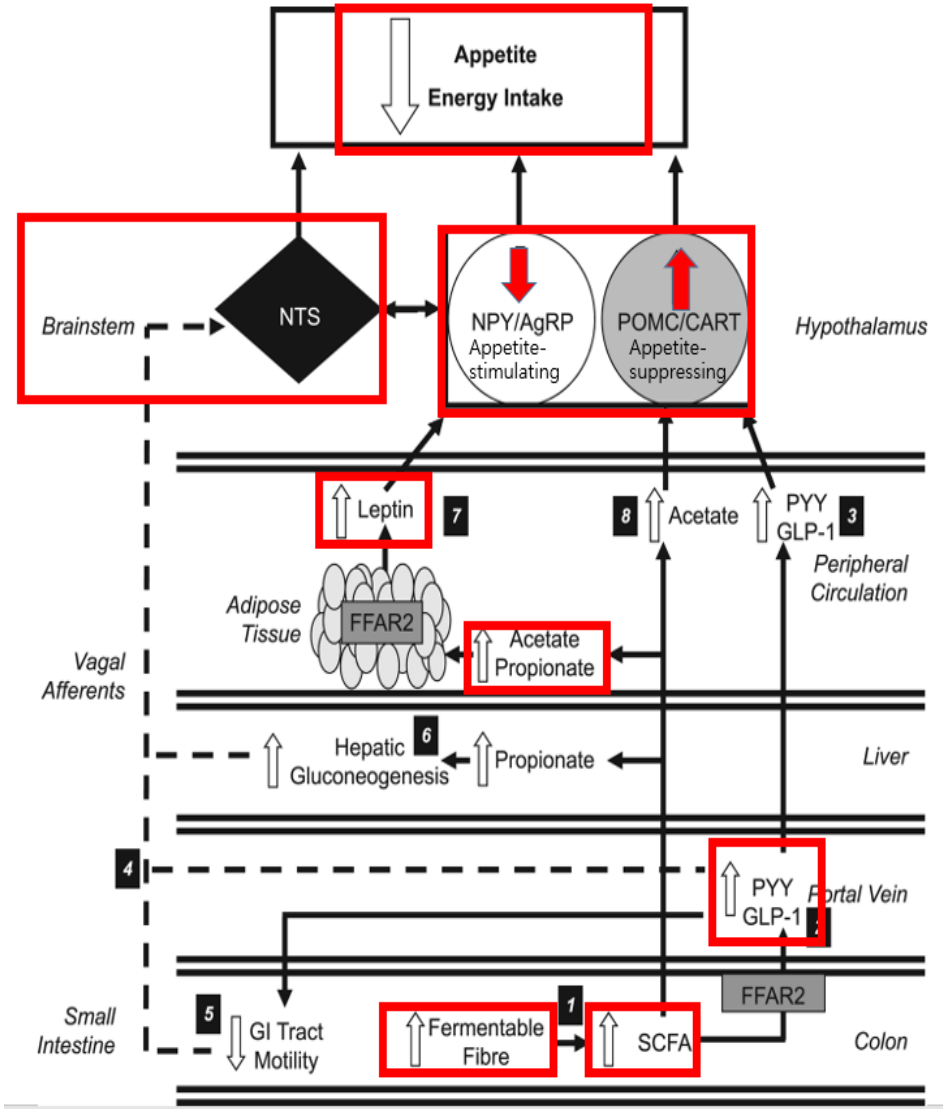


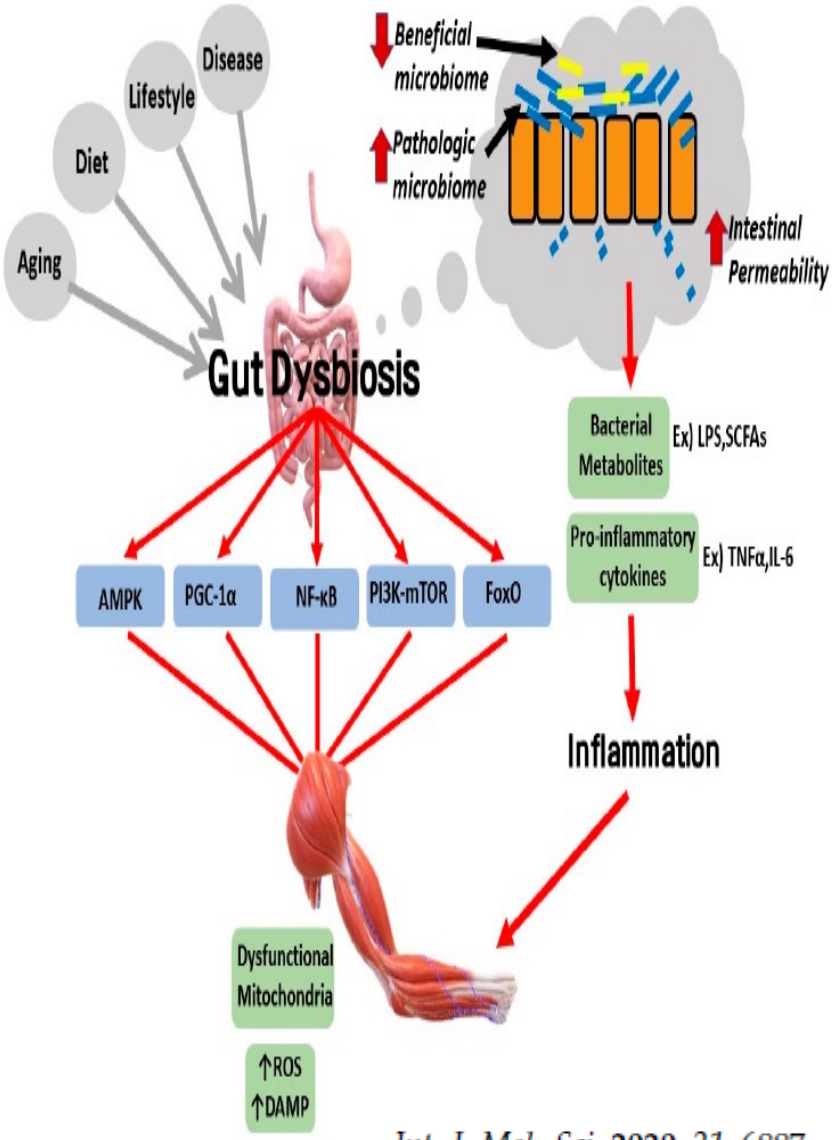
그림 3 뇌-장내 세균의 상호 작용에 따른 전신 상태

(출처: Martin CR, et al. Cell Mol Gastroenterol Hepatol 2018;6:133-48)

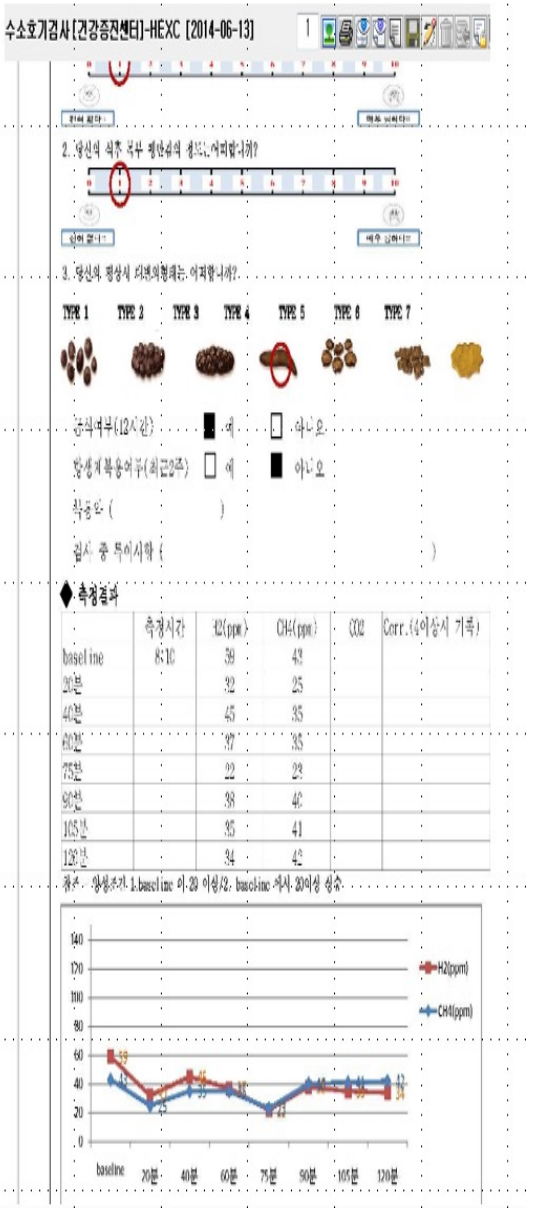


Proc Nutr Soc 2015;74:328-36

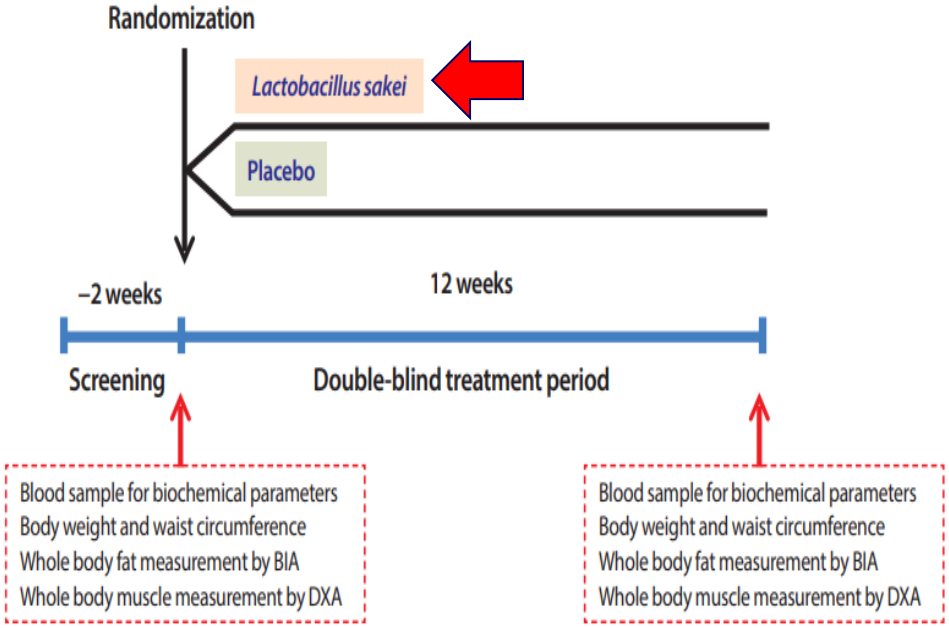
Small Intestine Bacterial Overgrowth



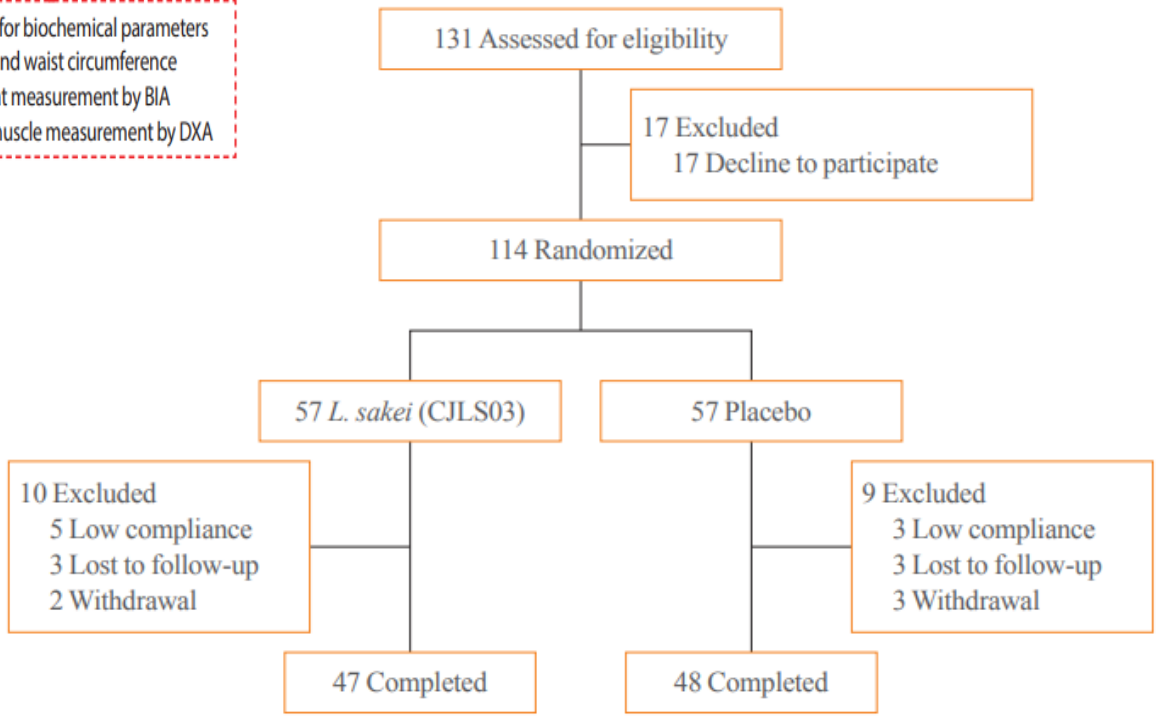
Int. J. Mol. Sci. **2020**, *21*, 6887;



Probiotics on body weight I



-Double blind RCT,
-114 Subjects
-BMI>25
-For 12 weeks



Endocrinol Metab (Seoul) 2020;35:425-34

Table 2. Changes in Body Composition in the *Lactobacillus sakei* and Placebo Groups after 12 Weeks

Variable	*L. sakei* (CJLS03) (n=47)			Placebo (n=48)			*P* value[a]
	Baseline	12 weeks	*P* value	Baseline	12 weeks	*P* value	
Body weight, kg	73.0±8.6	72.6±8.6	0.352	76.7±10.4	77.2±11.0	0.034	0.058
Body mass index, kg/m^2	28.2±2.3	28.0±2.5	0.360	28.5±2.5	28.7±2.7	0.033	0.065
Body fat, kg	27.0±5.1	26.8±5.3	0.454	27.4±5.8	28.0±6.1	0.003	0.018
Waist circumference, cm	91.0±5.6	90.3±5.6	0.017	91.1±7.1	91.3±7.6	0.301	0.013
Abdominal visceral fat, cm^2	131.7±33.5	130.7±34.6	0.554	131.4±32.7	134.6±34.0	0.003	0.035
Whole body muscle mass, kg	41.5±7.6	41.3±7.6	0.203	44.5±9.4	44.4±9.3	0.139	0.853

Values are expressed as mean±standard deviation.

[a]*P* values were calculated using Student's *t* test for the difference between groups in the change from the baseline to 12 weeks.

Endocrinol Metab (Seoul) 2020;35:425-34

Probiotics on body weight II

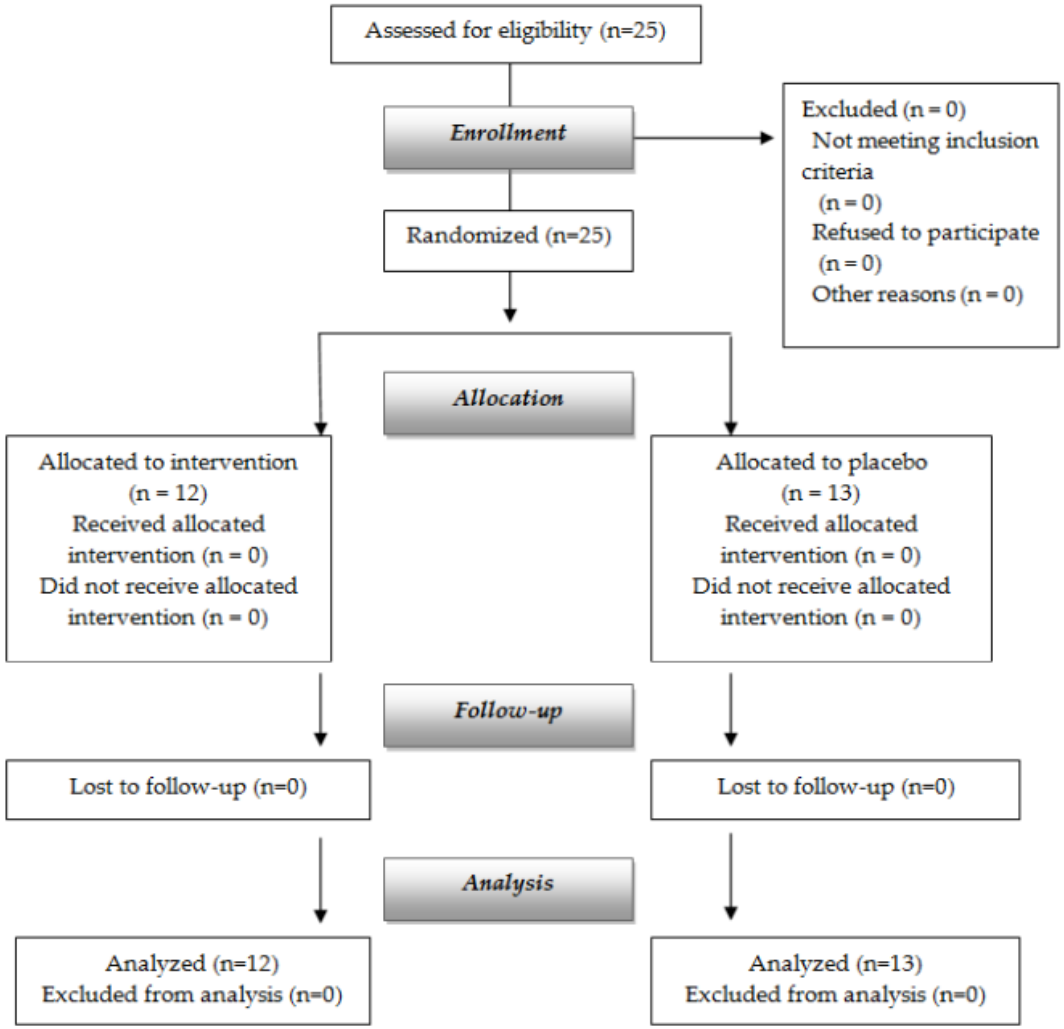


Figure 1. Flow chart of the study.

-25 subjects
-for 2 months
-Saccharomyces boulardii + Superoxide dismutase (Cu, Zn, **Mn**)
-BMI; 30~35

Nutrients 2021;13:2512

Table 2. Treatment effect from baseline analyzed using linear mixed models and treatment effect between groups.

Variables	Intervention	Placebo	Difference between Groups (Confidence Interval)	*p*-Value between Groups
	Δ T1-T0 (confidence interval)	**Δ T1-T0 (confidence interval)**		
DXA				
Free Fat Mass (kg)	0.04 (−0.85; 0.93)	0.20 (−0.65; 1.05)	−0.15 (−1.44; 1.13)	0.805
Fat Mass (kg)	−3.13 (−5.22; −1.05) *	−1.88 (−3.78; 0.02)	−1.25 (−4.21; 1.70)	0.385
Android fat (%)	−2.13 (−3.63; −0.63) *	−0.62 (−2.06; 0.82)	−1.51 (−3.67; 0.65)	0.160
Gynoid fat (%)	−1.01 (−2.40; 0.38)	−0.64 (−1.97; 0.69)	−0.37 (−2.37; 1.63)	0.702
VAT (g)	−132.16 (−349.27; 84.94)	−135.00 (−342.80; 72.80)	2.84 (−311.54; 317.22)	0.985
DXA Weight (kg)	−2.73 (−4.72; −0.74) *	−1.00 (−2.90; 0.90)	−1.73 (−4.60; 1.14)	0.223
Anthropometric measures				
BMI (kg/m^2)	−0.97 (−1.70; −0.25) *	−0.36 (−1.05; 0.34)	−0.62 (−1.67; 0.43)	0.235

Probiotics on body weight III

nutrients

MDPI

Article

Effect of MED-02 Containing Two Probiotic Strains, *Limosilactobacillus fermentum* MG4231 and MG4244, on Body Fat Reduction in Overweight or Obese Subjects: A Randomized, Multicenter, Double-Blind, Placebo-Controlled Study

Young Gyu Cho [1], Yun Jun Yang [2,*], Yeong Sook Yoon [2], Eon Sook Lee [2], Jun Hyung Lee [2], Yulah Jeong [3] and Chang Ho Kang [3]

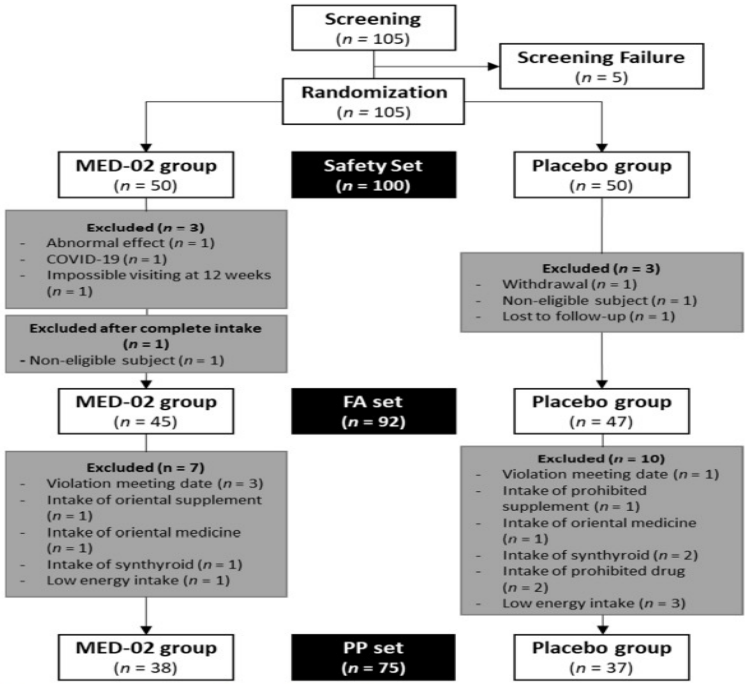
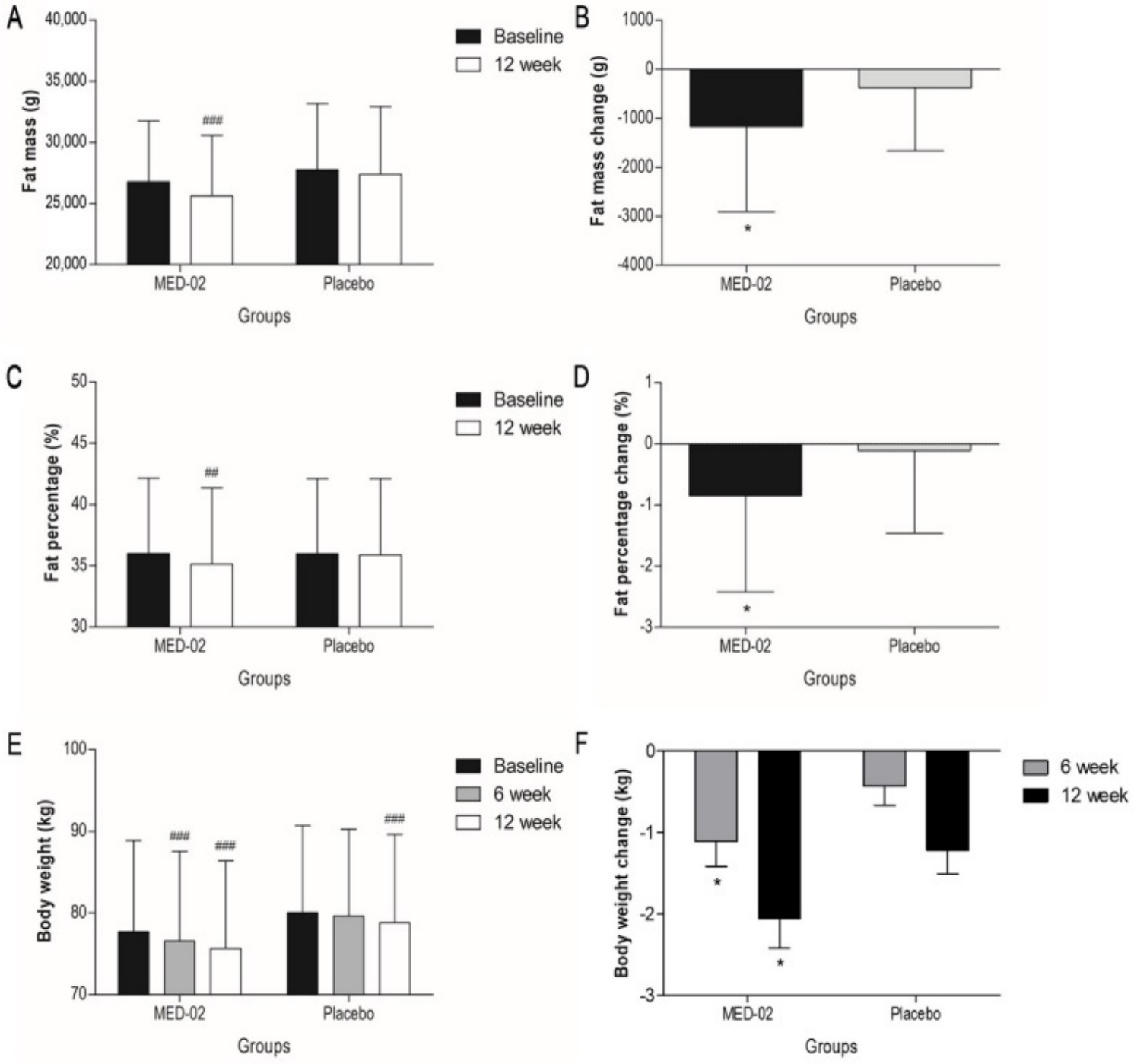


Figure 1. Flow diagram of the enrolled participants.

-Limosilactobacillus fermentum
-100 healthy obese, overweight subjects
-19~60 years
-BMI; 25~31.9
-For 12 weeks

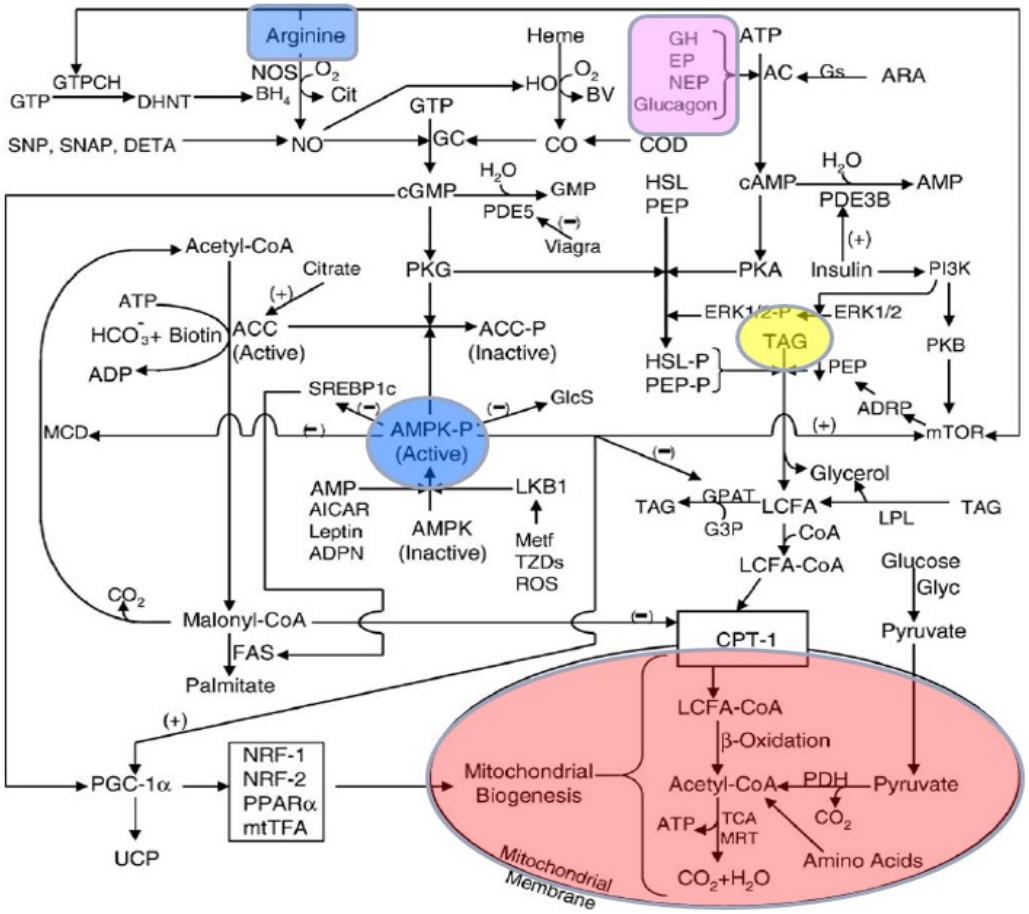
Nutrients 2022;14:3583



Nutrients 2022;14:3583

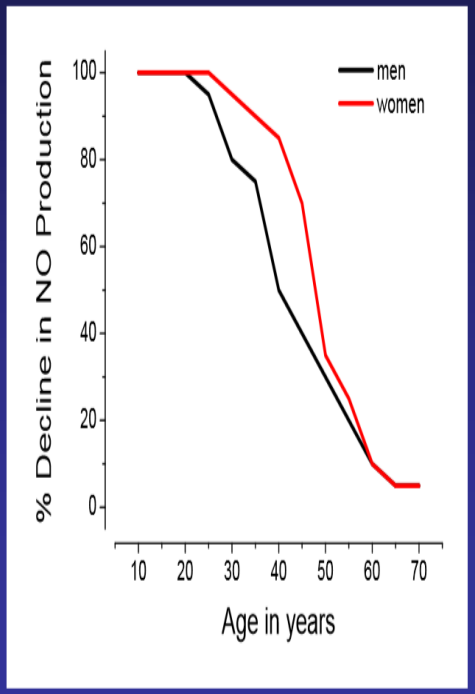
Nitric Oxide controls and regulates

- **Telomerase activity**
- **Mitochondrial biogenesis and function**
- **Mobilization of resident stem cells**



J of nutritional Biochemistry 17, 2006

Humans lose ability to produce NO with aging



Gerhard et al Hypertension 1996
Celermajer et al JACC 1994
Taddei et al Hypertension 2001
Egashira et al Circulation 1993

Estrogen on weight control

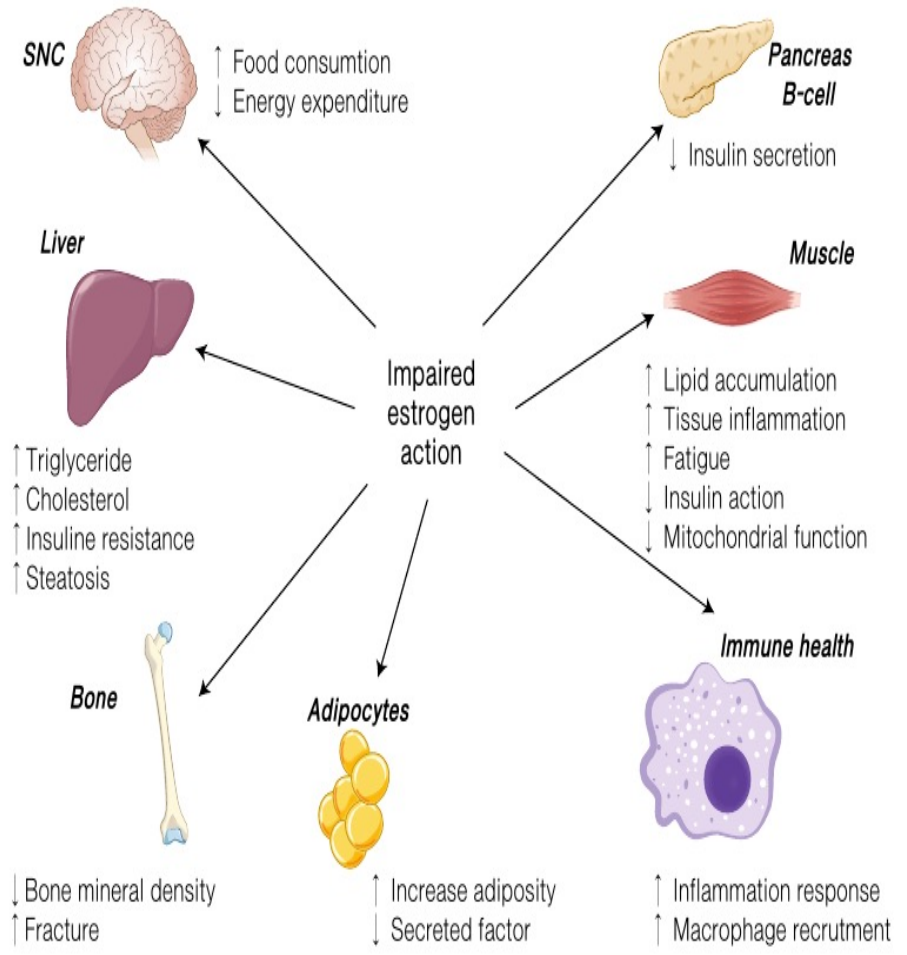


그림 10 비정상적인 에스트로젠의 영향

(출처: Menopause Rev 2017;16:61-5)

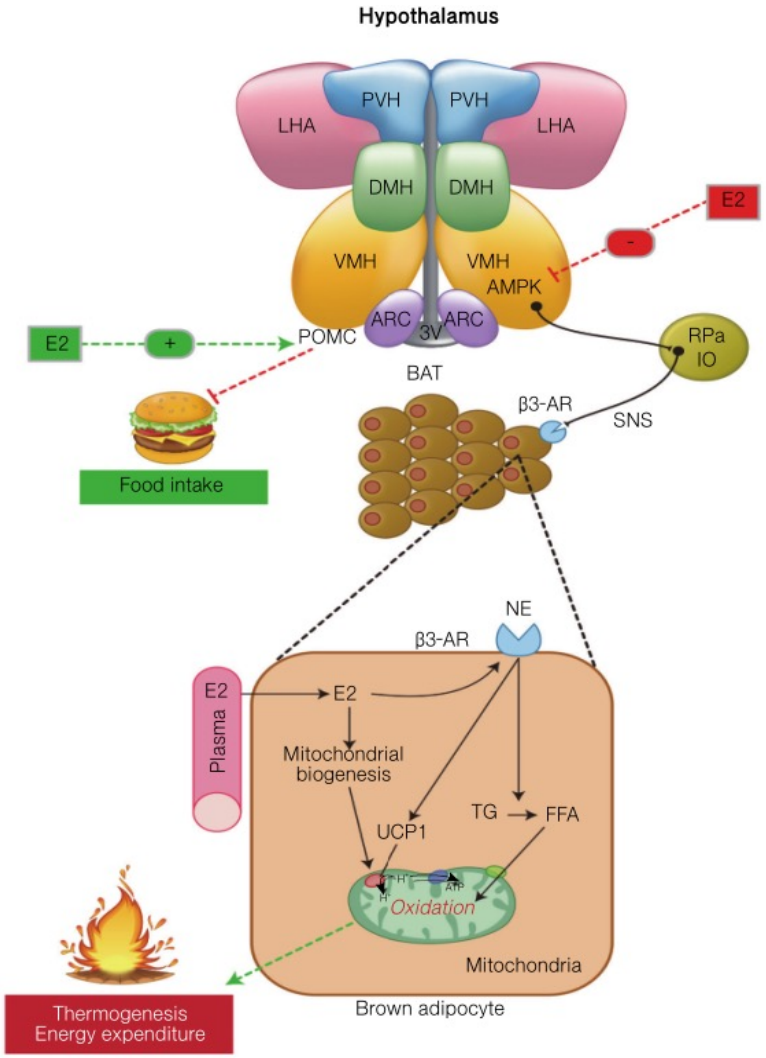


그림 11 정상적인 에스트로젠과 비정상적인 에스트로젠이 미치는 영향

(출처: López M, et al. Best Pract Res Clin Endocrinol Metab 2016:527-36)

Estrogen on NOS

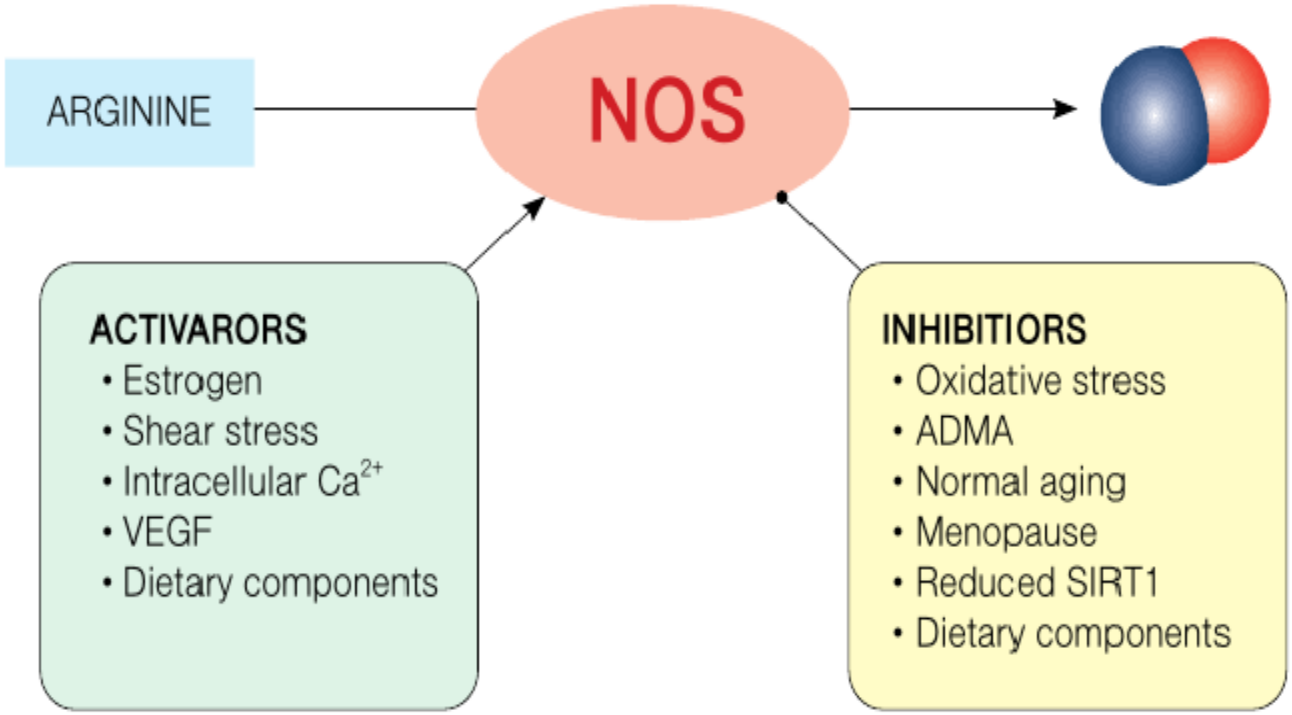
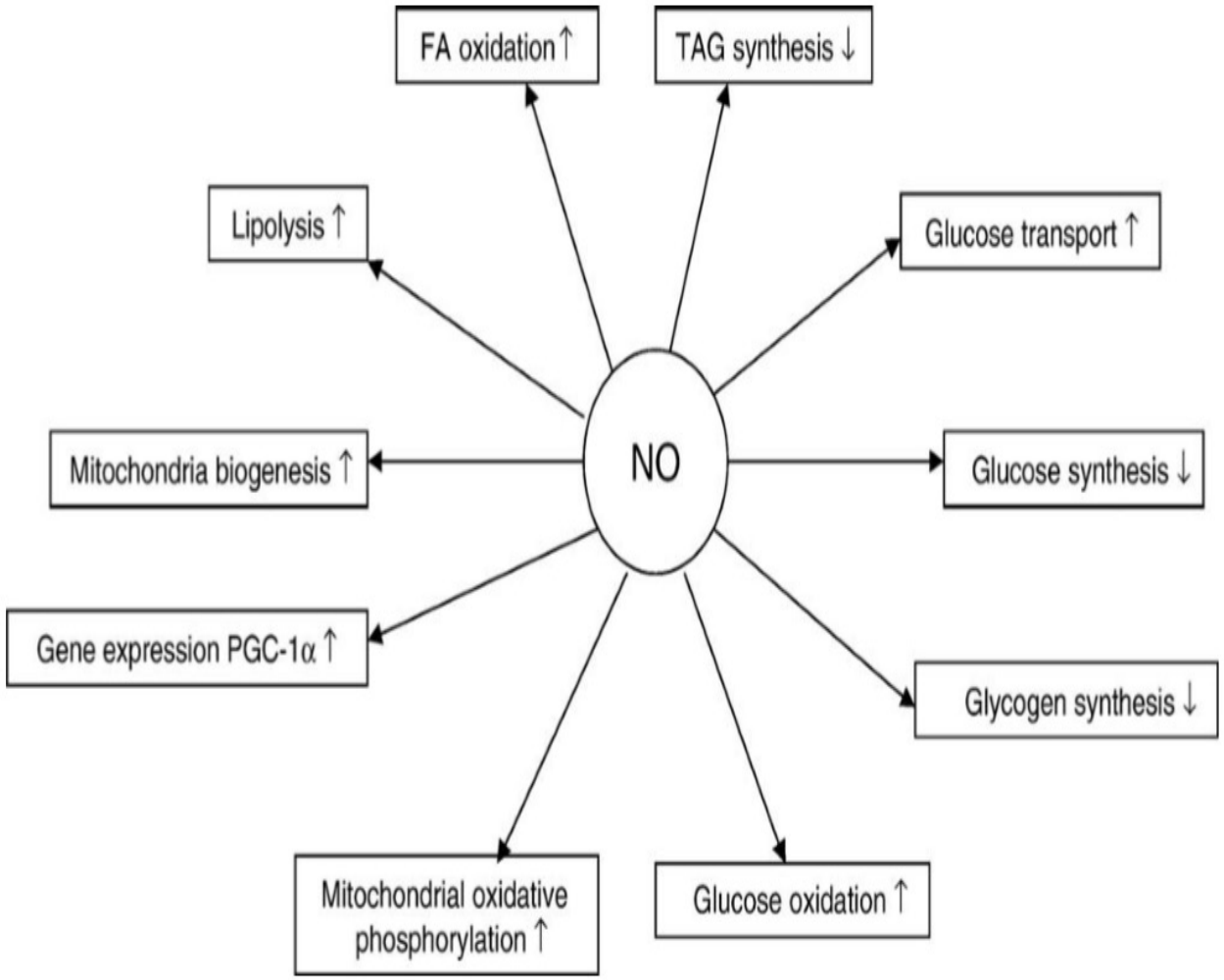


그림 12 에스트로젠의 기능

(출처: Nevzati E, et al. Acta Neurochir Suppl 2015;120:141-5)

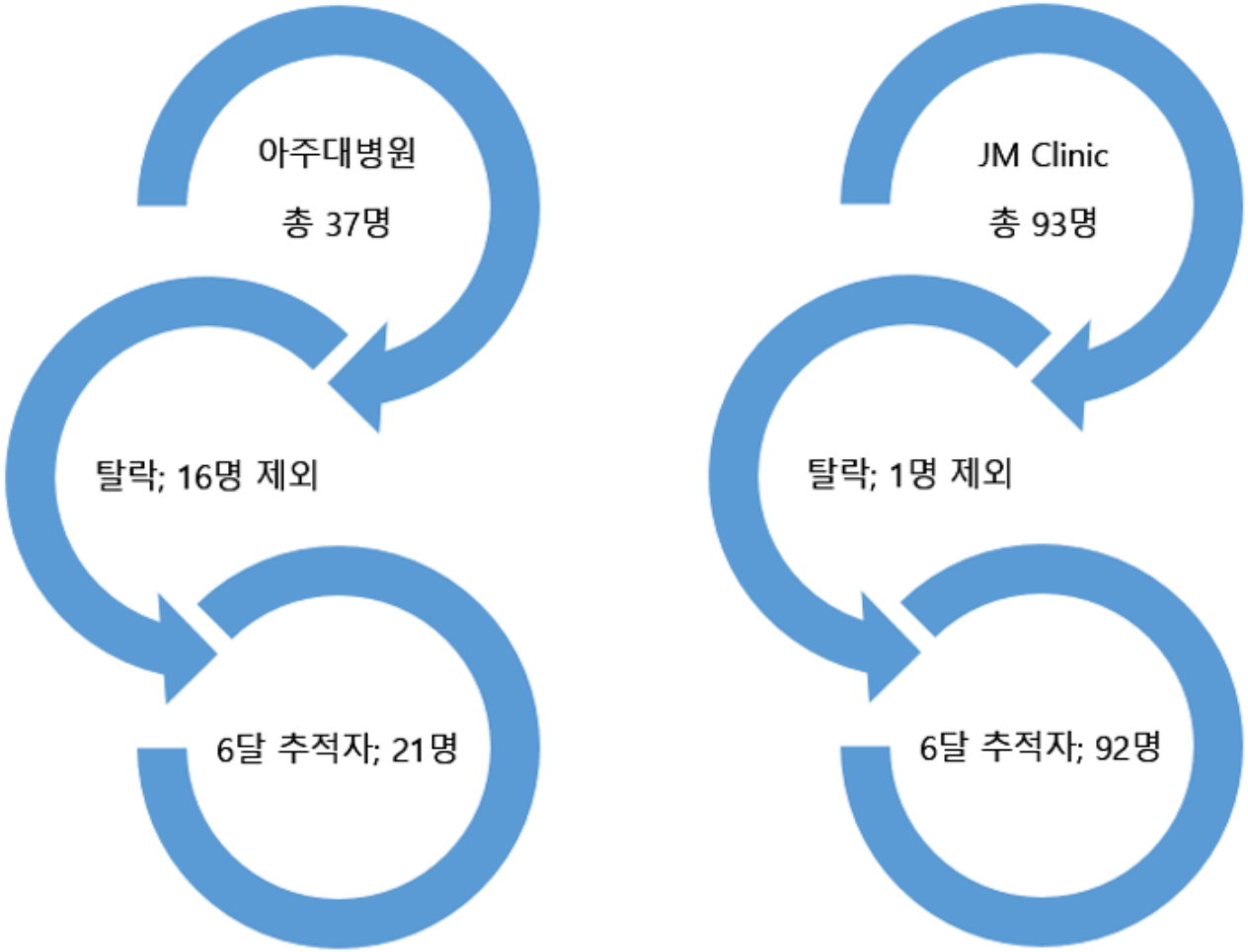
NO & Fat Oxidation.. Weight loss?

W.S. Jobgen et al. / Journal of Nutritional Biochemistry 17 (2006) 571–588

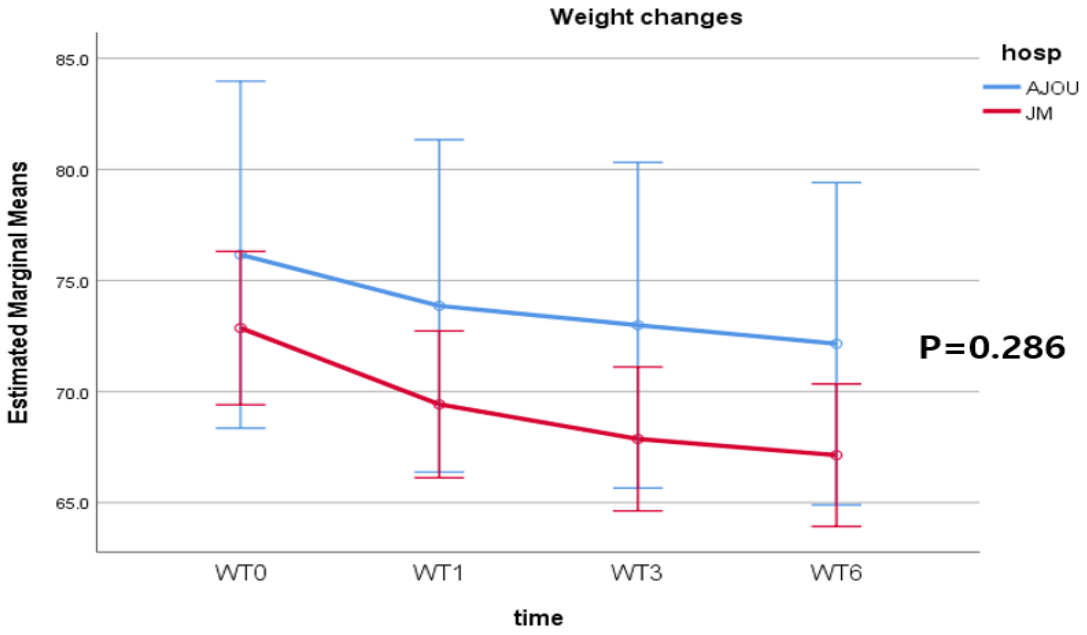


- **IV Arginine up to 30g**

Liraglutide vs. Liraglutide + L-Arginine (15g)

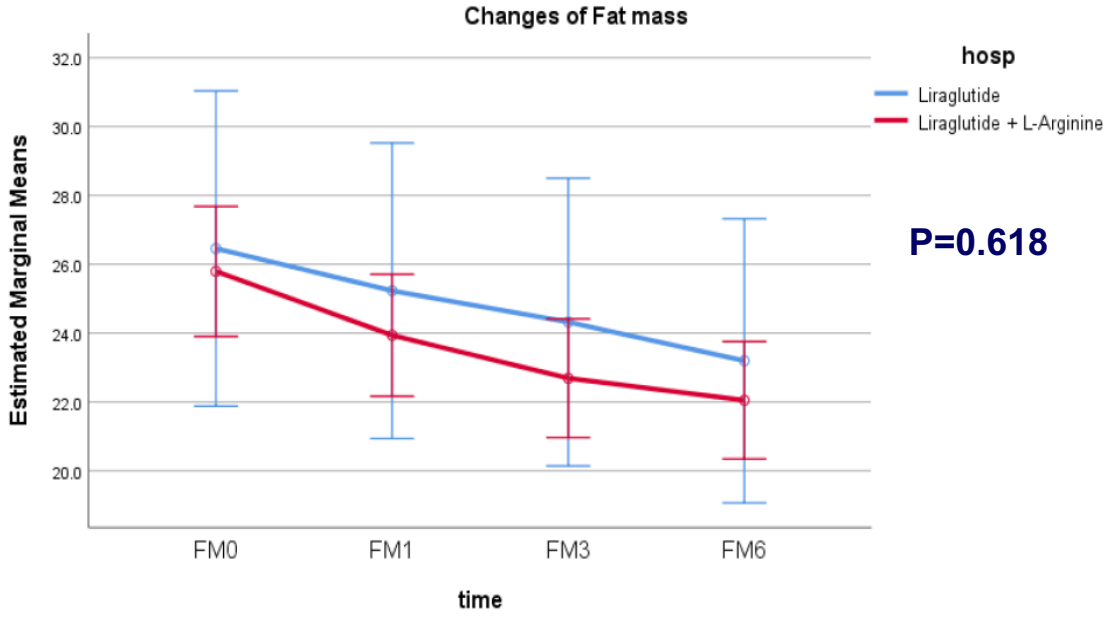


J Korean Inst Funct Med, Vol. 3 No. 1, 2020.05. pp.24-30



P=0.286

Values present mean (standard deviation) by repeated measured ANOVA



P=0.618

L-Arginine on obesity: A systemic review & Meta-analysis of RCT

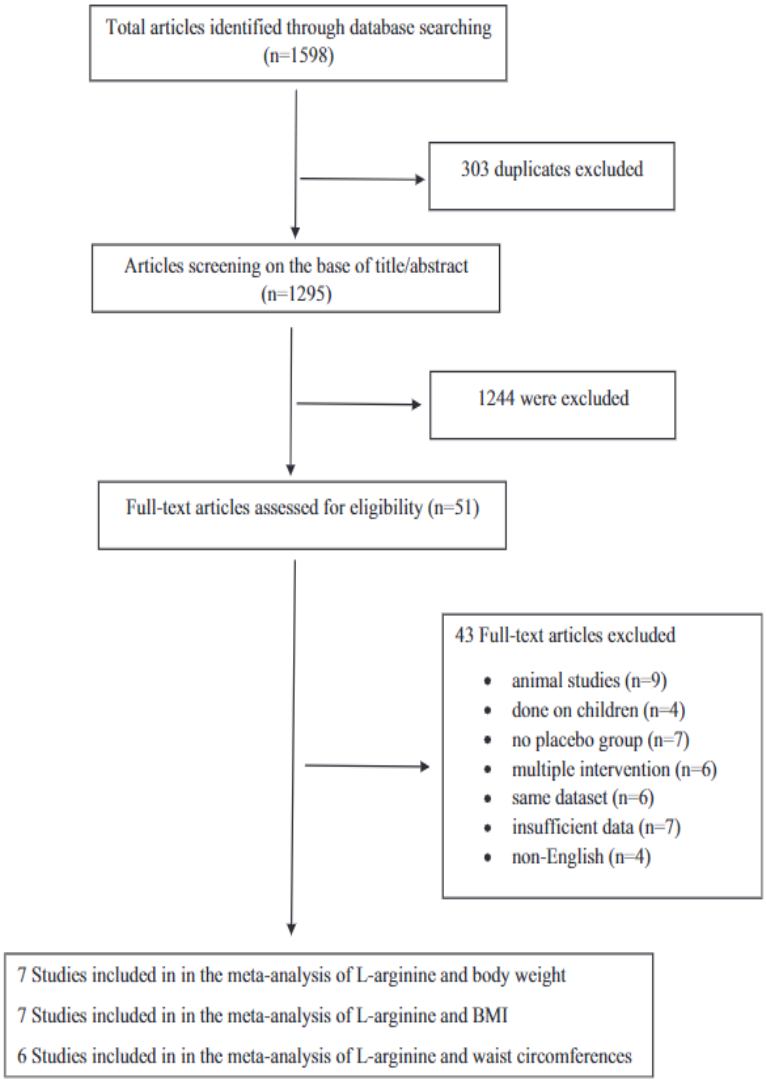


Figure 1. Summary of the process of study selection

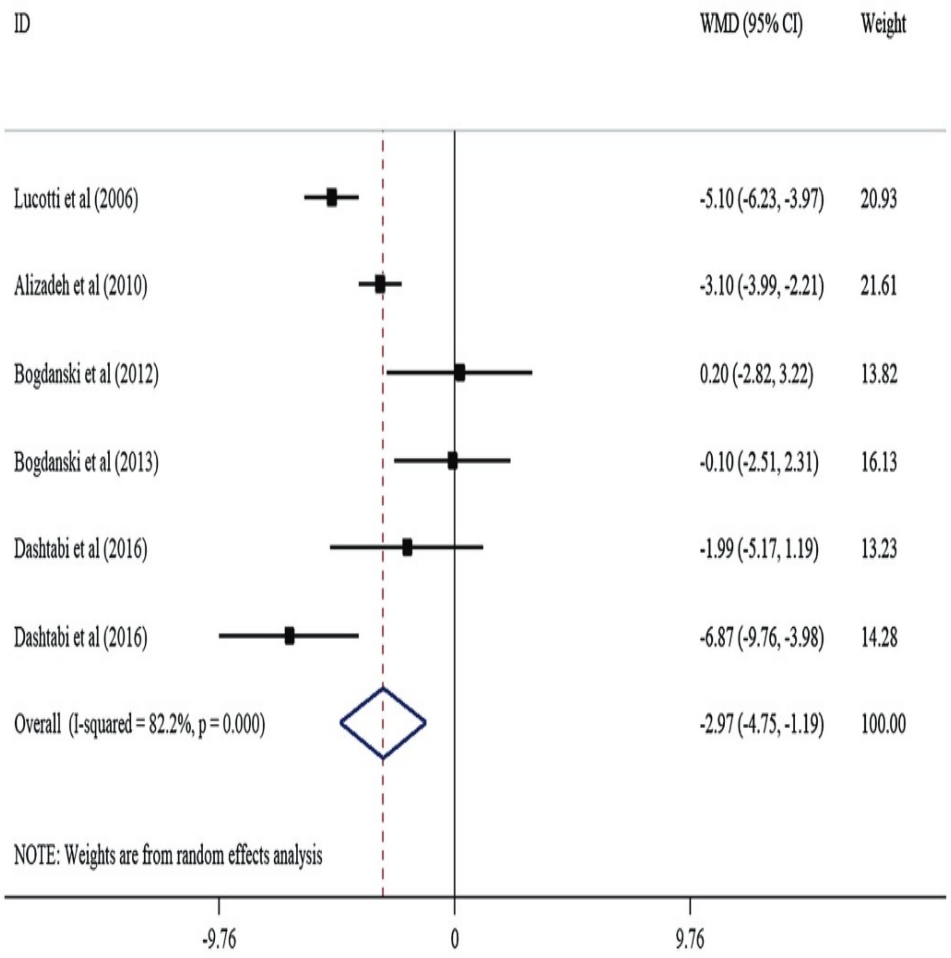


Figure 4. Forest plot of randomized controlled trials investigating the effects of L-arginine on waist circumference (WC).

Int J Vitam Nutr Res 2021;91:164-74

Oral Arginine + Leucine vs. physical activity on Obesity

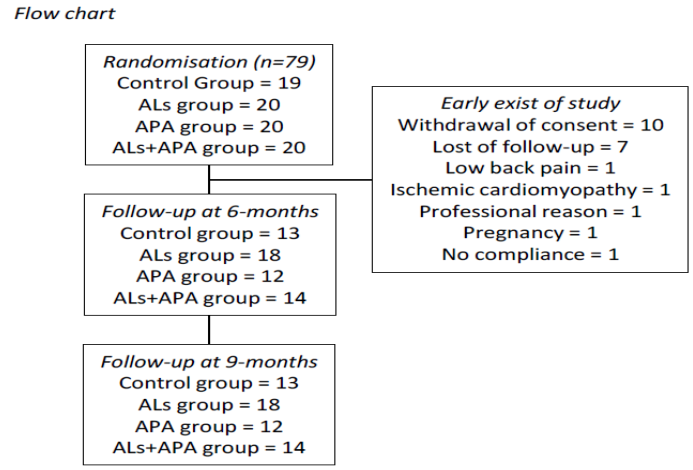


Figure 1. Flow chart. ALs, arginine and leucine supplementation; APA, adapted physical activity.

-6 months intervention, 9m F/U
-**9g arginine**, 21g leucine/day
-APA; 3times/week

Nutrients 2022,14,3708

Table 2. Demographic changes observed after 6 months of treatment: delta m0–m6.

	Control (n = 13)	ALs (n = 18)	APA (n = 12)	Als + APA (n = 14)	*p* Values
Body weight (kg)	−1.7 [−7.3; 0]	−3.65 [−7; 0]	−2.8 [−5.85; −1.3]	−4.05 [−6.2; −0.8]	0.9816
BMI (kg.m^{-2})	−0.64 [−2.41; −0.01]	−1.28 [−2.46; 0]	−0.91 [−2.1; −0.49]	−1.45 [−2.65; −0.3]	0.9887
Waist circumference (cm)	−5 [−10; −2]	−4 [−10; −3]	−5.5 [−10; −4]	−5 [−9; −3]	0.9340
Hip circumference (cm)	−6 [−11; −4]	−2 [−10; 0]	−1.5 [−9; 0]	−6 [−10; −3]	0.4373
Waist/hip ratio	0 [−0.02; 0.03]	−0.02 [−0.03; −0.01]	0 [−0.04; 0]	0.01 [−0.02; 0.03]	0.2758
Fat mass (kg)	−0.6 [−5.3; 0.3]	−0.9 [−4.7; −0.2]	−1.3 [−3.25; 0.2]	−3.15 [−6; −1.9]	0.4338
Fat mass (%)	−0.1 [−2.7; 1]	−0.95 [−5; 0.3]	−0.75 [−1.7; 0.25]	−2.7 [−3.3; −1]	0.2773
Fat free mass (kg)	−1.5 [−2.1; −0.2]	−0.6 [−3.2; 0.4]	−1.1 [−3.45; −0.05]	−1.05 [−1.4; 1.1]	0.8868
Fat free mass (%)	0.1 [−1; 2.7]	0.95 [−0.3; 5]	0.25 [0.05; 1.7]	2.7 [1; 3.3]	0.2638
Abdominal fat mass (kg)	−0.2 [−0.44; 0.24]	−0.2 [−1.2; 0]	−0.05 [−0.5; 0.18]	−0.7 [−0.9; −0.2]	0.1771

Data are expressed as median (quartiles 1 and 3). Continued data have were using the Kruskal–Wallis test and Dunn post tests. Values without a common letter significantly differ, $p < 0.05$. BMI, body mass index.

경구용 Arginine 제제; 임상 준비 중

아주대학교병원 e-IRB - 프로필 1 - Microsoft Edge

https://eirb.ajoumc.or.kr/Study/ResearchTab.aspx

연구계획심의의뢰서 심의신청

접수번호	2022-0913-00 1			과제진행상태	수정요청	연구상태	미승인
과제명	체중 감량이 필요한 비만 또는 과체중 환자를 대상으로 알룬정의 유효성 및 안전성을 평가하기 위한 다기관 공동, 이중 눈가림, 무작위배정, 위약 대조, 평행설계, 제 4 상 임상시험						
연구책임자	주남석	소속	가정의학과교실	심의 신청일	2022-11-04	접수일/접수자	

자료출처 : 식품의약품안전처

제품 기본정보

허가정보 바로가기 | 출력 | 정보 수정요청

제품명	알룬정 Alloon Tab.		
성분 / 함량	Alginic Acid 알긴산 200mg Carboxymethylcellulose Sodium 카르복시메틸셀룰로오스나트륨 100mg	동일성분 의약품	
첨가제	라우릴황산나트륨 무수인산수소칼슘 미결정셀룰로오스	첨가제 더보기	
도핑금지 약물정보	경기기간중 : 허용 경기기간외 : 허용 ※상세정보는 반드시 한국도핑방지위원회 홈페이지를 통해 확인해주세요.	상세정보 확인	
전문 / 일반	일반	단일 / 복합	복합
제조 / 수입사	휴온스		
제형	정제	투여경로	경구(내용고형)
성상	분홍색의 장방형 필름코팅정제		

등록 (2012-02-23) | HS1

2t, tid = 1,200mg
For 6 months

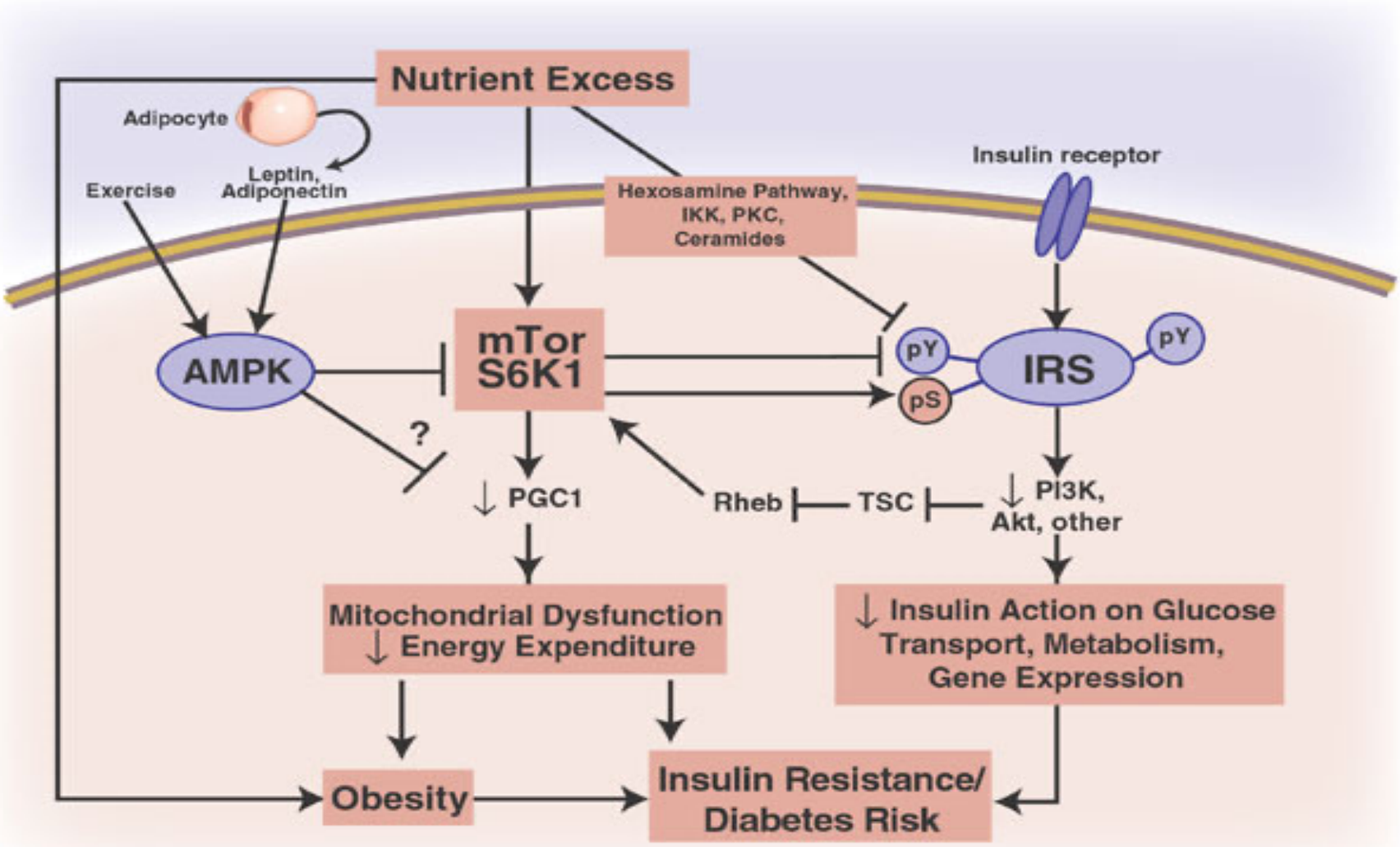
적게 먹는데, 살이 안 빠져요 vs. 많이 먹는데 살이 안쪄요

쯔양이 연일 화제입니다.

Calorie Restriction, Exercise?

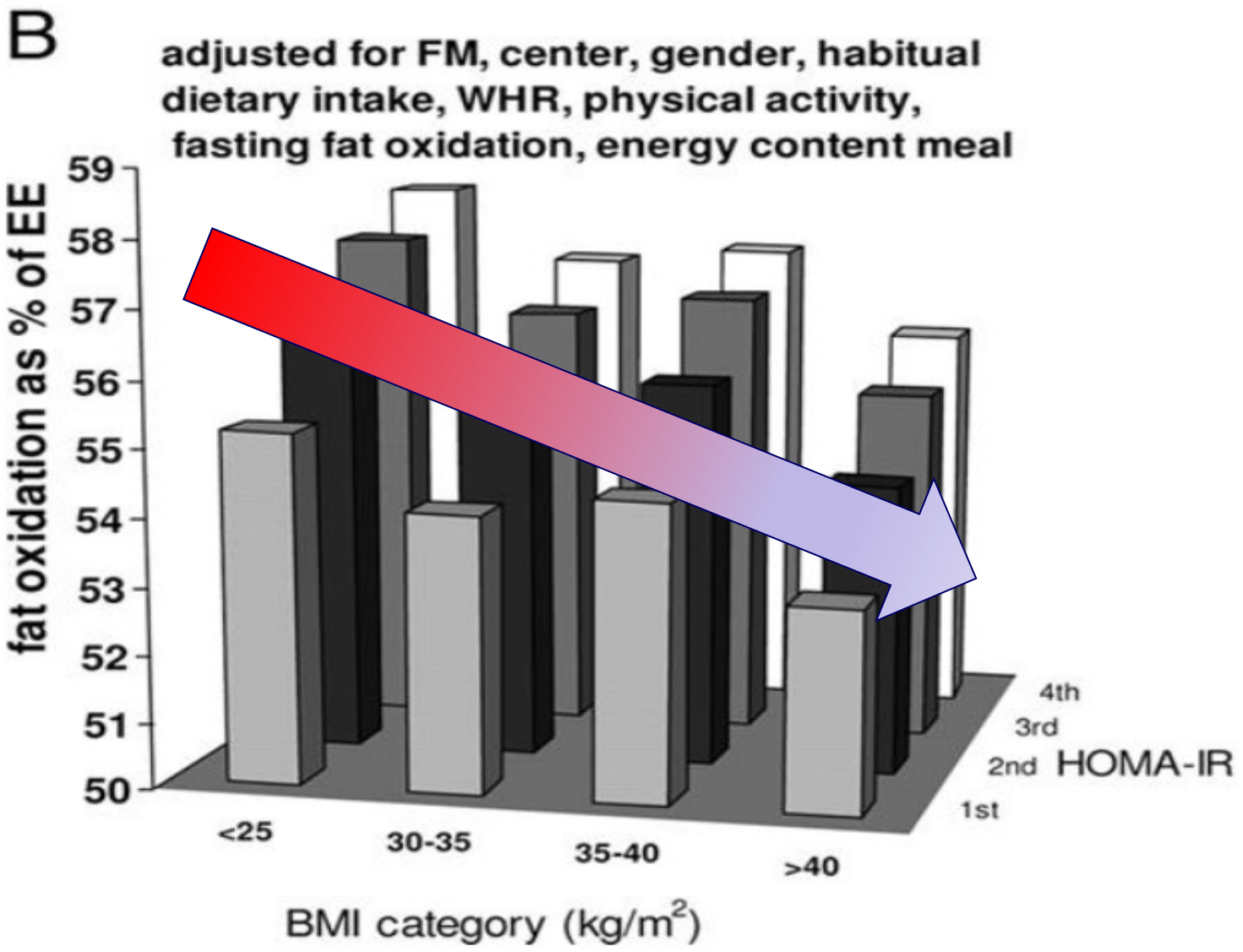
Answer: ↑ Mitochondrial Biogenesis

Elements to affect on Mitochondria Function



Nat Med 2004;10:1049-50

HOMA-IR & Fat Oxidation



J Clin Endocrinol Metab 2006;91:1462-9

Ketonuria & Obesity Phenotype

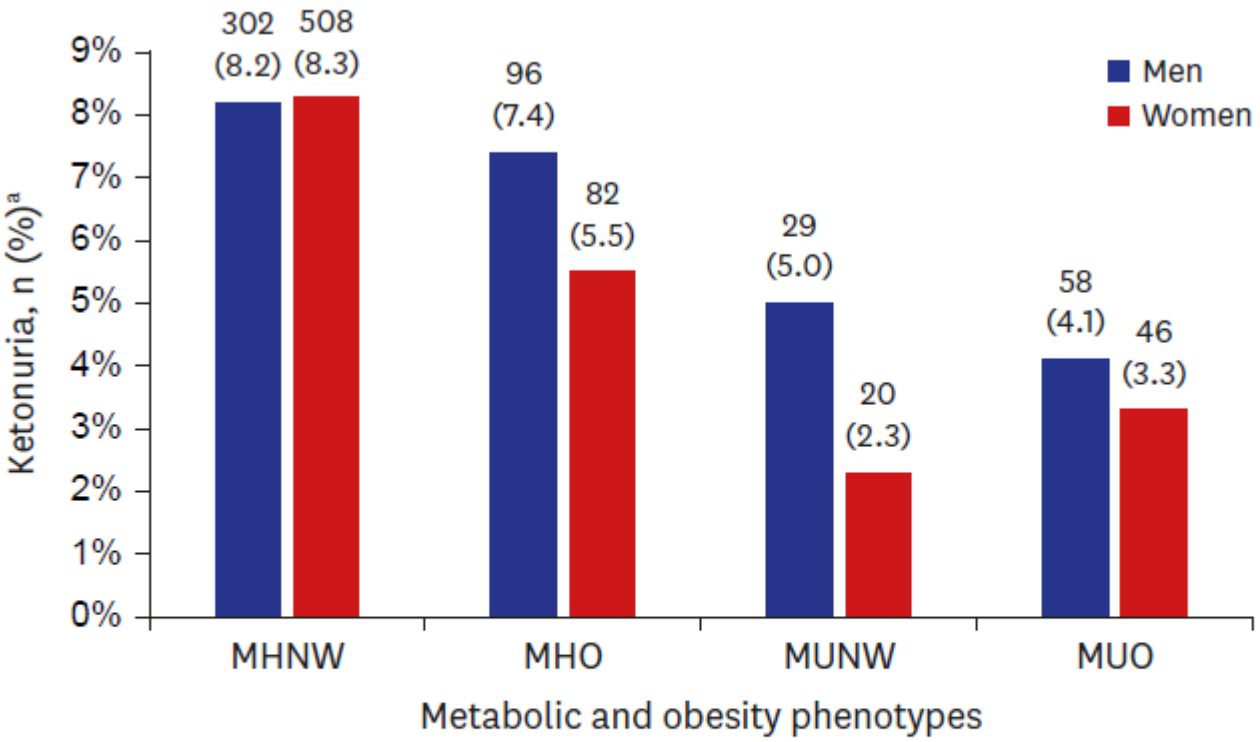


Fig. 2. Proportion of ketonuria in each metabolic and obesity phenotype.
P value < 0.001 both in men and women; *P* value is calculated by χ^2 test under complex sample analysis.
MHNW = metabolically healthy normal weight, MHO = metabolically healthy obese, MUNW = metabolically unhealthy normal weight, MUO = metabolically unhealthy obese.
[a]Values are presented as unweighted number (weighted %).

NS Joo et al. J Korean Med Sci. 2020;35:e273

Ketonuria & Weight reduction

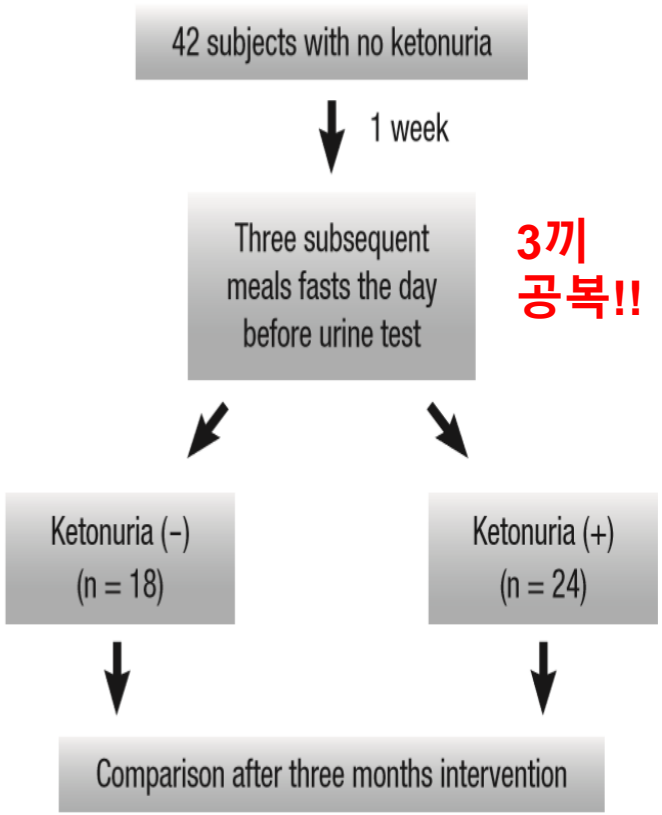


Table 2. Comparison of anthropometric changes between ketonuria group and non-ketonuria group after 3 months of an obesity control program application

Variables	Changes after 3 months		
	Urine-ketone (-) (n = 18)	Urine-ketone (+) (n = 24)	*P* value
Δ Weight (kg)	-1.17 ± 2.22	-8.65 ± 3.69	< 0.001
Δ BMI (kg/m^2)	-0.43 ± 0.86	-3.16 ± 1.25	< 0.001
Δ WC (cm)	-2.32 ± 1.01	-6.92 ± 1.22	< 0.001
Δ Fat mass (kg)	0.35 ± 2.70	-2.99 ± 2.17	< 0.001
Δ LBM (kg)	0.02 ± 1.77	-3.06 ± 2.76	< 0.001
Δ FFA (μEq/L)	13.6 ± 172.3	576.9 ± 390.0	< 0.001
Δ Insulin (μIU)	-2.95 ± 3.12	-2.94 ± 3.17	0.994

All values were mean ± standard deviation. *P* values was calculated by independent t test. Ketone (-), ketone (-) at initial urine test and ketone (-) at retest 1 week later; Ketone (+), ketone (-) at initial urine test and ketone (+) at retest 1 week later. BMI, body mass index; LBM, lean body mass; FFA, free fatty acid.

NS Joo & SM Kim J Korean Med Sci 2012;27:250-4

Exercise & Ketonuria

Table 3. Comparison of urinary ketones according to the kinds of exercise

Variable	Chi-square	Adjusted F	*P*
Walking* (day/wk, n=5,892)	1.481	0.469	0.624
Duration of walking† (hr/day, n=6,967)	3.786	2.795	0.095
Anaerobic exercise‡ (day/wk, n=8,356)	1.823	1.281	0.259
Aerobic exercise§ (yes/no, n=8,306)	7.338	5.354	0.021

P-values represent chi-square.
*Numbers of walking days into below 1 day and above; †Numbers of walking hours into below 1 hour and above; ‡Numbers of anaerobic exercise days into below 1 day above; §Engaging in more than 2 hours 30 minutes of moderate-intensity physical activity or 1 hour 15 minutes of high-intensity physical activity or a mixture of moderate and high intensity of physical activity.

Table 4. Ketonuria according to exercise

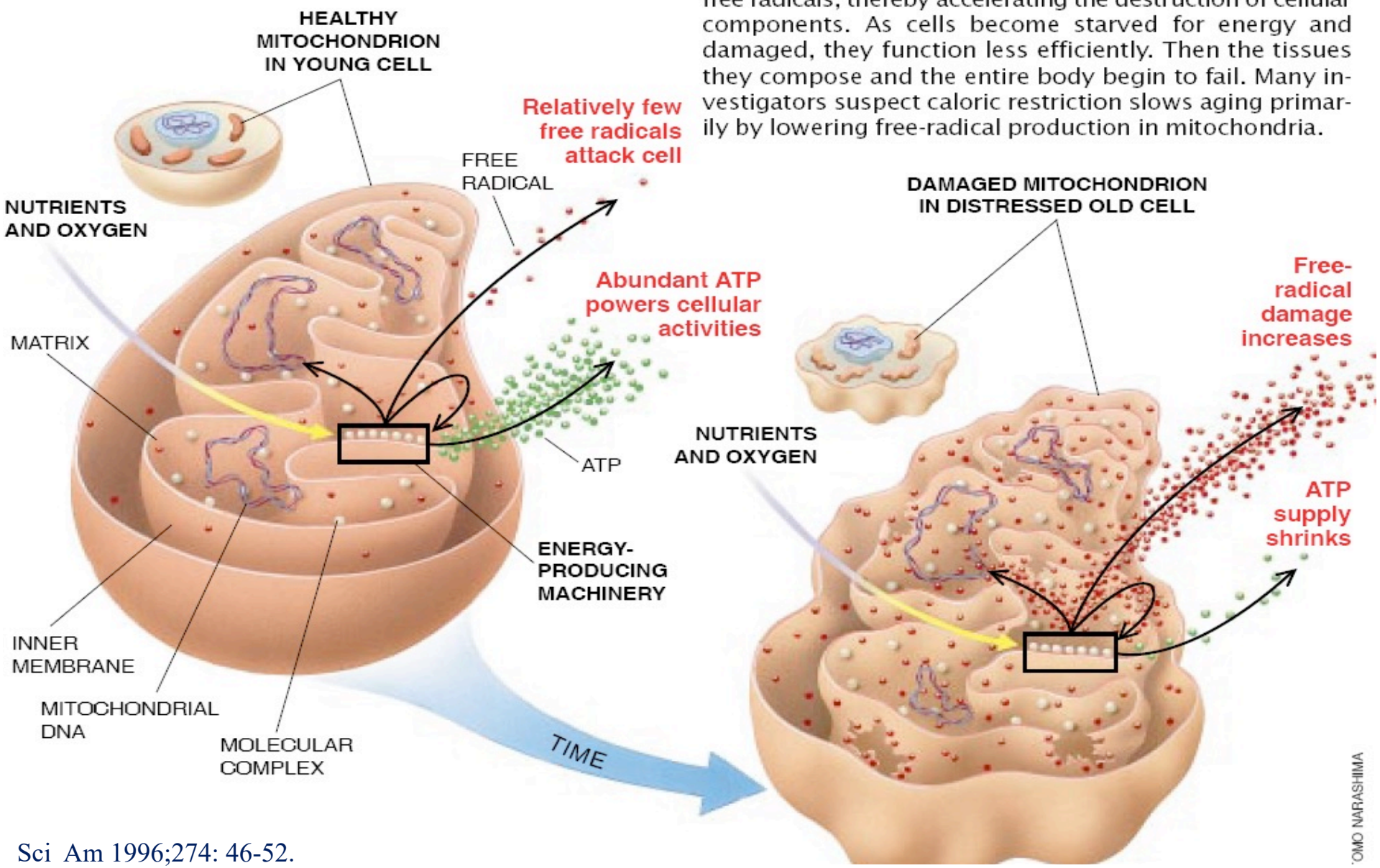
Variable	Model 1	Model 2	Model 3
Aerobic exercise*	1.28 (1.04–1.58)	1.29 (1.04–1.60)	1.00 (0.80–1.27)

Values are presented as odds ratio (95% confidence interval) by logistic regression under complex sample analysis.
*Engaging in more than 2 hours 30 minutes of moderate-intensity physical activity or 1 hour 15 minutes of high-intensity physical activity or a mixture of moderate and high intensity of physical activity.
Model 1, without adjustment; Model 2, adjusted for body mass index, carbohydrate, and potassium consumption; Model 3, adjusted for age, sex, and triglycerides in addition to the factors listed in Model 2.

NS Joo et al. J Obes Metab Synd 2020;29:143-9

Mitochondria Deteriorate with Age

free radicals, thereby accelerating the destruction of cellular components. As cells become starved for energy and damaged, they function less efficiently. Then the tissues they compose and the entire body begin to fail. Many investigators suspect caloric restriction slows aging primarily by lowering free-radical production in mitochondria.



Sci Am 1996;274: 46-52.

Causes of 2nd Mitochondrial Failure

- ↑Oxidative Stress
- ↑Nitric Oxide (NO) **iNOS**
- ↑SCFA (esp. Propionate)
- ↑TNF-α & Inflammation
- ↓Folate & B-Vitamins
- ↓Mineral Co-Factors
- ↓Co-Q 10
- ↓Glutathione (GSH)
- ↓Carnitine

⇑ Oxidative Stress

↓

Activation of NF-kB

↓

Up-regulation of stress and inflammation genes including inducible NOS (iNOS)

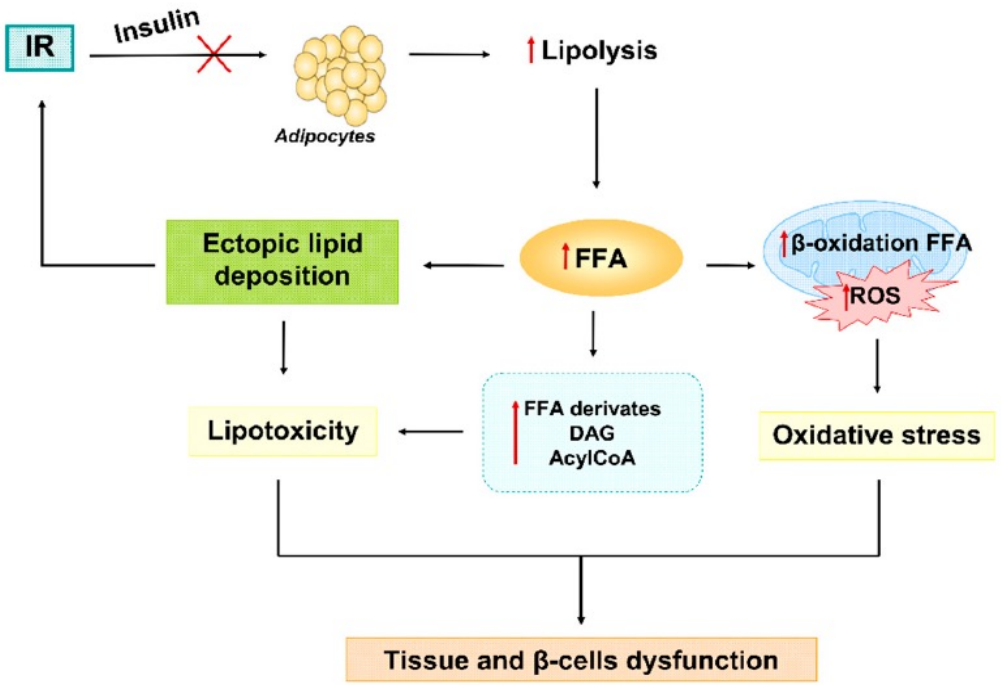
↓

⇑ RNS, NO, $*ONO2^-$

↓

Increased Cellular Damage

- **↑Oxidative Stress**
- Exposure to Medications
- Exposure to Heavy Metals
- Exposure to Chemicals
- Exposure to PCBs
- Exposure to Pesticides

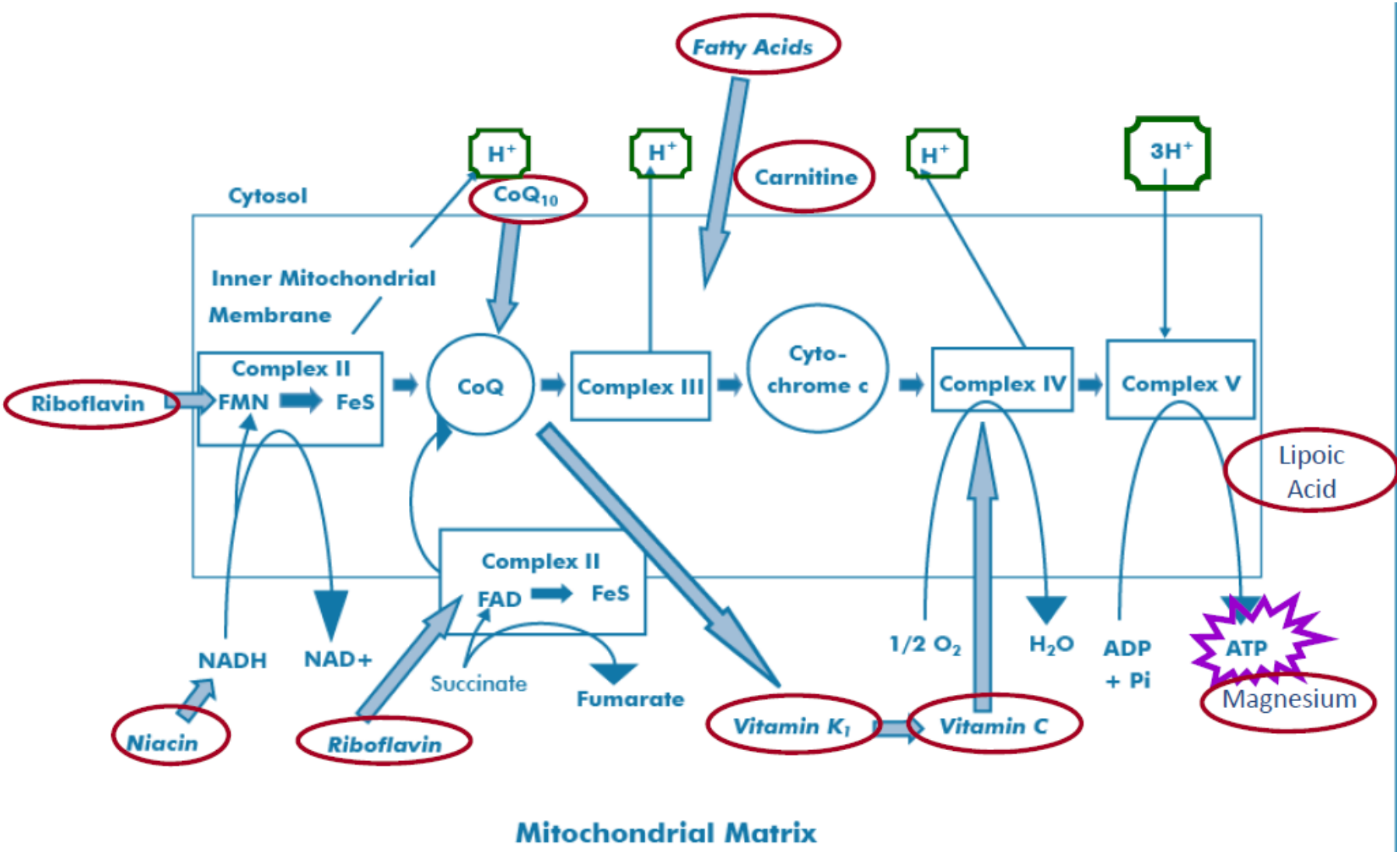


J. Clin. Med. **2019**, *8*, 1385;

Oxidative Stress Markers

- Elevated lipid peroxides; TG ↑, HDL ↓
- HOMA IR ↑ (glucose*Insulin/405) >2.3
- Non-alcoholic fatty liver
- Lean central obesity; metabolic unhealthy subjects
- 8-OHDG in Urine Organic acid

Empower Mitochondria Function



TCA Cycle intermediates in Urine Organic Analysis

- Citrate high + cis-Aconitate low; Arginine !!!
- Cis-aconitate high; cysteine 1000mg, Check IDA
- Isocitrate; lipoic acid, 25mg/kg/day, Mg 400mg, manganese 20mg
- α-KG (if low); α-KG, 300mg; arginine , 1000mg; glutamine , 1-5g
- α-KG (if high); B-complex, tid, lipoic acid 100mg
- Succinate (if low); isoleucine 1000mg tid, valine 1000mg tid
- Succinate (if high); CoQ10 50mg tid, Mg 500mg
- Fumarate (if low); tyrosine 1000mg bid, phenylalinine 500mg bid
- Malate (if high); CoQ10 50mg tid, B3 100mg tid
- Hydroxymethylglutarate (HMG) (if low or high); CoQ10 50mg tid

Mitochondrial Resusciatation

Mitochondrial Function Up!!

- CoQ10.. Oral 100~200mg/day
- Lipoic acid
- Acetyl-L-carnitine
- Magnesium
- Vitamin B-complex

Mitochondrial Biogenesis Up!!

- Lipoic acid
- Arginine
- Omega-3 PUFAs
- Resveratrol
- Quercetin
- Ketogenic Diet
- Branched chain amino acids (BCAA)
- Caffeine

Source: Evans JL (2013) *The Secret Life of Mitochondria (Smashwords; ISBN 9781301331024)*

Myers' Protocol

Ingredient	Dose	Nutrient
Magnesium chloride hexahydrate 20%	2-5 mL	Magnesium
Calcium gluconate 10%	1-3 mL	Calcium
Hydroxocobalamin 1,000 mcg/mL	1 mL	Vitamin B_{12}
Pyridoxine hydrochloride 100 mg/mL	1 mL	Vitamin B_6
Dexpanthenol 250 mg/mL	1 mL	Vitamin B_5
B complex 100	1 mL	Vitamin B complex
Vitamin C 222 mg/mL	4-20 mL	Vitamin C

$350

FM in AUMC

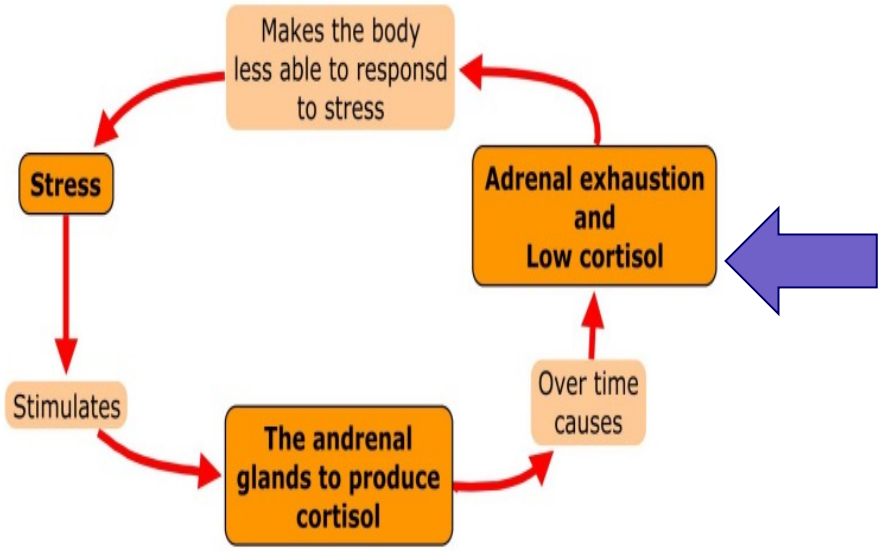
Megacorbin-C 10g/20ml Inj	1 VIA
0.9% NS 250ml/Bag	200 ML
Beecom hexa Inj 2ml	1 AMP
Dutenol Inj 500mg/2ml	1 AMP
Thiamine Inj 50mg/2ml	1 AMP
Kyominotin Inj 20ml	2 AMP
MagneSIUM Inj 10% 2g/20ml	1 AMP
Sod. Bicarbonate Inj 8.4% 1.68g/20ml	8 ML
sig IV ONCE 150 ml/hr <약국용> <원내>	

$50

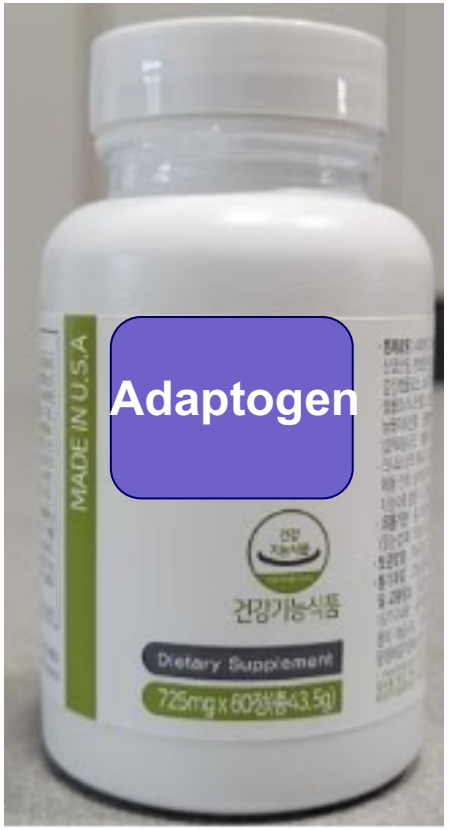
RCT? NONE!!

Chronic Stress & Adrenal Fatigue

What is Adrenal Fatigue?



The adrenals produce several hormones such as adrenaline, which is responsible for "fight or flight" response.



Textbook of Functional Medicine

DHEA

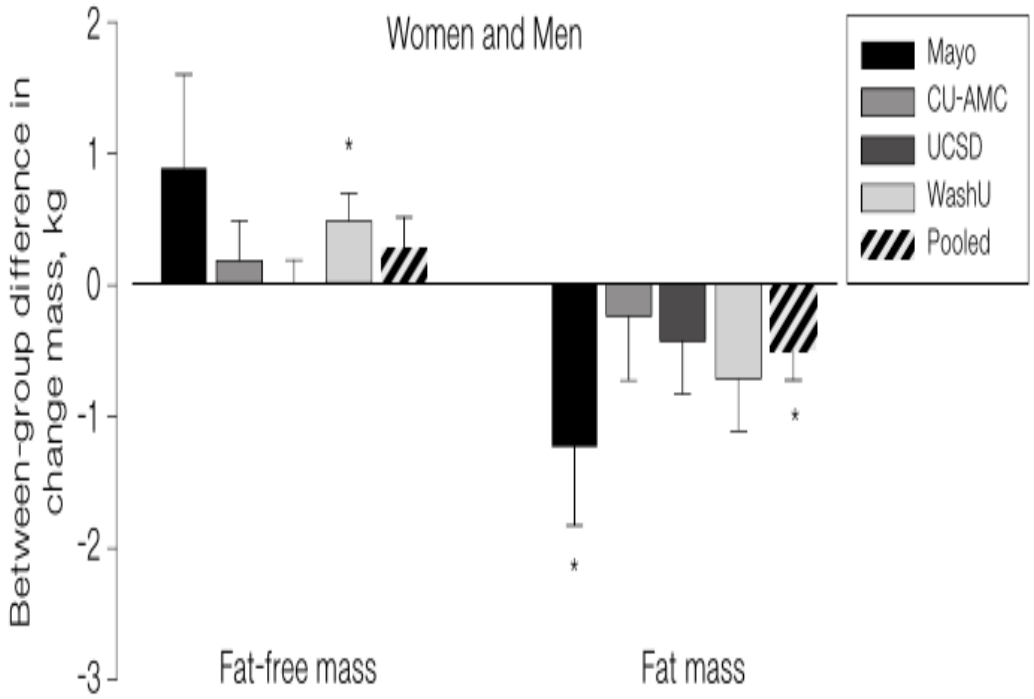


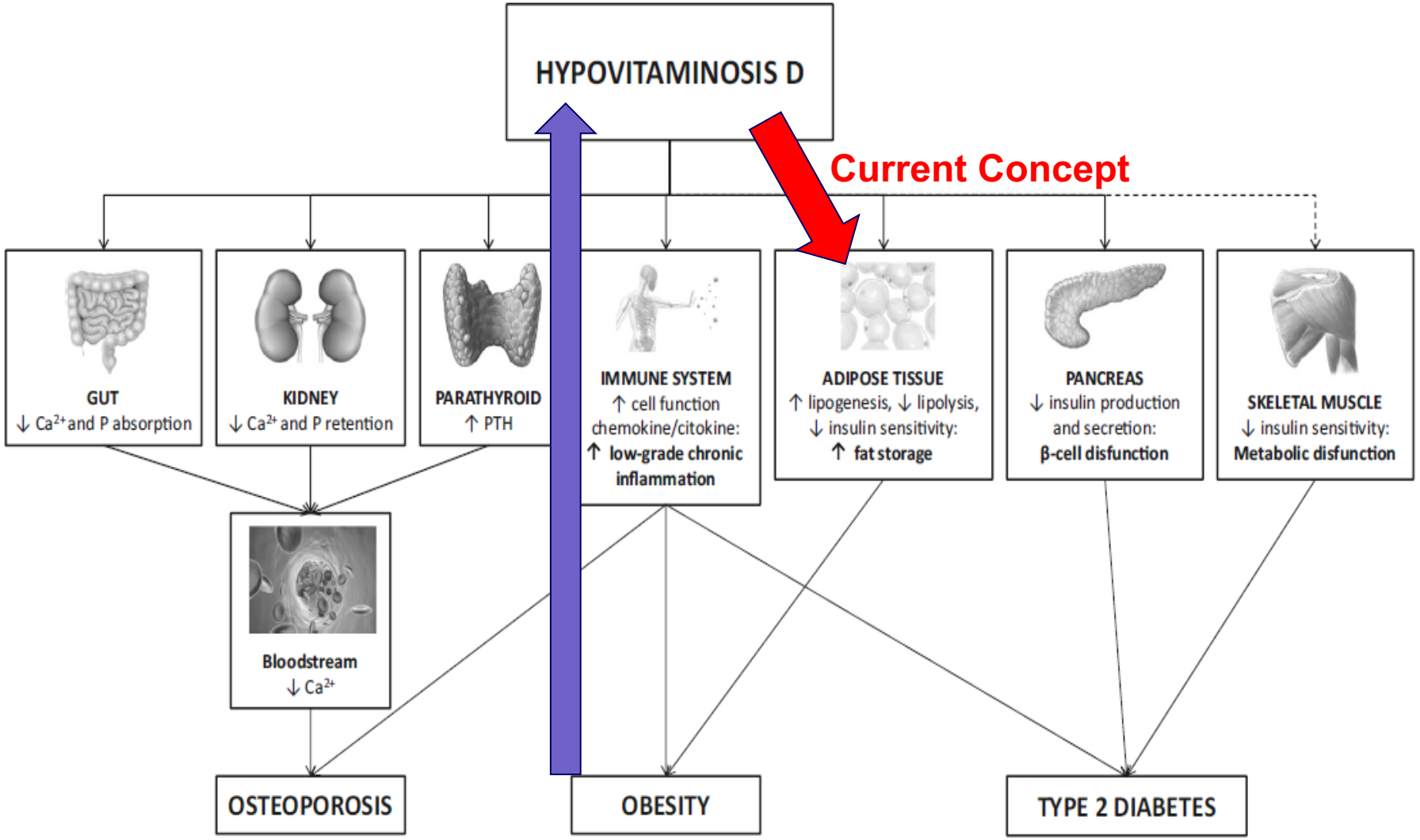
그림 19 DHEA 투여의 근육량 증가

(출처: Jankowski CM, et al. Clin Endocrinol (Oxf) 2019;90:293-300)

Recover Adrenal gland Function

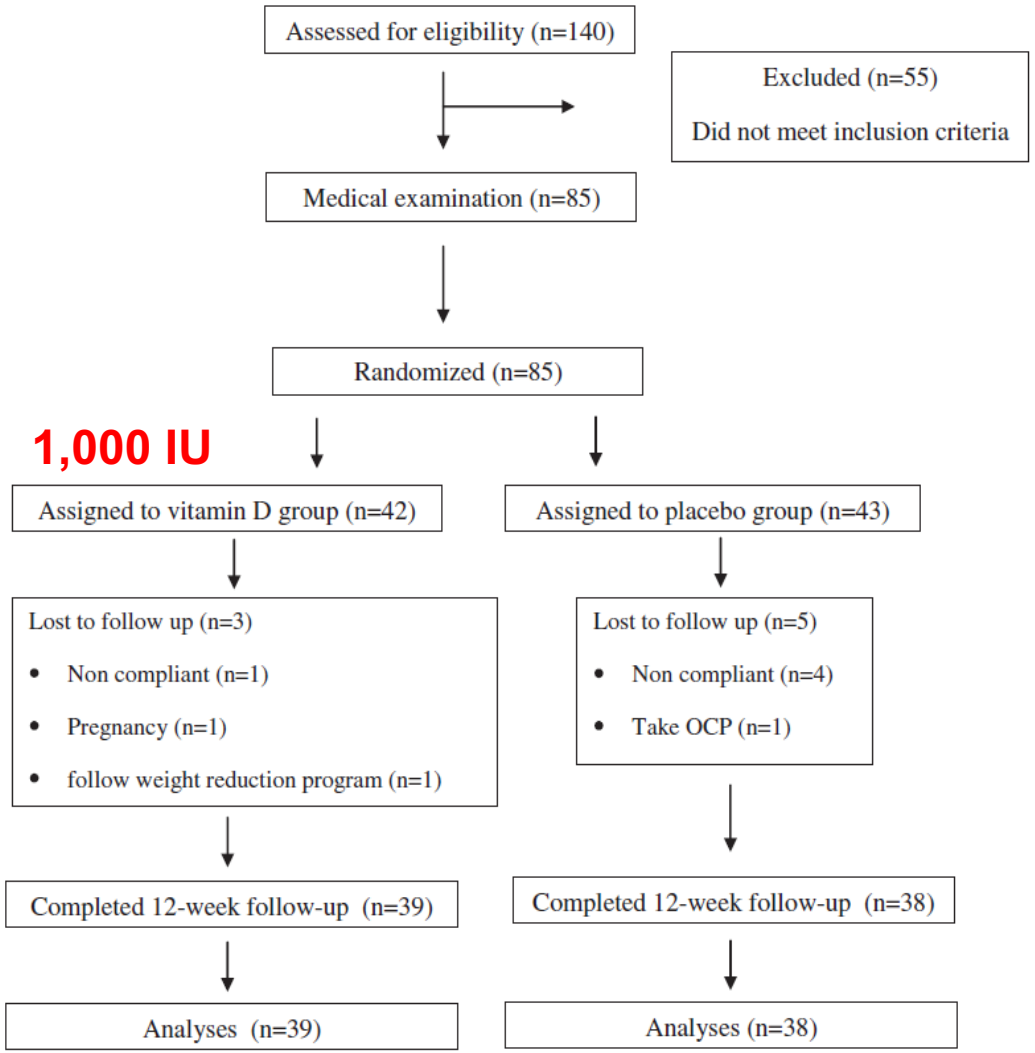
- Refrain high carbohydrate
- High protein diet
- Brief walk, not hard exercise
- Enough rest and proper sleep
- IVNT..Myers' cocktail
- Adaptogens; evaluate morning cortisol/DHEA

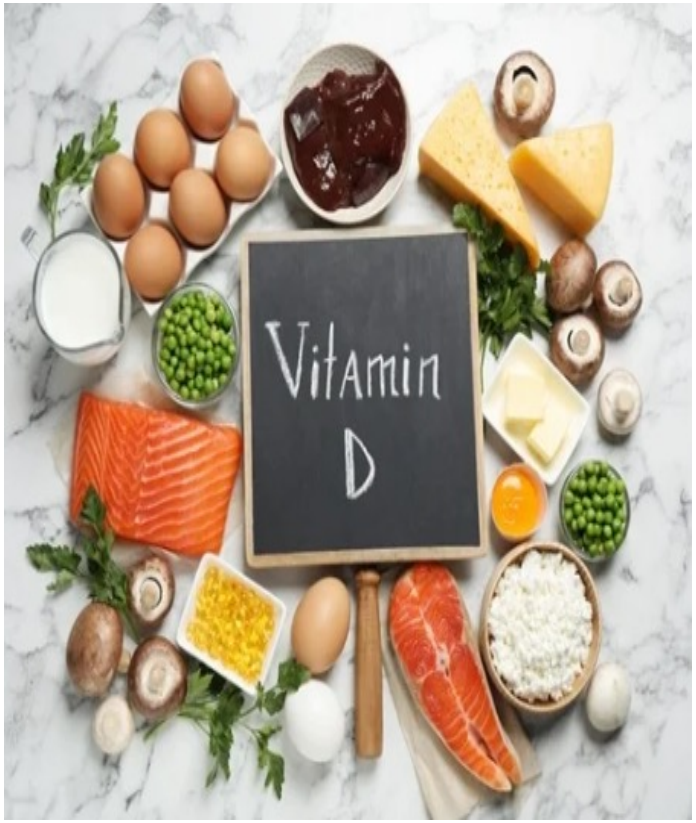
Obesity vs. Low Vitamin D;
Causality or Casualty?



Int J Obes Suppl 2019;9:20-31

A 12-week double-blind randomized clinical trial of vitamin D_3 supplementation on body fat mass in healthy overweight and obese women





Nutr J 2012;11:78

Vitamin D supplementation

Table 2 Anthropometric, dietary and serum variables in the subject groups after vitamin D3 supplementation and changes in variables between measurement periods

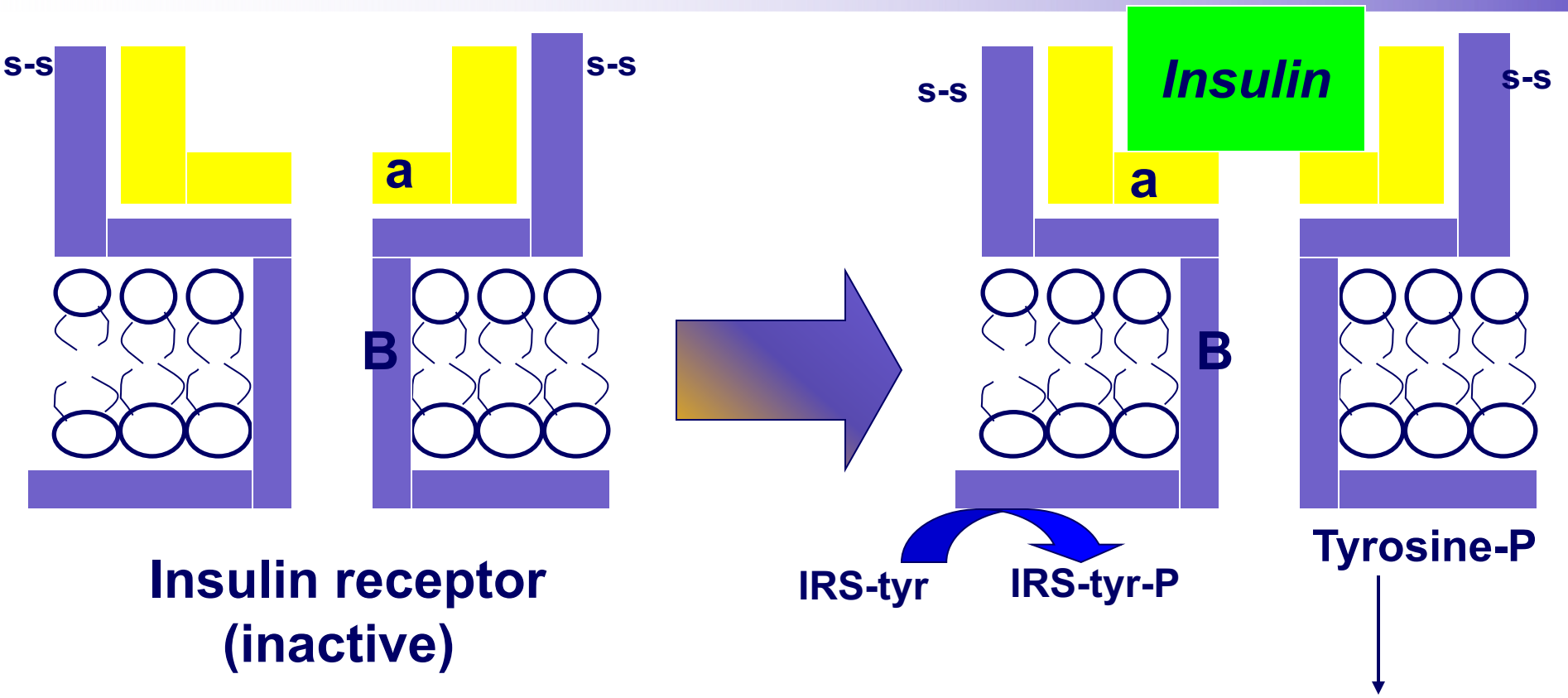
Characteristics	Vitamin D group		Placebo group		P-value[a]
	Week 12	Change[b]	Week 12	Change	
Body weight (kg)	73.5±10.4[3]	-0.3±1.5	75±12.3	-0.1±1.7	0.71
Waist circumference (cm)	89.5±8.8	-0.3±4.3	91.6±13	0.4±4.1	0.38
Hip circumference (cm)	107.6±7.9	-0.39±2.4	107.3±7.2	-0.9±2.4	0.36
BMI (kg/m^2)	30±4	-0.13±0.6	29.5±4.6	-0.04±0.6	0.50
Fat mass(kg)	28.2±7.5	-2.7±2.1	28.6±8.9	-0.47±2.1	<0.001
Fat free mass (kg)	45.5±4.9	1.8±2.1	46.2±5	0.4±2.1	<0.001
Physical activity (METminutes/week)	892±1488	-10±1627	1081±1372	379±1137	0.23
Energy intake (kcal/d)	2010±1289	143.7±1358.4	1852±992	-208±920.9	0.32
Carbohydrate intake (g/d)	312±186	31.8±194.6	294±164	-34.3±143	0.23
Fiber intake (g/d)	16±12	1±11.7	14±7	-4.3±11.3	0.10
Protein intake (g/d)	72±53	7.8±54.3	66±32	-9.3±35.6	0.29
Fat intake (g/d)	53±43	-2.3±52.2	45±36	-4.2±39.3	0.48
Dietary calcium intake (mg/d)	829±533	-43.9±674.4	625±454	-51.8±509.5	0.18
Dietary vitamin D intake (μg/d)	0.4±0.47	-0.09±0.77	0.37±0.35	-0.04±0.52	0.70
25(OH) D (nmol/L)	75±22	38.2±32	51.5±31	4.6±14	<0.001
PTH (pmol/L)	1.2±0.5	-0.2±0.5	1.7±0.8	0.2±0.5	<0.001
Calcium (mmol/L)	2.2±0.1	-0.02±0.1	2.3±0.09	-0.02±0.1	0.81
Phosphorus (mmol/L)	0.9±0.09	-0.12±0.1	1±0.09	-0.09±0.1	0.21

[a]An analysis of covariance (ANCOVA) was used to adjust mean differences on all dependent variables.
[b]After 12 weeks.
Mean ± SD (all such values).

Nutr J 2012;11:78

Chromium (Cr)

GTF(Cr, Mn)



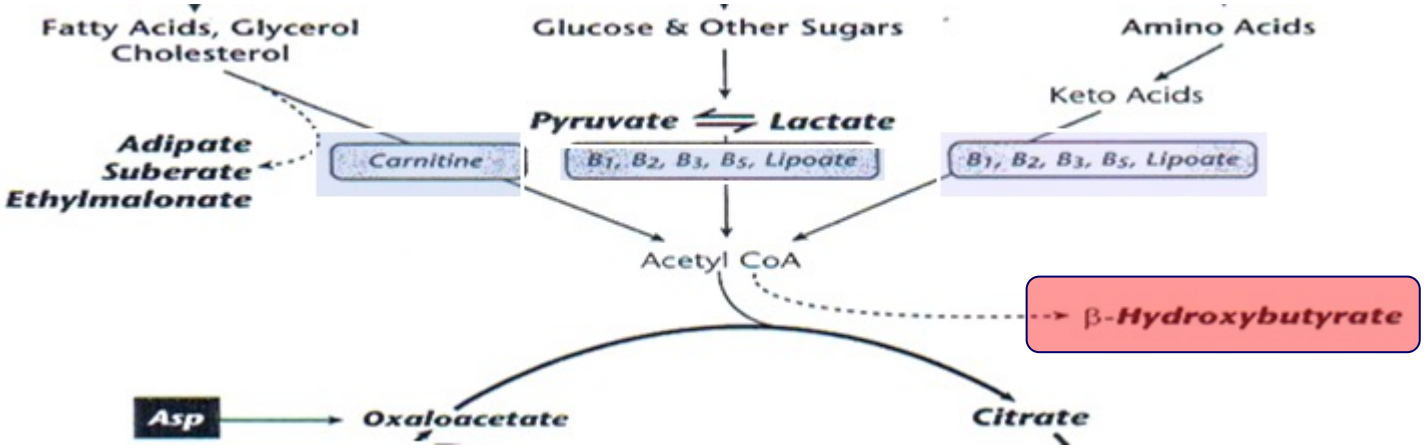
Insulin receptor (inactive)

Phospholyated IRS promotes Activation of other proteinkinase And phosphatase lead to Biologic action of insulin

IRS:Insulin-Receptor-Substrate
GTF:Glucose-Tolerance-Factor

In high Carbohydrate diet

- Ketone body
- Due to failure of glucose utilization as with DM
- Production increased d/t oxidation of FFA
- Excess acetyl-CoA conversion
- Defects of CYP oxidase enz. in ETC. ;iron dependent
- Restriction of carbohydrate
- **Tx; chromium (picolinate 1000μg), Lipoic acid 600mg**



Chromium Supplementation on body fat

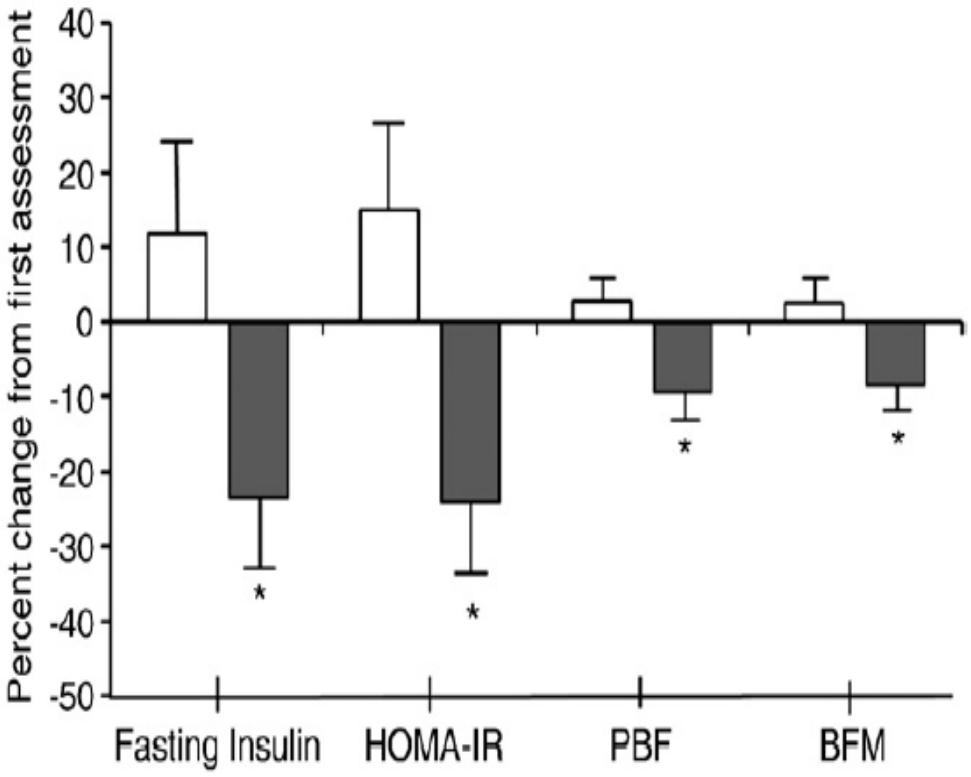


Fig. 1. Mean percent change in fasting insulin level, HOMA-IR, percentage body fat (PBF) and body fat mass (BFM) in overweight children taking either chromium chloride (black bars) or placebo (white bars) for 6 weeks, compared with baseline. Chromium supplementation reduced insulin resistance and body fatness while placebo did not make any significant change. *$P<.05$.

-25 overweight children
-9~12 years old
-RCT
-400ug Cr vs. placebo
-For 6 weeks

N-S Joo et al. J Nutr Biochem 2011;22:1030-34

Omega 3 fatty acid & Obesity

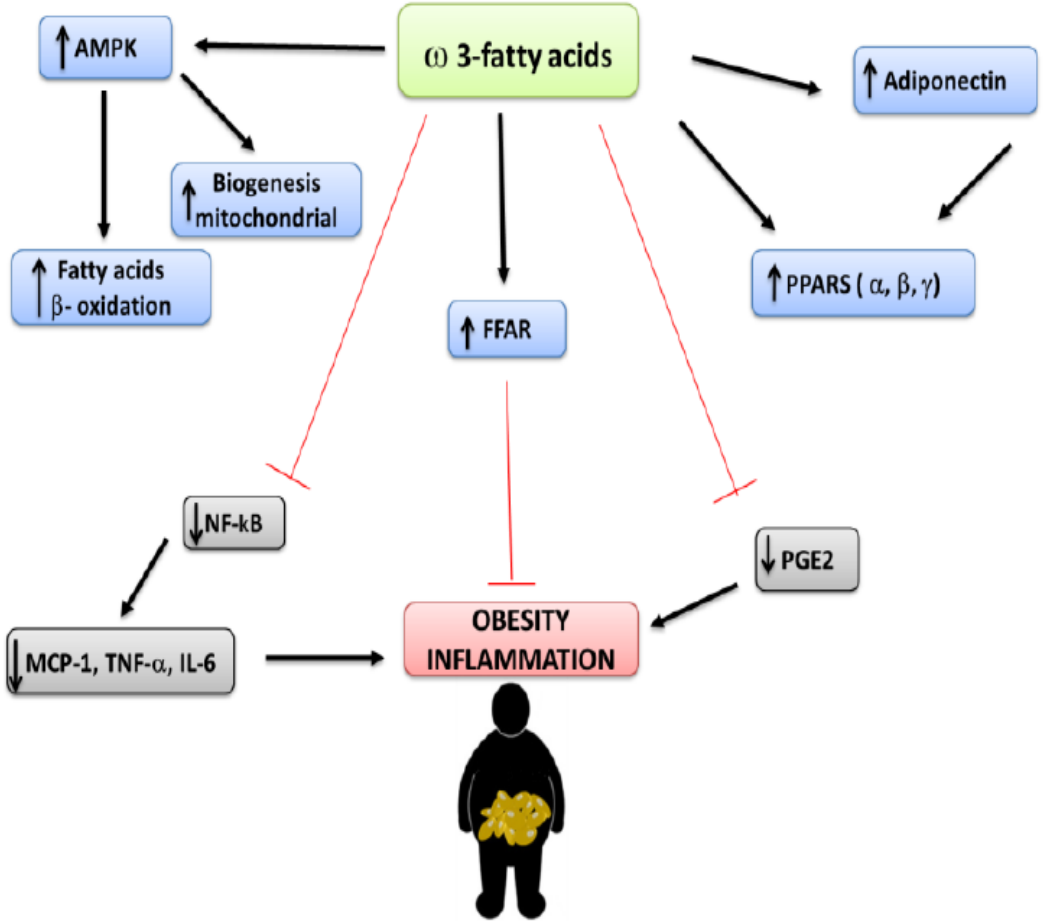


Figure 3. Some signaling mechanisms mediating effects of ω-3PUFAs.

Nutrients. 2020;12:2751

Omega 3 fatty acid on weight loss

Table IV. Total and abdominal fat

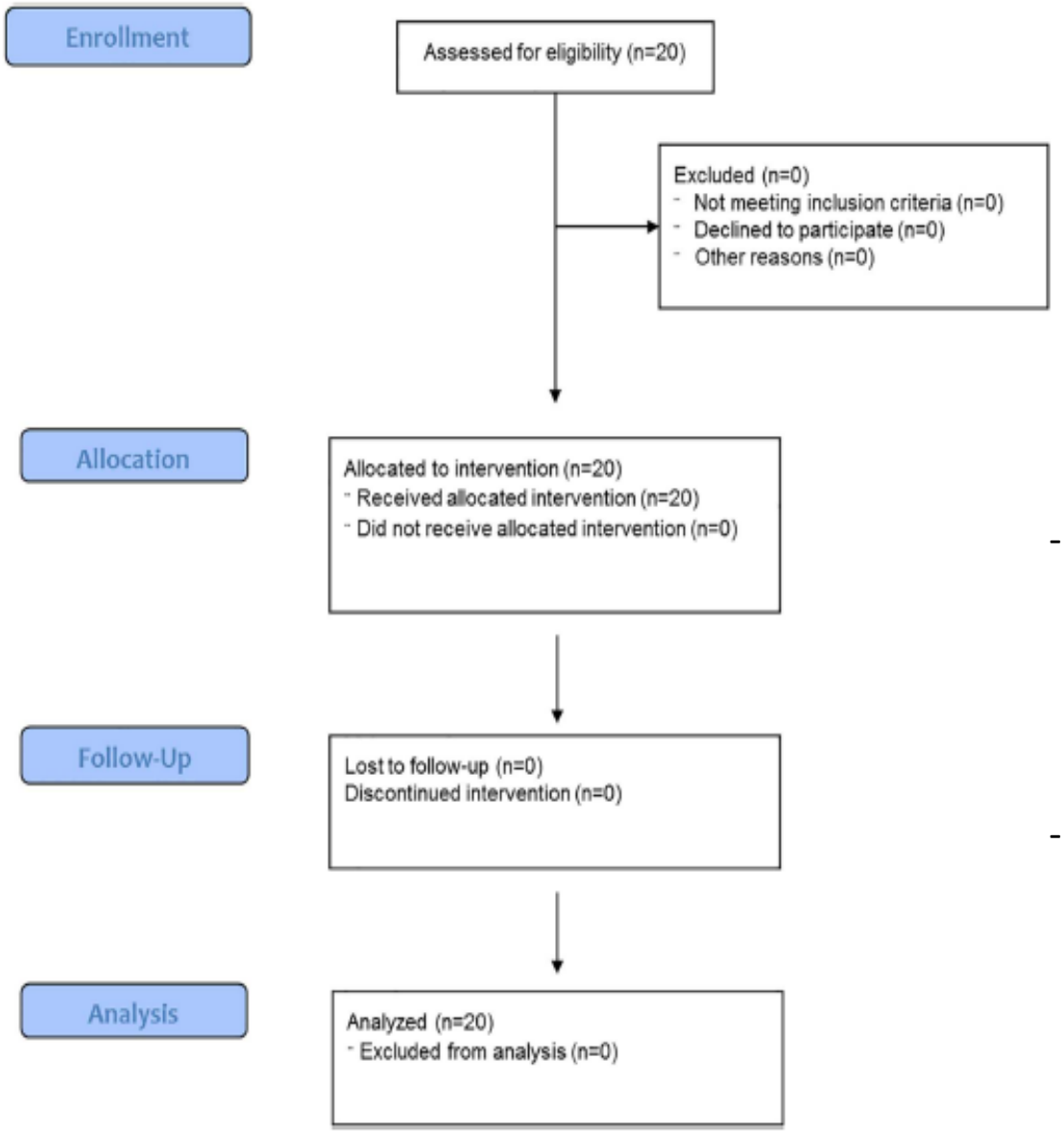
Group	Onset	4th week	8th week	12th week
Fat mass (kg)				
Control	31.51 ± 5.18*	29.45 ± 5.37*	28.12 ± 6.08*	26.68 ± 4.98*
Omega-3	28.63 ± 6.11*	26.57 ± 6.61*	24.64 ± 6.96*	23.83 ± 6.42*
Total	30.07 ± 5.78*	28.01 ± 6.12*	26.38 ± 6.69*	25.25 ± 5.85*
Fat percentage				
Control	35.43 ± 5.05*	34.50 ± 6.01*	33.64 ± 6.72*	32.89 ± 6.23*
Omega-3	33.91 ± 6.21*	32.57 ± 6.83*	30.92 ± 7.38*	30.27 ± 6.94*
Total	34.67 ± 5.64*	33.54 ± 6.42*	32.28 ± 7.10*	31.58 ± 6.64*
Abdominal fat mass (kg)				
Control	16.08 ± 2.79*†	15.17 ± 2.90*†	14.51 ± 3.08*†	13.82 ± 2.72*†
Omega-3	14.29 ± 3.85*†	12.98 ± 4.30*†	11.96 ± 4.60*†	11.39 ± 4.44*†
Total	15.18 ± 3.44*	14.08 ± 3.78*	13.23 ± 4.08*	12.60 ± 3.83*
Abdominal fat percentage				
Control	17.96 ± 1.94*†	17.67 ± 2.70*†	17.27 ± 2.94*†	16.91 ± 2.75*†
Omega-3	16.69 ± 3.08*†	15.63 ± 4.18*†	15.34 ± 3.65*†	14.10 ± ±4.36*†
Total	17.33 ± 2.62*	16.65 ± 3.62*	16.30 ± 3.42*	15.50 ± 3.87*

*Mean ± SD. *$p < 0.05$ within time; †$p \leq 0.05$ between groups.*

-BMI; 27~35
-Age; 30~60
-Omega 3;
580mg EPA +
390mg DHA,
50mg others
-12 weeks

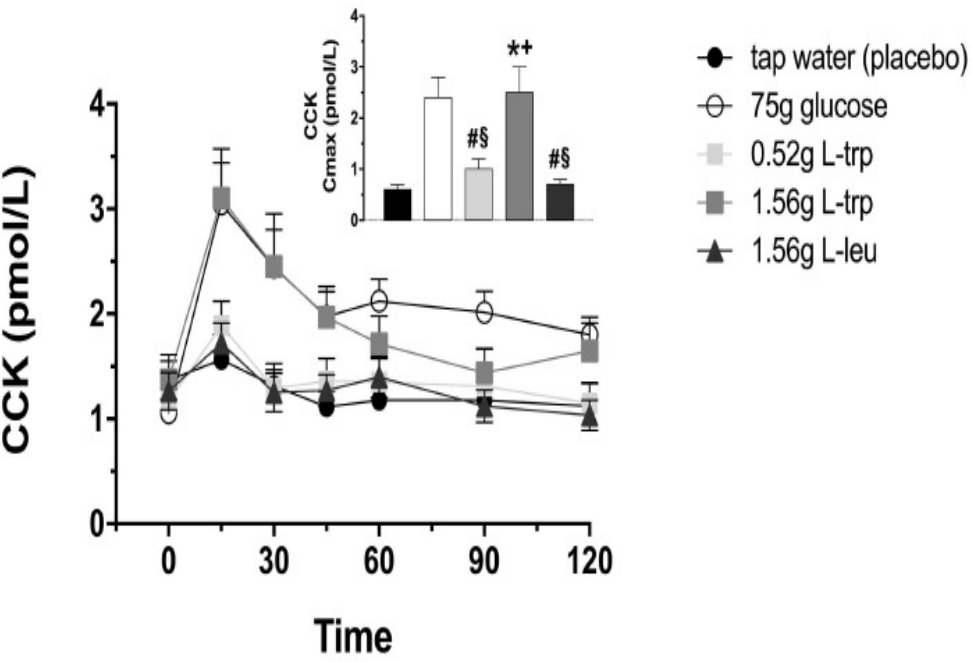
Nutr Hosp 2022;39:803-13

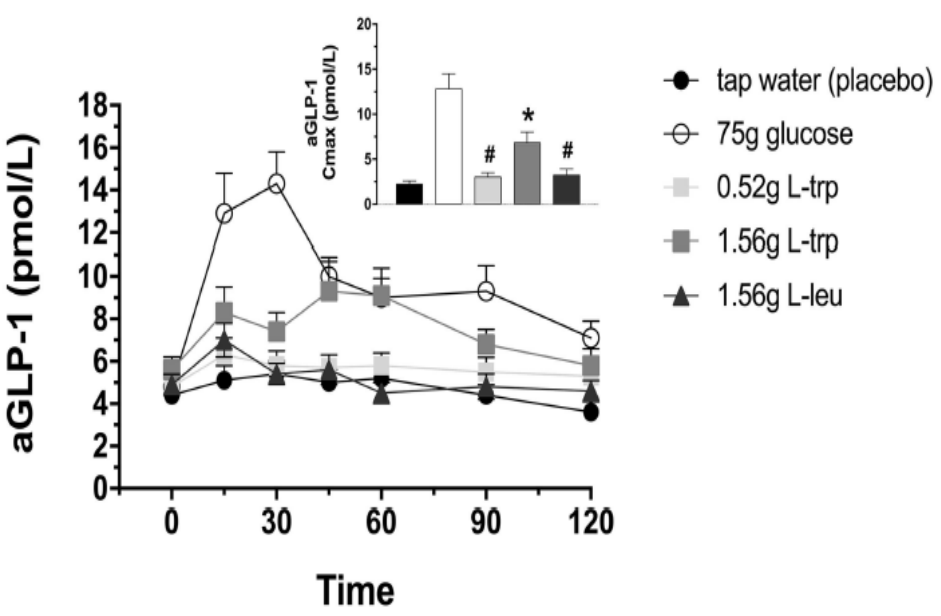
L-tryptophan

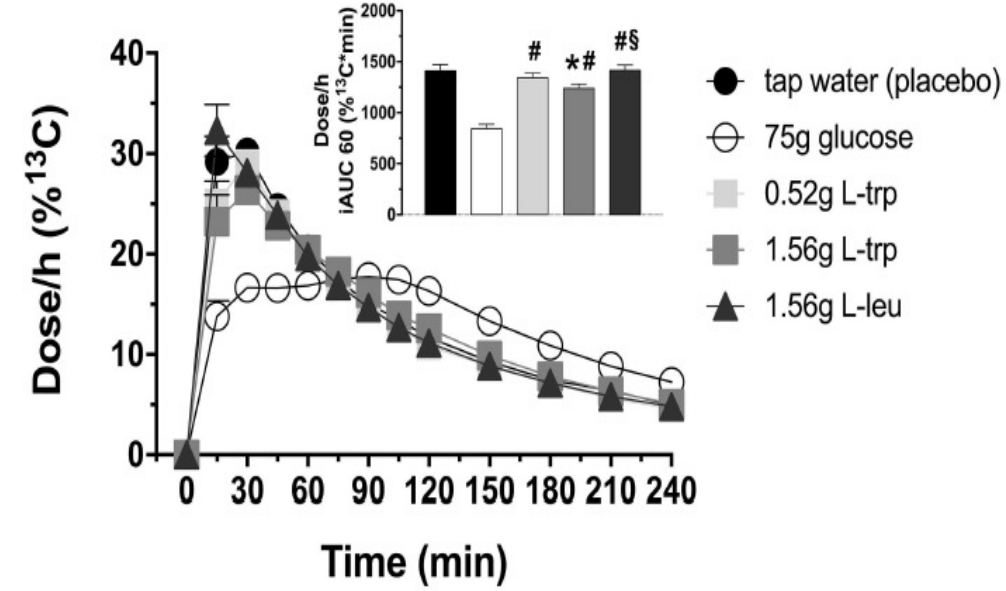


- 대상자는 남성과 여성 각각 10명으로, 마른 대상자 10명 + 비당뇨성 비만 대상자 10명을 포함
- **Randomized, double-blind, Parallel-Group Trial**

PLoS One 2016;11:e0166758







트립토판 500mg — 불면증 완화 및 포만감 형성

식물성 멜라토닌
타트체리 농축액 2,000mg
(멜라토닌 함유) — 불면증 완화

테아닌&마그네슘
& 비타민 B6 — 스트레스 완화&심신 안정

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Take Home Messages

- **Remember Main Treatment Options; medication, exercise, etc.**
- **Green tea, caffeine (coffee); Recommend usual drink**
- **Rebalance Gut microbiota**
  - SIBO Treatment; Normix 2t, tid, 2 weeks ~ 4weeks, maximum 3 months
  - **Consider Probiotics**
- **Exercise + enough dietary or supplementary Protein intake, if no contra-indication**
- **Consider to use Vitamin D (keep serum 25OHD, 40~60ng/ml), & omega 3 fatty acids (if exist CVD risk), tryptophan (PMS or sleep disturbance)**
- **Support Mitochondria function or remove ROS by IVNT**
  - **Myers' Cocktail, weekly or biweekly**
  - **± Arginine 30g iv or daily 9g oral**
- **Rebalance Hormones; recover adrenal function by adaptogens**
  - **In case of fatigue**