

FITOESTEROLES

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UDELAR

ECV

- ◆ 1ª Causa de muerte en mundo occidental
- ◆ Origen complejo, influyen muchos factores
- ◆ Colesterol plasmático elevado: indicador de riesgo

1ª ENCUESTA NACIONAL DE FACTORES DE RIESGO ECNT

COLESTEROL ELEVADO

- Colesterol total medio: **186.4 mg/dl**
- Porcentaje de adultos con colesterol total elevado (≥ 200 mg/dl): **33.3%**
- Porcentaje de adultos con colesterol total elevado (250 mg/dl): **5.8%**

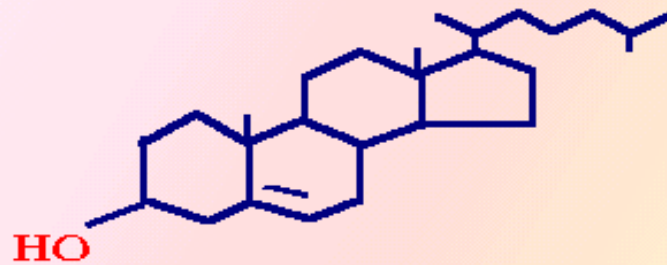
Manejo hipercolesterolemia

- ◆ Medidas en estilo de vida: alimentación, actividad física
- ◆ Inclusión de fármacos

Cómo llega el colesterol al plasma?

Como resultado de diferentes mecanismos

Estructura del colesterol



" Pool del Colesterol Orgánico "

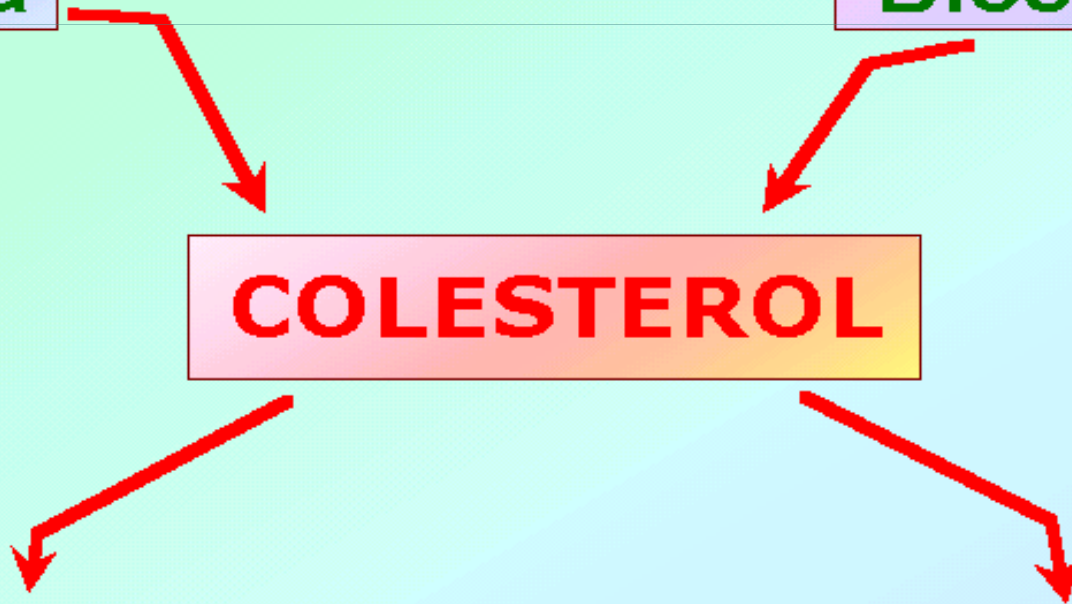
Dieta

Biosíntesis

COLESTEROL

Excreción

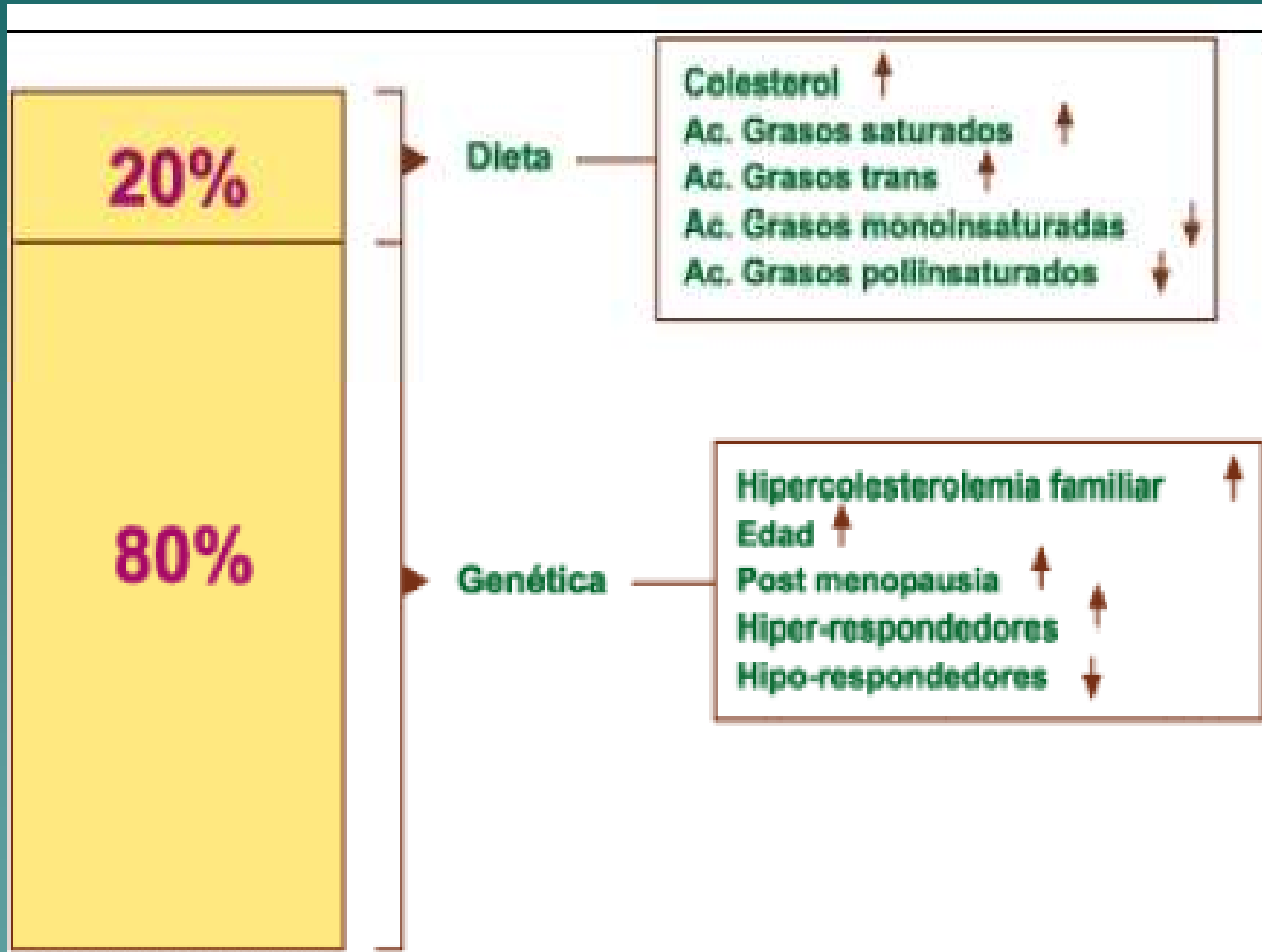
Uso metabólico



Estos mecanismos se ven afectados por diversos factores

- ◆ Edad
- ◆ Sexo
- ◆ Hábitos alimentarios
- ◆ Genotipo de cada persona

COLESTEROL PLASMÁTICO



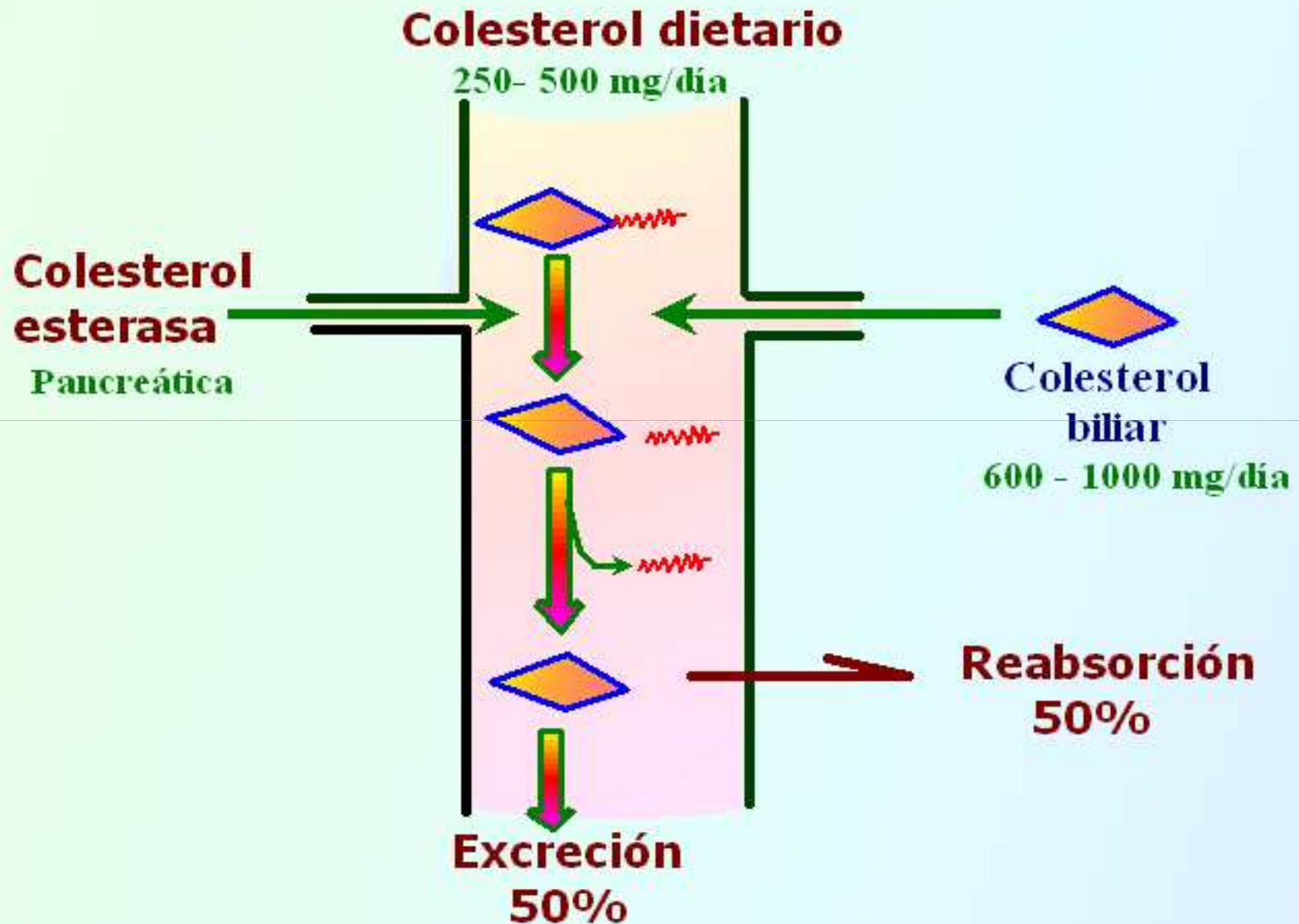
Colesterol a nivel intestinal

- ◆ Dietético: 250 a 500 mg/d (o más)
- ◆ Secreción biliar: 600-1000 mg/d



TOTAL: 850-1500 mg/d

Origen y destino del colesterol intestinal



Digestión y absorción del colesterol

Alimentos de origen animal

Bilis



Colesterol esterificado

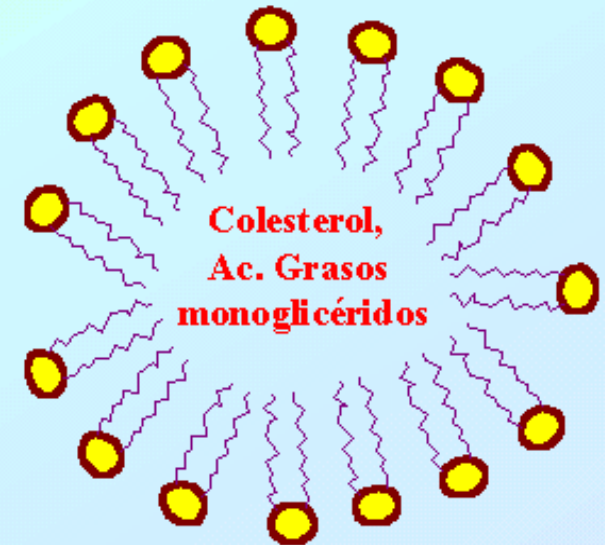
Colesterol esterasa pancreática

Páncreas



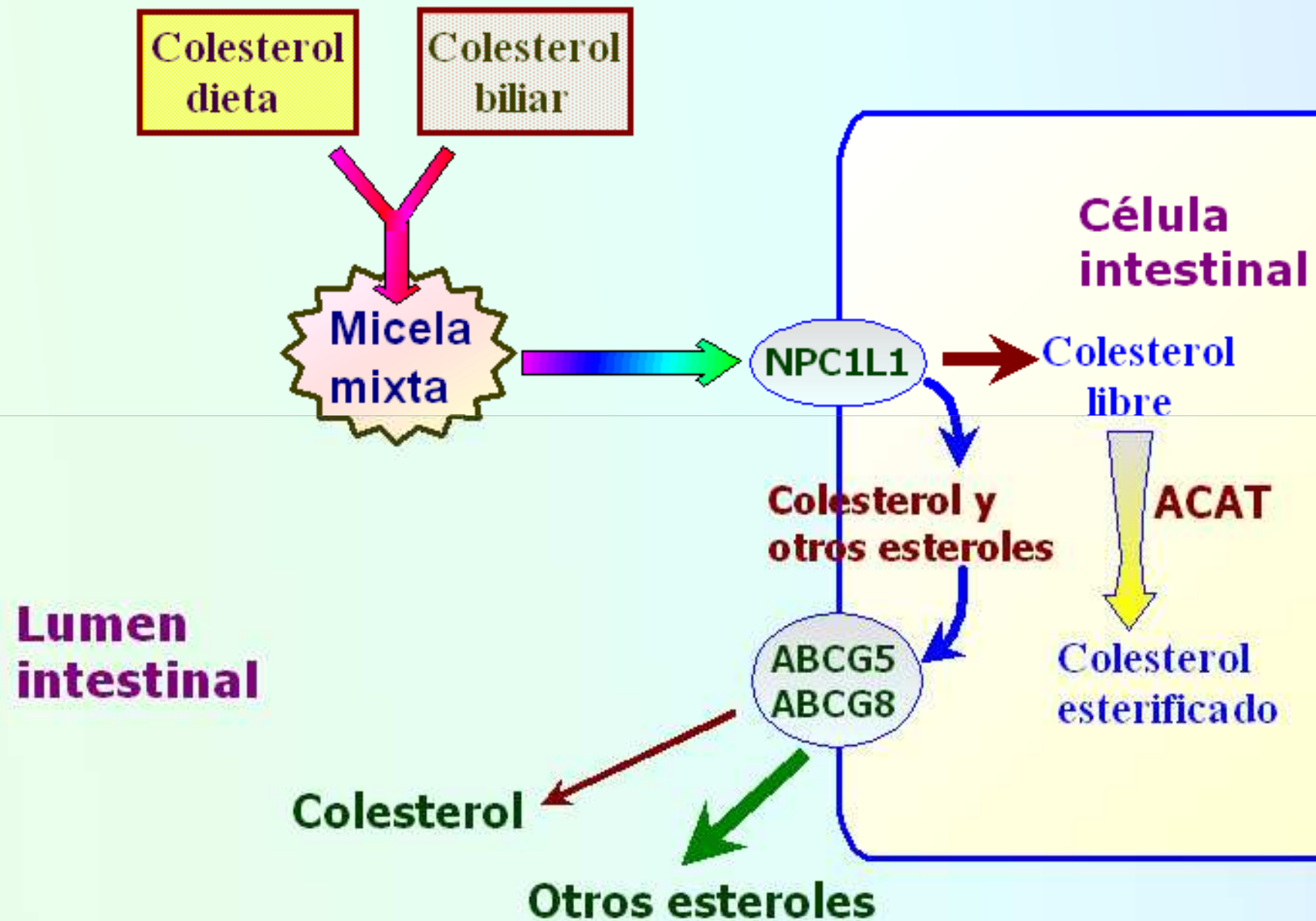
Fosfolípidos y colesterol

Ac. Grasos y monoglicéridos dietarios



Micela Mixta

Aspectos moleculares de la absorción del colesterol intestinal



FITOESTEROLES - FITOESTANOLES

- ◆ Esteroles de origen vegetal
- ◆ Estructura química similar al colesterol
- ◆ Presentes en hojas, tallos, semillas, frutas

FITOESTEROLES

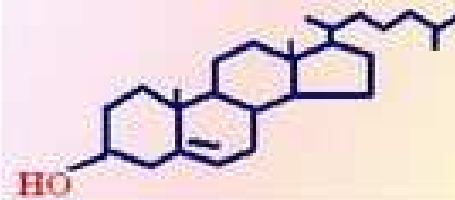
- ◆ Ingesta diaria variable: 160-500 mg/d
- ◆ Hay más de 25 estructuras químicas identificadas
- ◆ 3 son las que están en mayor proporción (95-98%): sitosterol, campesterol, stigmasterol
- ◆ Fitoestanoles: Reducción química del doble enlace de los fitoesteroles

Estructura de fitoesteroles y de fitoestanoles

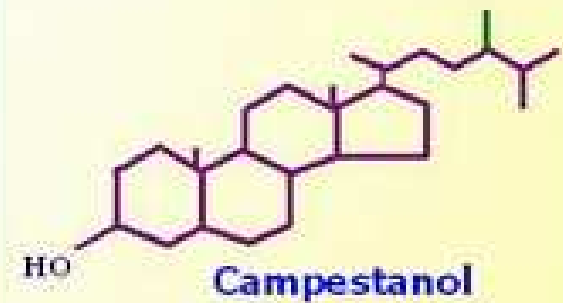
Fitoesteroles



Estructura del colesterol



Fitoestanoles



Efectos fisiológicos

- ◆ Antiinflamatorios
- ◆ Antitumorales
- ◆ Bactericidas
- ◆ Fungicidas
- ◆ HIPOCOLESTEROLEMIANTE (efecto más evidenciado científicamente)

Mecanismos de acción

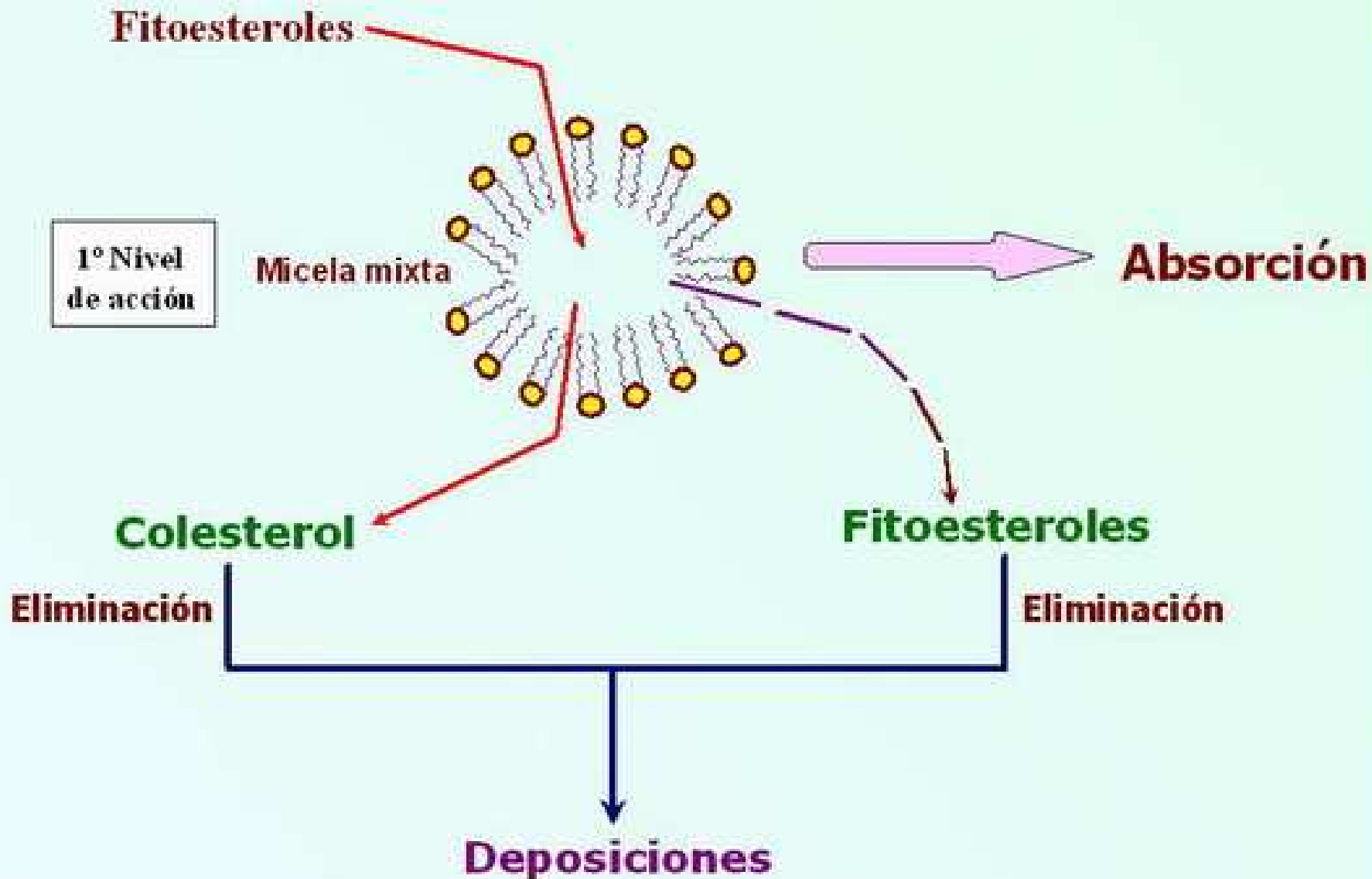
- ◆ **Luz intestinal:**

- Inhiben absorción de colesterol, por competencia al ingresar a la micela

- ◆ **Enterocito:**

- Inhiben reesterificación del colesterol
- Aumentan la actividad y síntesis de los transportadores del colesterol desde las células al lumen intestinal

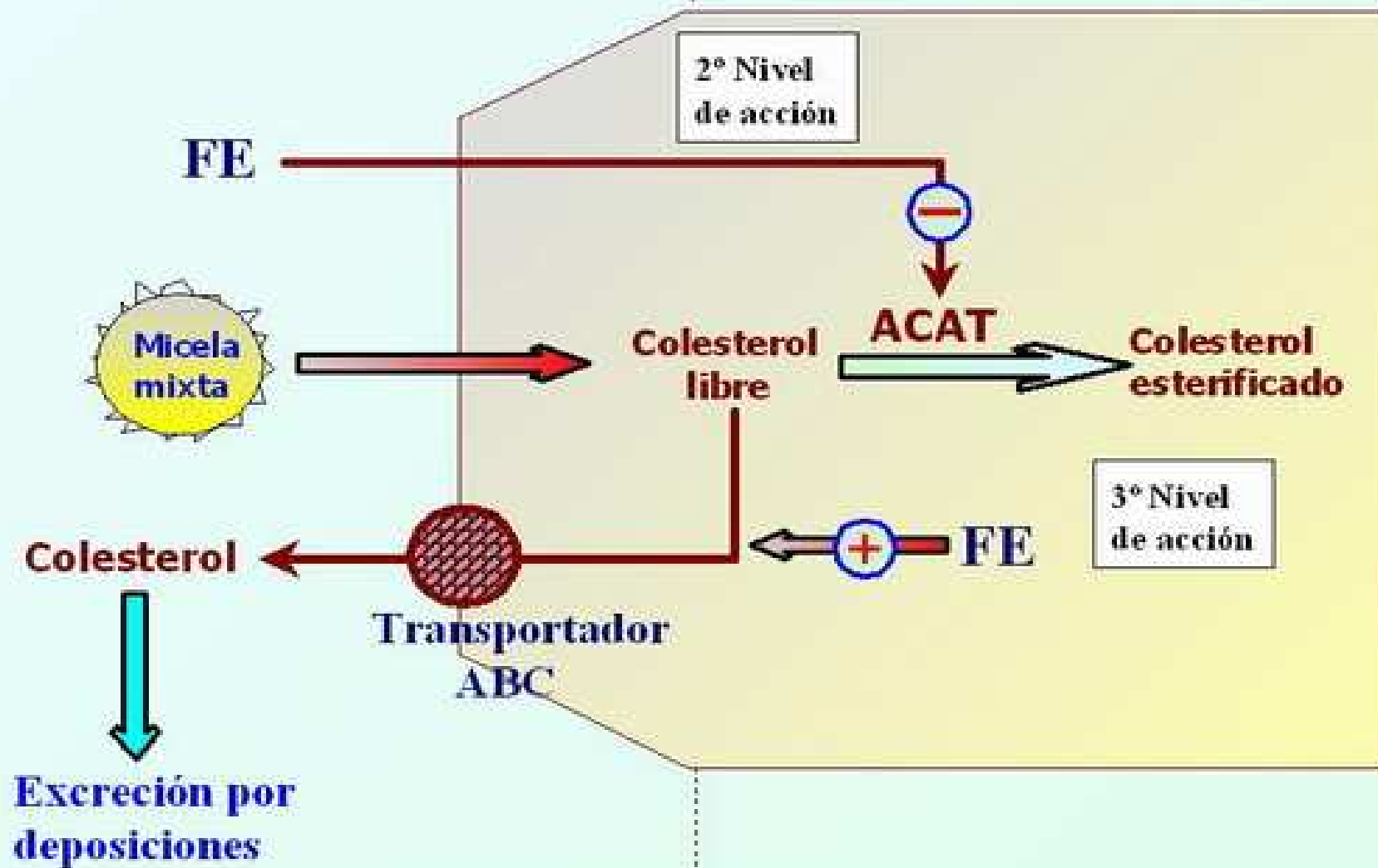
Efecto de fitoesteroles en el intestino delgado



Efecto de fitoesteroles a nivel de la célula intestinal

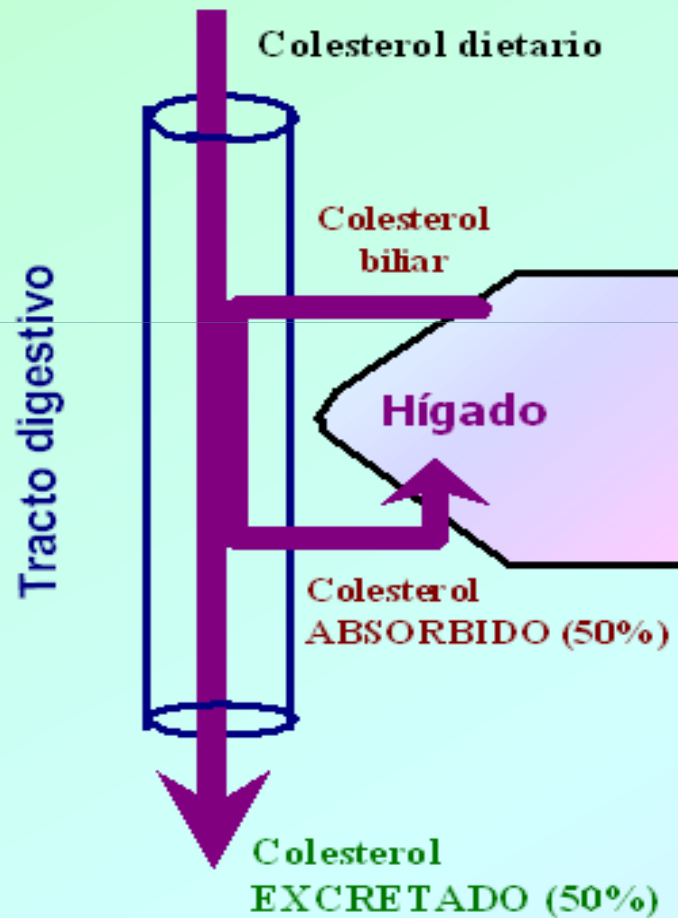
Lúmen intestinal

Célula intestinal

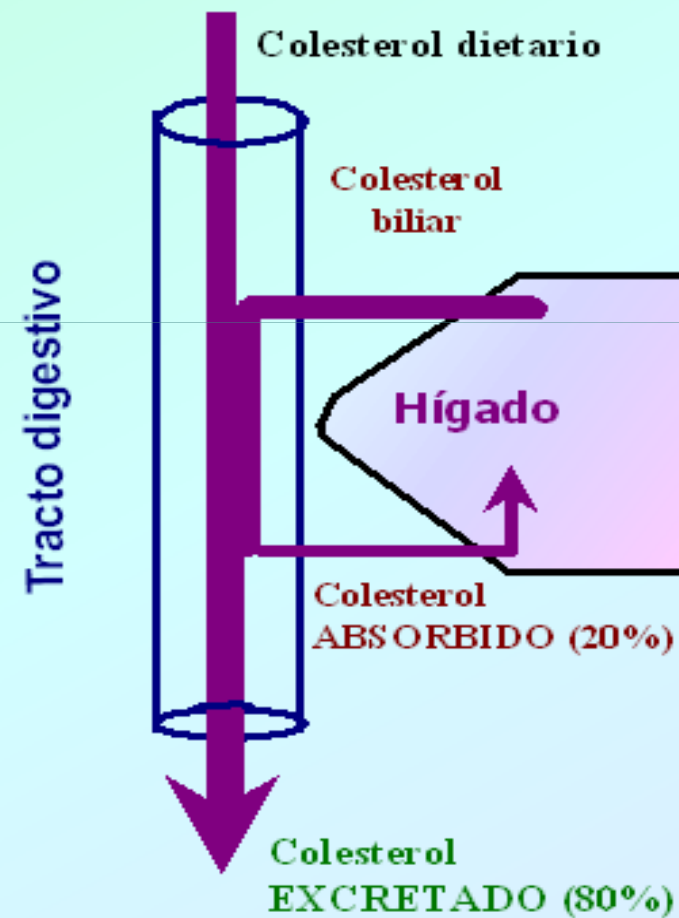


Efecto de fitoesteroles sobre la absorción y excreción del colesterol dietario

A. Dieta normal



B. Dieta enriquecida con fitoesteroles



TOXICIDAD

- ◆ En general los estudios realizados no muestran casi efectos secundarios
- ◆ Sugerencia: No superar el aporte de 8,6g/d (no hay estudios con dosis mayores)*
- ◆ Considerar consumo de productos enriquecidos

EFECTOS ADVERSOS

- ◆ Disminución de concentración de vitaminas liposolubles en plasma*:
 - β caroteno: hasta 25%
 - Vit E: hasta 8%
- ◆ Actúan protegiendo al LDL de oxidarse:
Al bajar LDL por fitoesteroles, se necesita menor cantidad de antioxidantes
- ◆ Por ajustes: Vit. E se mantiene, β caroteno disminuye entre 8 y 19%
- ◆ Sugerencia: aumentar consumo de alimentos fuente

PRODUCTOS ADICIONADOS

- ◆ Yogures
- ◆ Margarinas
- ◆ Aderezos para ensaladas
- ◆ Barritas de cereal

Mejor solubilidad en medio graso

Table 5. Blood lipid-lipoprotein level responses to sterols/stanol consumption and carotenoid/tocopherol concentrations across recent trials (continued)

| First author, (y), (reference) | Population/duration | Intervention (type) | Major findings |
|--------------------------------|---|--|---|
| Davidson et al (2001) (67) | N=84 men and women with mildly elevated LDL cholesterol level (130 mg/dL ^a); 8 wk | 0, 3.0, 6.0, and 9.0 g/d plant sterol esters were provided in 14 g reduced-fat spread and 46 g reduced-fat salad dressing per day. Subjects followed usual diet (randomized, double-blind, controlled design) | LDL cholesterol level decreased by 5%, 2.6% and 9% in the 3, 6, and 9 g/d groups, respectively, vs 1.3% in the 0 g/d group. The changes were not statistically significant. TC and HDL cholesterol levels did change. TG level increased in the control group, which was significantly different from the 3.0 g/d arm ($P<0.05$). Serum α - and <i>trans</i> -beta carotene levels were reduced in the 9.0 g/d group vs controls ($P<0.05$), but all carotenoid values were within normal ranges |
| Ntanios et al (2002) (66) | N=53 subjects (TC=213 mg/dL ^a); subjects stratified into cohorts on the basis of TC (<198 mg/dL ^a or >198 mg/dL ^a); 3 wk | 7.5 g spread at breakfast and 7.5 g at lunch or dinner were consumed. All subjects followed habitual Japanese diet (double-blind, controlled design) | TC and LDL cholesterol levels were 6% and 9% lower for all subjects, respectively, after consumption of free sterols ($P<0.001$). For the TC <198 mg/dL ^a group, TC and LDL cholesterol levels decreased 5% and 8%, respectively ($P<0.001$) and for the TC >198 mg/dL ^a group, they were 7% and 11% lower, respectively ($P<0.001$). The decreases were similar between the two cohorts. HDL cholesterol and TG levels did not change in any group. Plasma β -carotene was lower (21%) in subjects consuming plant sterols ($P<0.001$). Plasma vitamin A and E levels did not differ |
| Noakes (2002) (81) | n=20 men, n=26 women with hypercholesterolemia; 3 wk | 25 g spreads per day, 3-way comparison study with 2.3 g sterol esters or 2.5 g stanol esters vs control. In addition, participants were advised to eat ≥ 5 servings of vegetables and fruit per day, of which ≥ 1 serving was from a high-carotenoid source. Subjects followed diets low in total and saturated fat (randomized double-blind, crossover design). | TC decreased 6.1% and 7.3% on sterol ester and stanol ester treatments, respectively ($P<0.001$), and LDL cholesterol level decreased 7.7% and 9.5%, respectively ($P<0.001$). The decreases on sterol vs stanol ester treatments were similar. HDL cholesterol and TG levels did not change. Consumption of 1 serving per day of high-carotenoid fruit or vegetable resulted in plasma carotenoid levels in the treatment groups that were similar to the control group. |
| Vanstone 2002 (79) | N=15 participants with primary familial hyperlipidemia; 3 wk | Four treatments: plant sterols (1.8 g/d); plant stanols (1.8 g/d); 50:50 mix of sterols and stanols (1.8 g/d); corn starch control. Subjects followed an average Canadian diet (randomized, crossover design) | TC level decreased 7.8%, 11.9%, 13.1% vs control, respectively ($P<0.01$). LDL cholesterol level decreased 11.3%, 13.4%, 16.0% vs control ($P<0.03$). HDL cholesterol and TG levels did not change. |
| Quilez (2003) (63) | N=57 patients with normocholesterolemia; 8 wk | 3.2 g/d sterol esters in croissants and magdalenas; also enriched in α -tocopherol and beta carotene. Subjects followed an average Western diet (randomized double-blind, placebo-controlled design) | TC and LDL cholesterol levels decreased by 8.9% and 14.7%, respectively ($P<0.001$). HDL cholesterol and TG levels did not change nor did plasma tocopherol or carotenoid levels. |

(continued)

Table 5. Blood lipid-lipoprotein level responses to sterols/stanol consumption and carotenoid/tocopherol concentrations across recent trials (continued)

| First author, (y), (reference) | Population/duration | Intervention (type) | Major findings |
|--------------------------------|---|---|---|
| Hendriks (2003) (64) | N=185 participants with normo- or mild hypercholesterolemia participants; 39 wk | 20 g spread with 1.6 g sterol esters per day. Subjects followed an average Dutch diet (randomized double-blind, placebo-controlled parallel arm design) | TC and LDL cholesterol levels decreased by 4% and 6%, respectively ($0.01 < P < 0.05$). β -Carotene concentrations decreased 15%-25% but carotenoid concentrations were not lower when expressed relative to LDL cholesterol. |
| Dewaraj (2004) (75) | N=72 free-living adults with mild hypercholesterolemia; 8 wk | Orange juice fortified with plant sterols (2 g/d). Subjects followed an average American diet (randomized, placebo-controlled design) | TC and LDL cholesterol levels decreased 7.2% and 12.4%, respectively ($P < 0.01$). HDL cholesterol and TG levels did not change. |
| Jauhainen (2006) (68) | N=67 men and women with mild hypercholesterolemia; 5 wk | 2 g plant stanols/d provided in 50 g low-fat cheese. Subject were instructed to follow their usual diet. (randomized, double-blind parallel arm design) | TC decreased 6% ($P < 0.001$), LDL cholesterol level decreased 10% ($P < 0.001$). HDL cholesterol and TG levels did not change. |
| Gylling (2006) (71) | N=38 women with mild hypercholesterolemia without heart disease; 12 mo | 3 g stanol ester/d provided in 24 g margarine for up to 6 mo. For remaining 6 mo, subjects were randomized to 2 g or 3 g stanol ester/d (double-blind, randomized parallel arm design) | LDL cholesterol level decreased 10% ($P < 0.05$) with 2 g/d and 17% with 3 g/d ($P < 0.01$) |
| Goldberg (2006) (69) | N=26 patients with hypercholesterolemia on statin therapy; 6 wk | Stanol tablets (1.8 g/d) were given to subjects following an American Heart Association heart-healthy diet and on long-term statin therapy (double-blind, placebo-controlled parallel arm design) | LDL cholesterol level decreased 9.1% ($P = 0.007$), TC decreased 12.9 mg/dL ^a ($P = 0.03$). HDL cholesterol and TG levels did not change. |
| Castro Cabezas (2006) (70) | N=20 patients on lipid-lowering medications (11 treatment subjects); 6 wk | Stanol margarine (30-35 g/d); 3 g plant stanols given. Subjects followed a habitual diet (single-blind, randomized design). | LDL cholesterol level decreased 15.6% in the treatment group and 7.7% in the control group (no significant difference between groups). HDL cholesterol and TG levels did not change. |

^aTC = total cholesterol.

^bLDL = low-density lipoprotein.

^cTo convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.0259. To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.7. Cholesterol of 193 mg/dL = 5.00 mmol/L.

^dHDL = high-density lipoprotein.

^eTG = triglycerides.

^fTo convert mg/dL triglycerides to mmol/L, multiply mg/dL by 0.0113. To convert mmol/L triglycerides to mg/dL, multiply mmol/L by 88.6. Triglycerides of 159 mg/dL = 1.80 mmol/L.

- ◆ Trabajos con 2 a 3g de fitoesteroles diarios muestran hasta 15% de descenso del CT y LDLc.
- ◆ De utilizar productos adicionados considerar sustitución isocalórica por otros
- ◆ Trabajos que combinan fitoesteroles con estatinas muestran que los efectos se suman

Niños y adolescentes

Estudio en Noruega:

- ◆ Cambios en el lípidos plasmáticos y vitaminas liposolubles con ingesta de margarina con esteroides
- ◆ 37 niños, 20 padres con hipercolesterolemia familiar.
- ◆ Dosis esteroides: 1,2g/d niños-1,6g/d padres
- ◆ Seguimiento: 6 meses

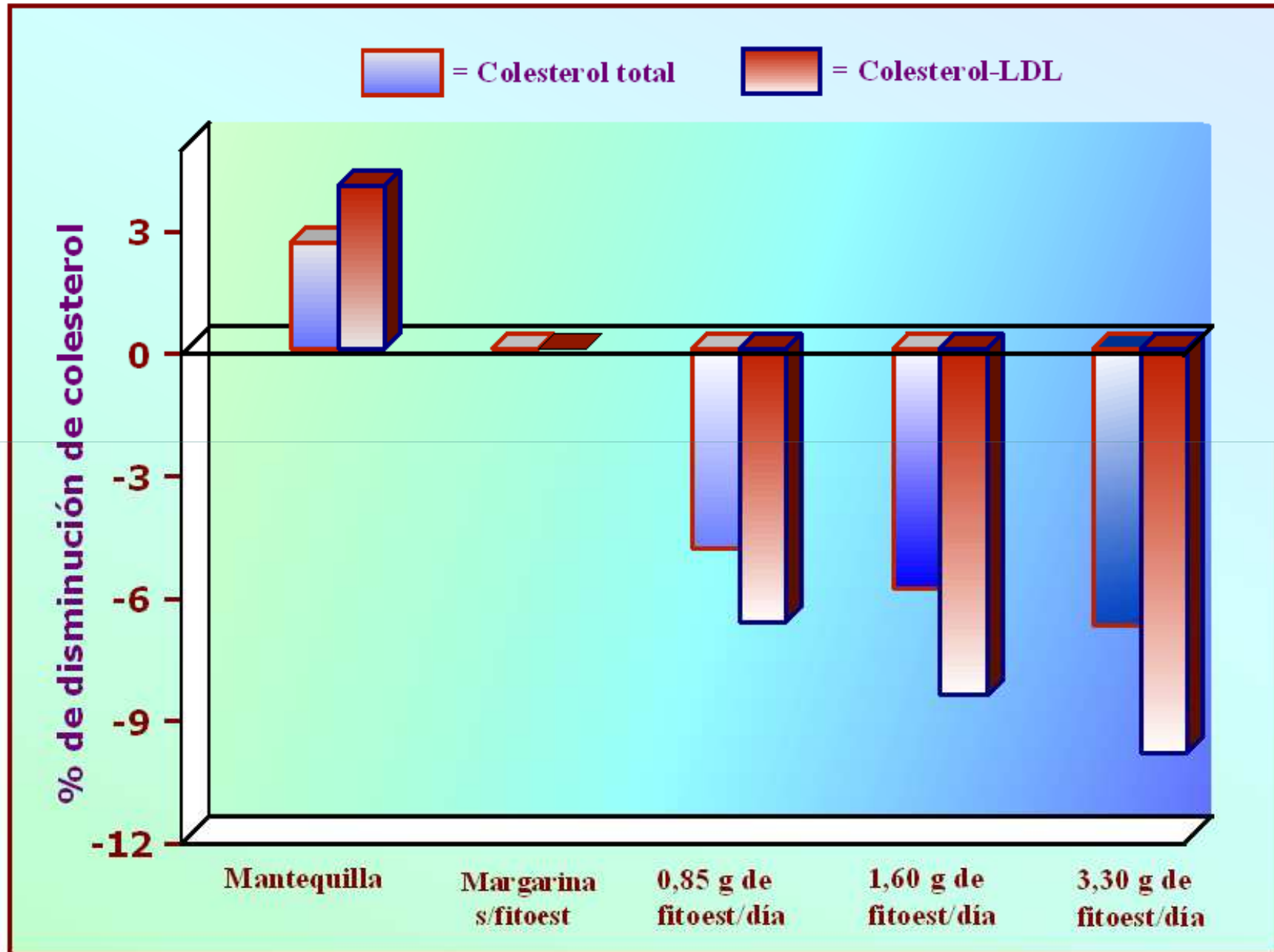
Resultados

- ◆ CT: ↓ 9,1% en padres y niños
- ◆ LDLc: ↓ 11,4% en niños y 11% en padres
- ◆ β caroteno: Incambiado en padres
↓ 10,9% en niños (luego aumenta en seguimiento)

Contenido de fitoesteroles de algunos aceites

| Alimento | Fitoesteroles mg/ 100 g porción comestible |
|--------------------------|---|
| Aceite de maíz | 952 |
| Aceite de girasol | 725 |
| Aceite de cártamo | 444 |
| Aceite de soja | 221 |
| Aceite de oliva | 176 |
| Almendras | 143 |
| Habas | 76 |
| Maíz | 70 |
| Trigo | 69 |
| Aceite de palma | 49 |
| Lechuga | 38 |
| Plátano | 16 |
| Manzana | 17 |
| Tomate | 7 |

Efecto del consumo de mantequilla, margarina y de margarinas con diferentes cantidades de fitoesteroles en el colesterol total y en el colesterol-LDL*



Incorporación de los fitoesteroles/fitoestanoles al "portfolio" reductor del colesterol-LDL de acuerdo al Adult Treatment Panel III (ATP III) del National Cholesterol Education Program (NCEP)*

| Modificación de la dieta | Recomendación | Reducción aproximada (%) del colesterol-LDL |
|--|-------------------------------------|--|
| Grasa saturadas | reducción a < 7% calorías | 8% - 10% |
| Fitoesteroles/fitoestanoles | 2g/día a 3g/día | 6% - 10% |
| Reducción de colesterol dietario | menos de 200mg/día | 3% - 5% |
| Incorporación de fibra | 5 - 10g/día fibra soluble | 3% - 5% |
| Reducción de peso | 4 a 5 Kg de reducción | 5% - 8% |
| Efecto total de reducción de colesterol-LDL | | 25% - 30% |

MUCHAS GRACIAS!