Role of Plant Flavonoids in Skin Health

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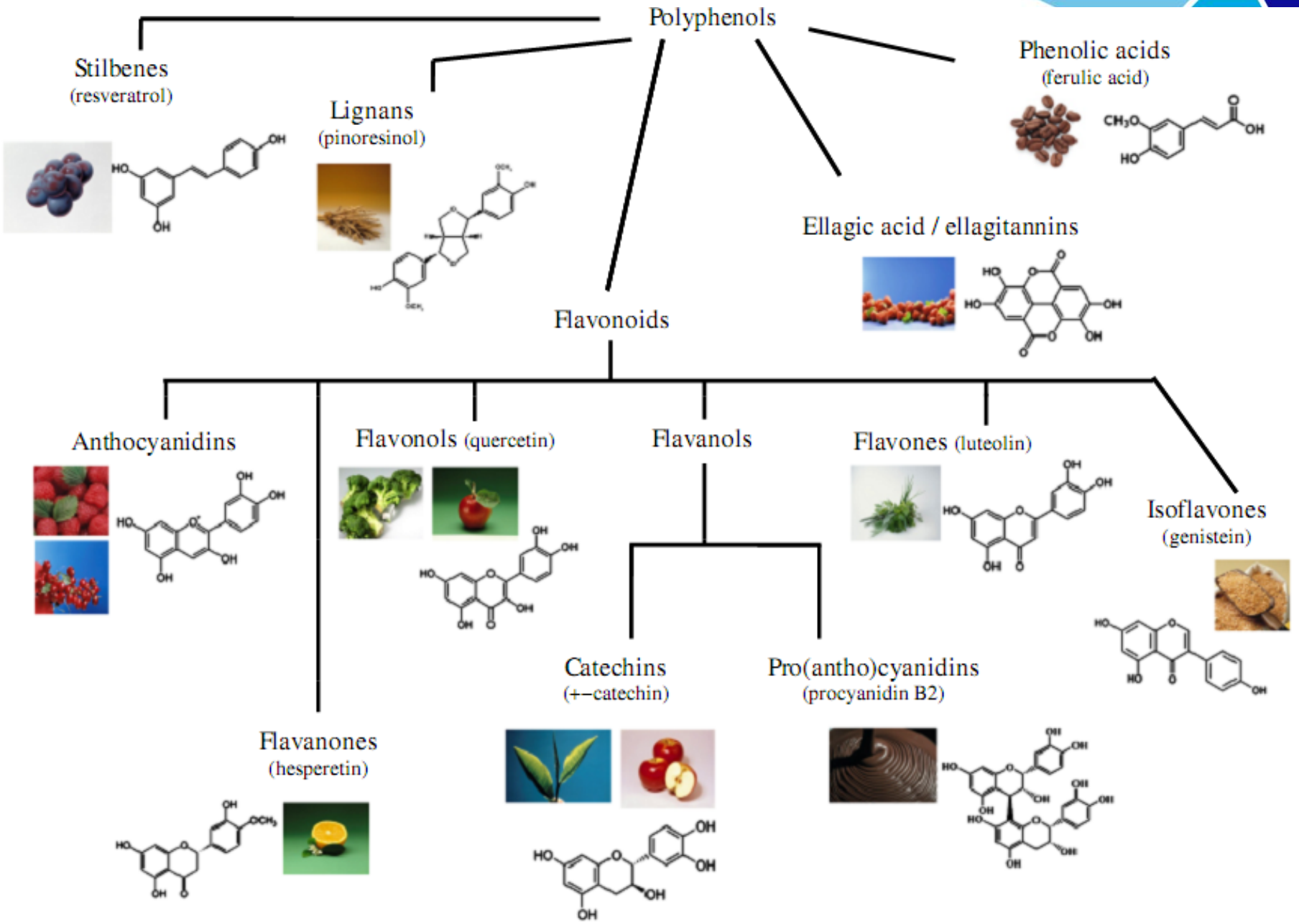
Presented at 5th Comoceutical Summit Conference
Renaissance Shanghai Pudong Hotel
25th ~ 26th Oct, 2012



Different classes of polyphenols, their known plant and fruit sources

Source: Clin Exp Allergy, 41, 1346–1359

Multiple benefits of flavonoids

Plant flavonoids possess a range of biological activity:

- Estrogen-like activity
- Direct influence on extracellular matrix
- Cardiovascular protective effect
- Anti-inflammatory and anti-allergic effect
- Photoprotection
- Anti-microbial activity

Source: Clin Dermatol, 2008, 26, 347–357

Estrogen-like activity

Phytoestrogens

- Naturally found in plant foods and structurally related to endogenous estrogens;
- Present in many diets, especially in Asia;
- Classified into flavonoids and liganins;
- Demonstrating higher binding affinity for estrogen receptor (ER) β which is dominantly expressed in skin and its appendages, than for ERα.

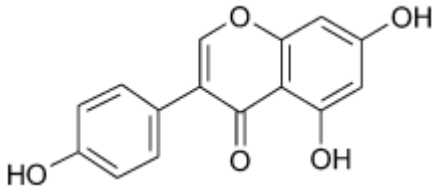


Fig. Structure of genistein

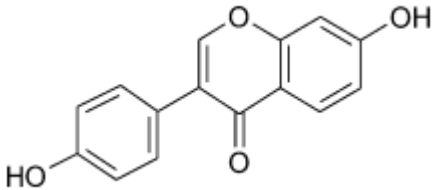


Fig. Structure of daidzein

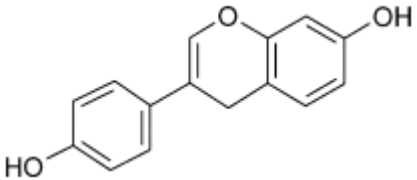
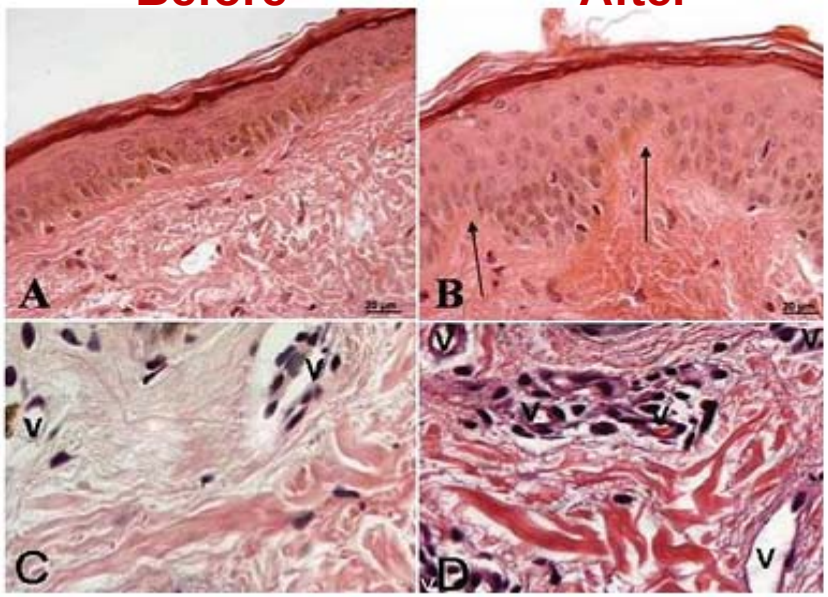


Fig. Structure of equol

Estrogen-like activity



6-month isoflavonoid rich soy extract human intervention study

Fig. A histological gluteal skin section from a patient before (A, C) and after (B, D) treatment with isoflavones.

The arrows indicate the dermal papillae, and "v" are the vessels. (A and B 250x; C and D 450x, H.E.)

Table Skin histological parameters in postmenopausal subjects (n=30)

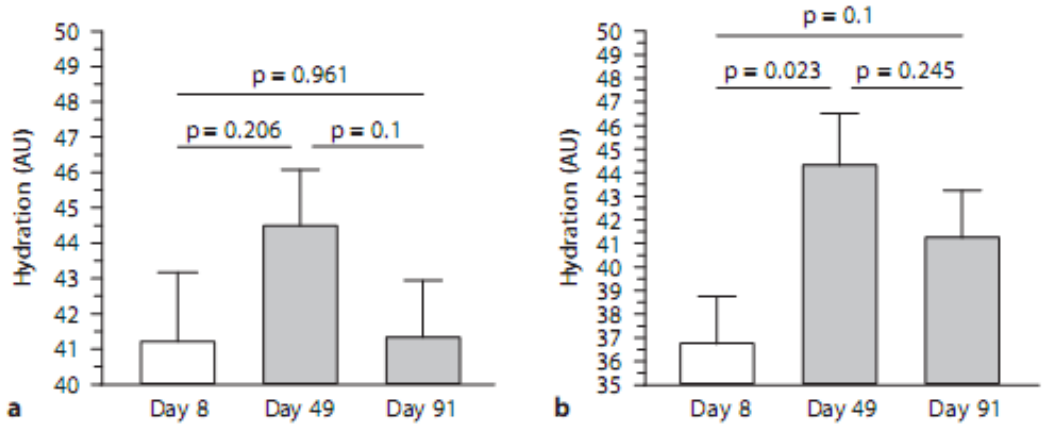
Parameters	Before treatment	After treatment
epithelial thickness (μm)	560.8 ± 4.4	613 ± 4.6*
epidermal papillar index (%)	10.4 ± 1.9	14.7 ± 4.0*
dermal collagen (no units)	152.0 ± 2.2	163.0 ± 2.3*
elastic fibers (no units)	525.4 ± 4.2	611.2 ± 4.6*
dermal vessels (number per slide)	64.2 ± 1.4	1.1 ± 1.6*

*$p<0.01$ compared to data before treatment by paired Student's t-test.

Source: Clinics 2009, 64:505-10

Direct effect of extracellular matrix - Pycnogenol

a.Whole study population (n = 20) **b. Subjects with dry skin (n=13)**



12-week Pycnogenol human intervention study

Fig. **Skin hydration** assessed with a Corneometer CM 825. The statistical significance was obtained by t test, and p values less than 0.05 were considered statistically significant.

a. Cutometer MPA 580 - R2 **b. Cutometer MPA 580 - R7**

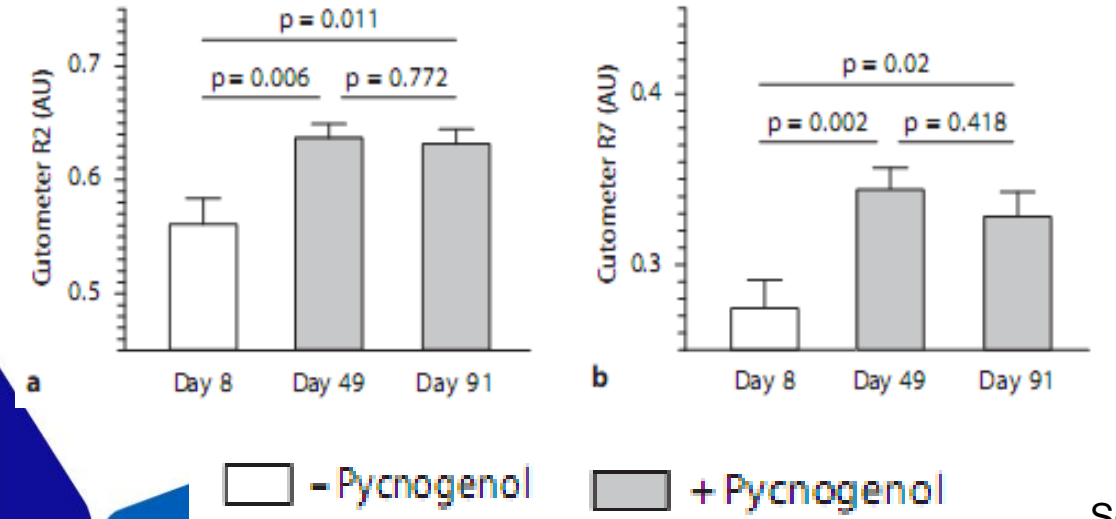
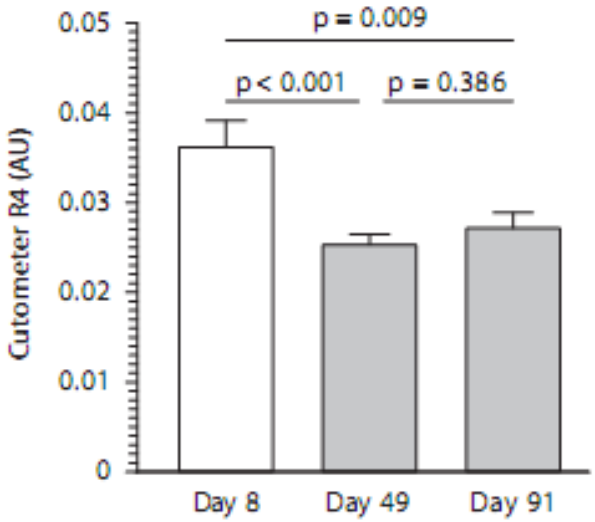


Fig. **Skin elasticity** measured with Cutometer MPA 580. The statistical significance was obtained by t test, and p values less than 0.05 were considered statistically significant.

Source: Skin Pharmacol Physiol 2012;25:86–92

Direct effect of extracellular matrix - Pycnogenol

Cutometer MPA 580 – R4



12-week Pycnogenol human intervention study

Fig. **Skin fatigue** assessed by cutometry. The statistical significance was obtained by t test, and p values less than 0.05 were considered statistically significant.

Hyaluronic acid synthase-1 (HAS-1)

Collagen (COL) 1A1 & 1A2

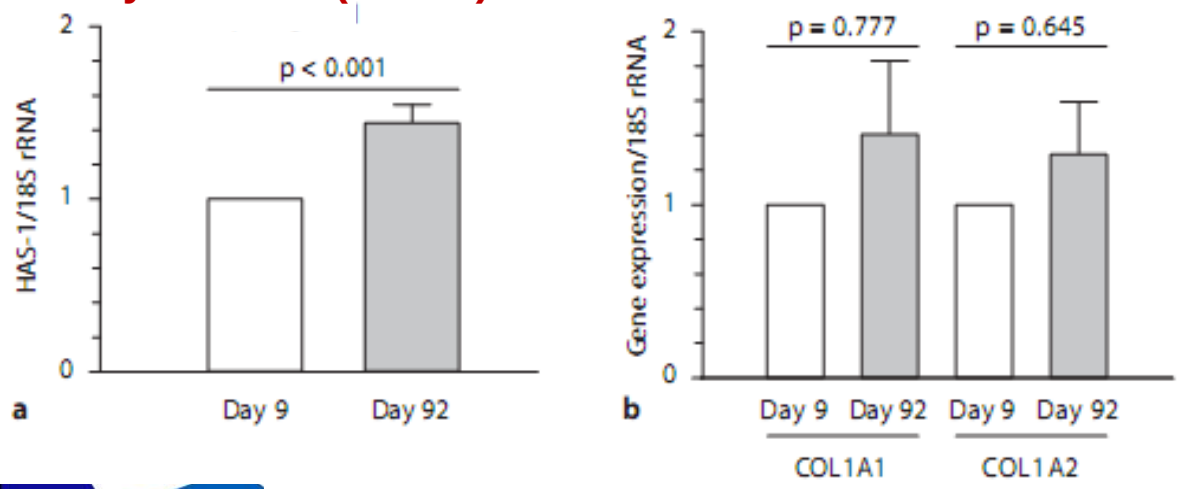


Fig. **Gene expression** of HAS-1, collagen (COL) 1A1 and 1A2. Statistical significance was evaluated by Wilcoxon signed-rank test.

Source: Skin Pharmacol Physiol 2012;25:86–92

Direct effect of extracellular matrix – Cocoa polyphenols

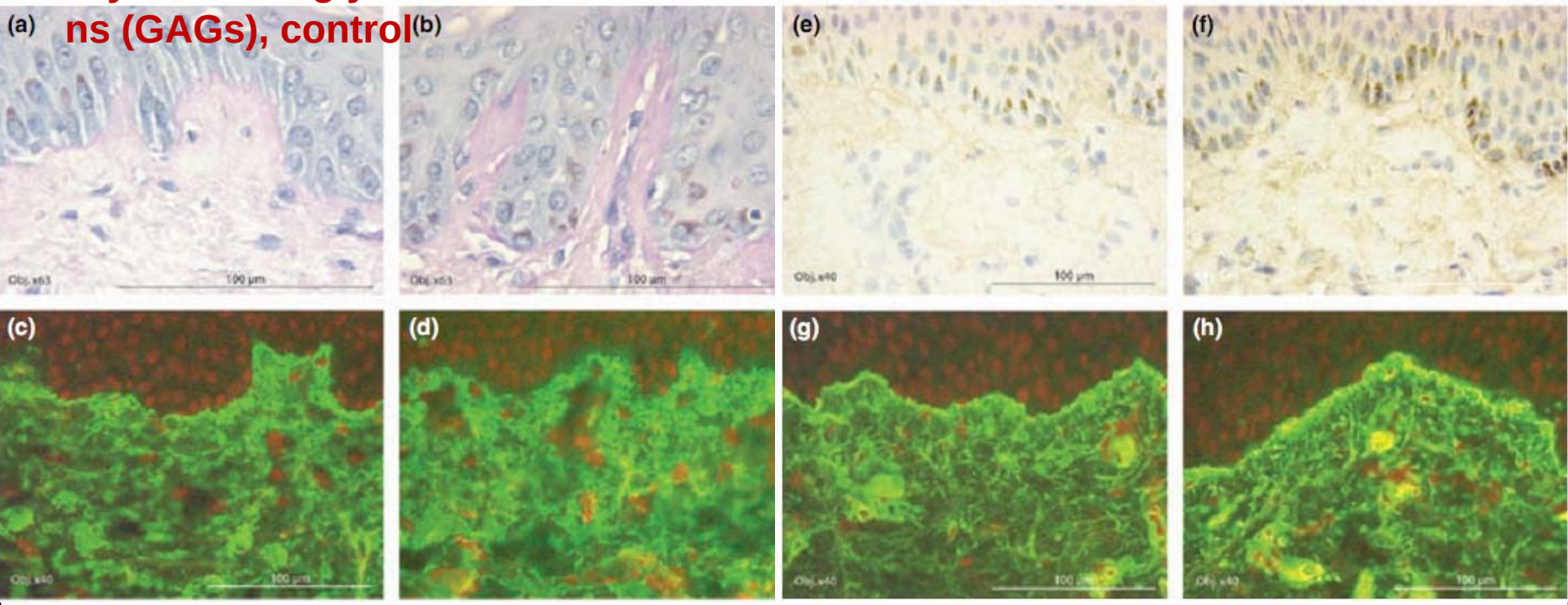
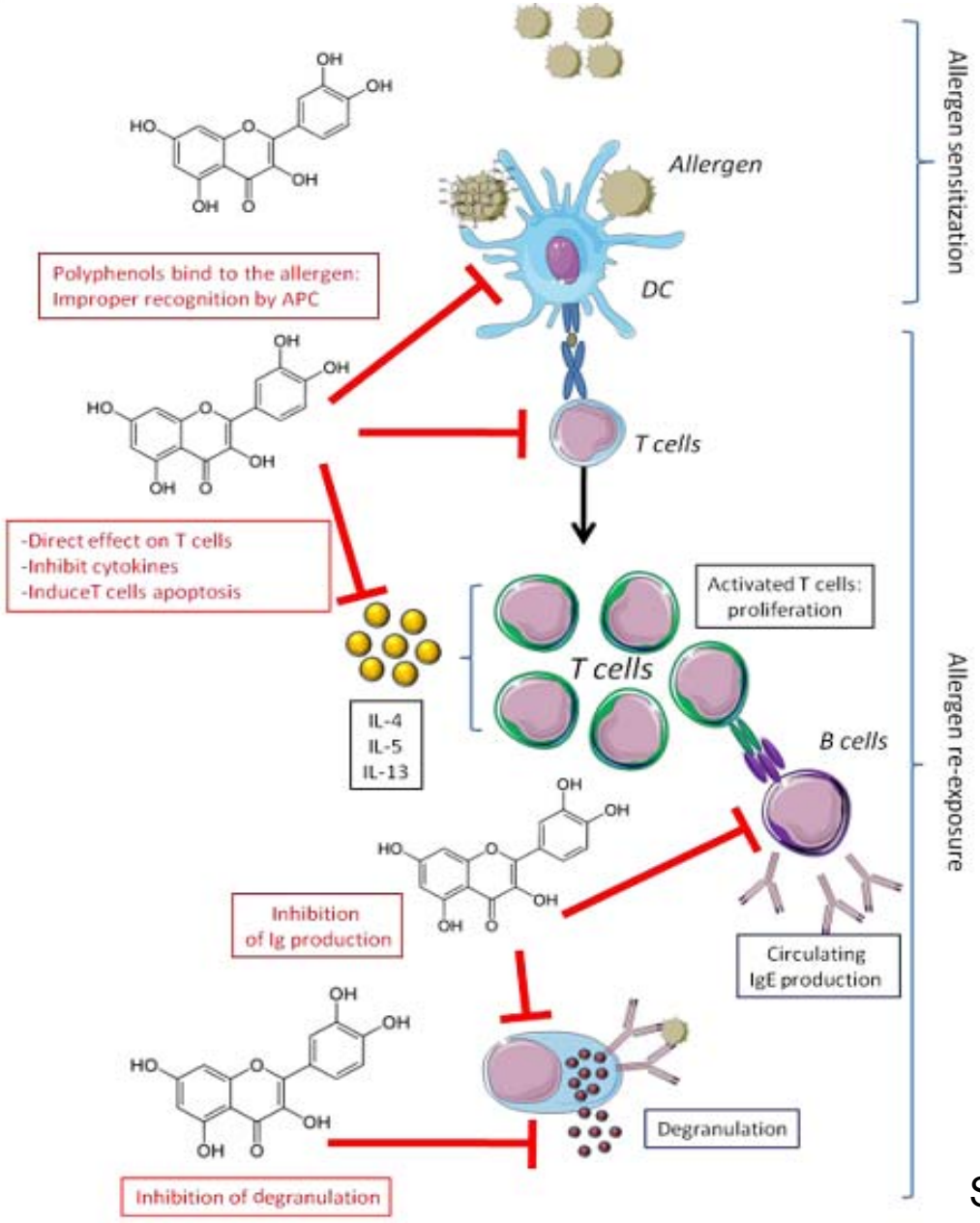


Fig. Effect of cocoa polyphenols blended in cocoa butter (CPP) on extracelluar matrix in *ex vivo* human skin.

Source: Int J Cos Sci. 2008, 30: 339–45

Anti-allergic/anti-inflammatory effect



Multiple anti-allergic mechanisms:

- Polyphenols bind to allergen
- Direct effect on T cell, e.g. inhibiting cytokines, inducing T cell apoptosis
- Inhibition of Ig production
- Inhibition of degranulation

Source: Clin Exp Allergy, 2011, 41: 1346–1359

Anti-inflammatory effect – Oolong tea

Before

After

Fig. A 21-year-old patient with recalcitrant atopic dermatitis.

6-month open clinical trial

Patients: 121 patients (mean age, 24 yrs) with refractory atopic dermatitis (AD).

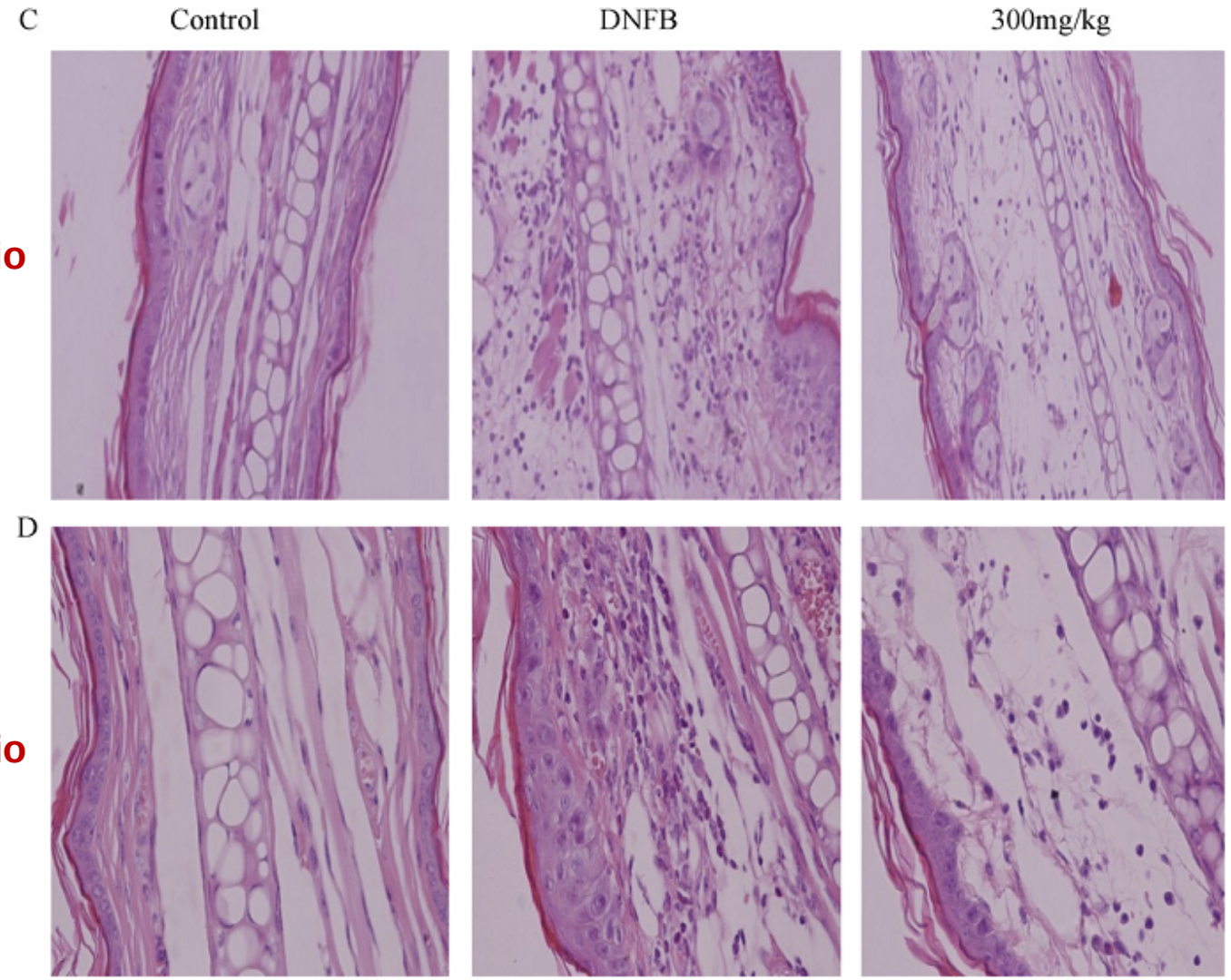
Intervention: Drinking oolong tea 3 times daily for 6 month. 10 g of dried oolong tea leaves was placed in 1000 mL boiling water and steeped for 5 min. The oolong tea was divided into 3 parts and drunk after 3 regular meals.

Efficacy of 1- and 6-Month Oolong Tea Treatment in 118 Patients With Atopic Dermatitis

Period of Oolong Tea Treatment, mo	Clinical Response to Oolong Tea, No. (%) of Patients				
	Markedly Improved	Moderately Improved	Slightly Improved	Unchanged	Worsened
1	20 (17)	54 (46)	18 (15)	22 (19)	4 (3)
6	9 (8)	56 (47)	29 (24)	21 (18)	3 (3)

Source: Arch Dermatol, 2001, 137: 42-43.

Anti-inflammatory effect – Grape seed proanthocyanidins



original magnification 200×

original magnification 400×

Fig. 8-day orally administered grape seed proanthocyanidins (GSPs) reduced ear swelling induced by 2,4-dinitrofluorobenzene (DNFB) in mice.

Source: Toxicol Let 2012, 210:1–8

Anti-inflammatory effect

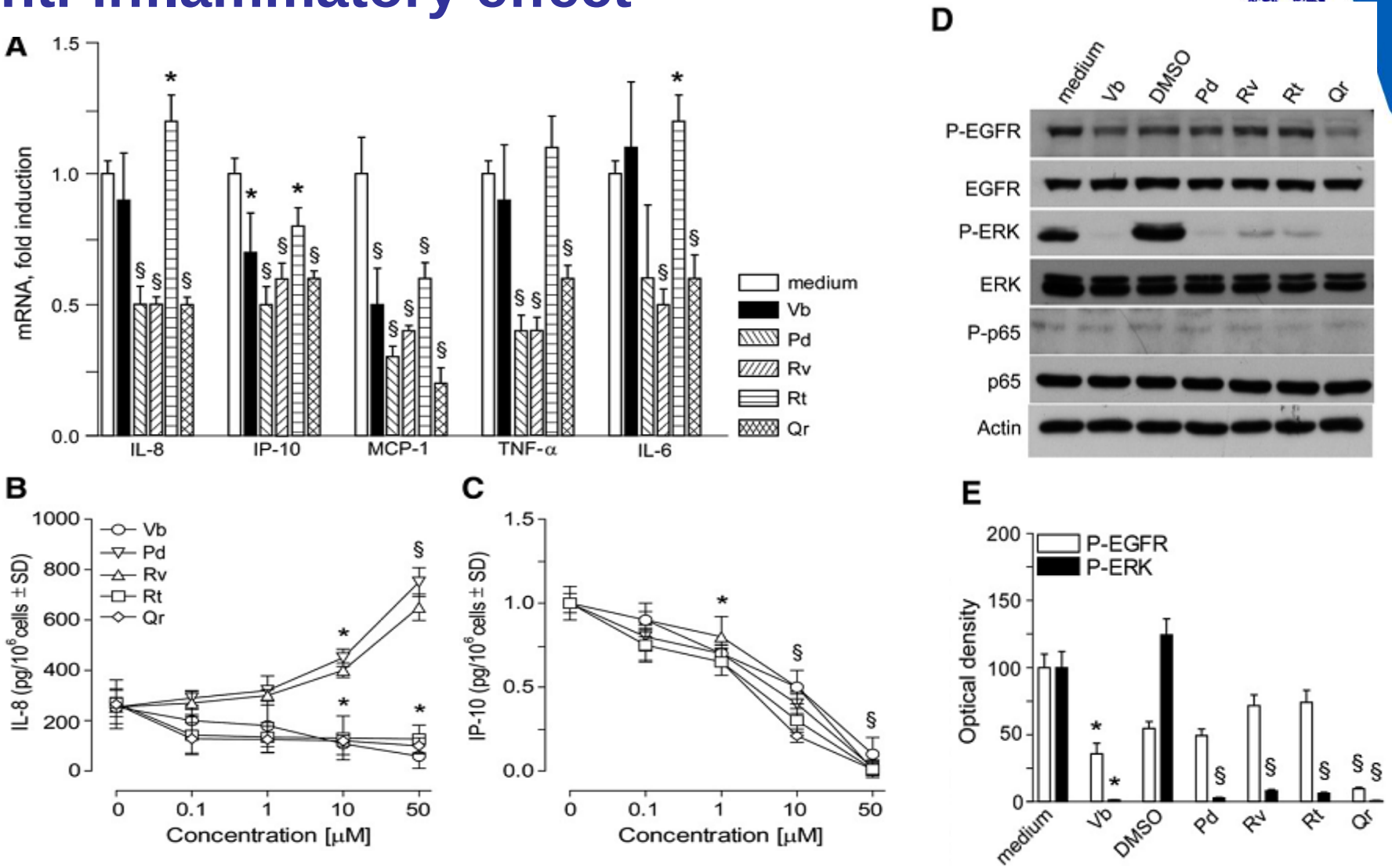
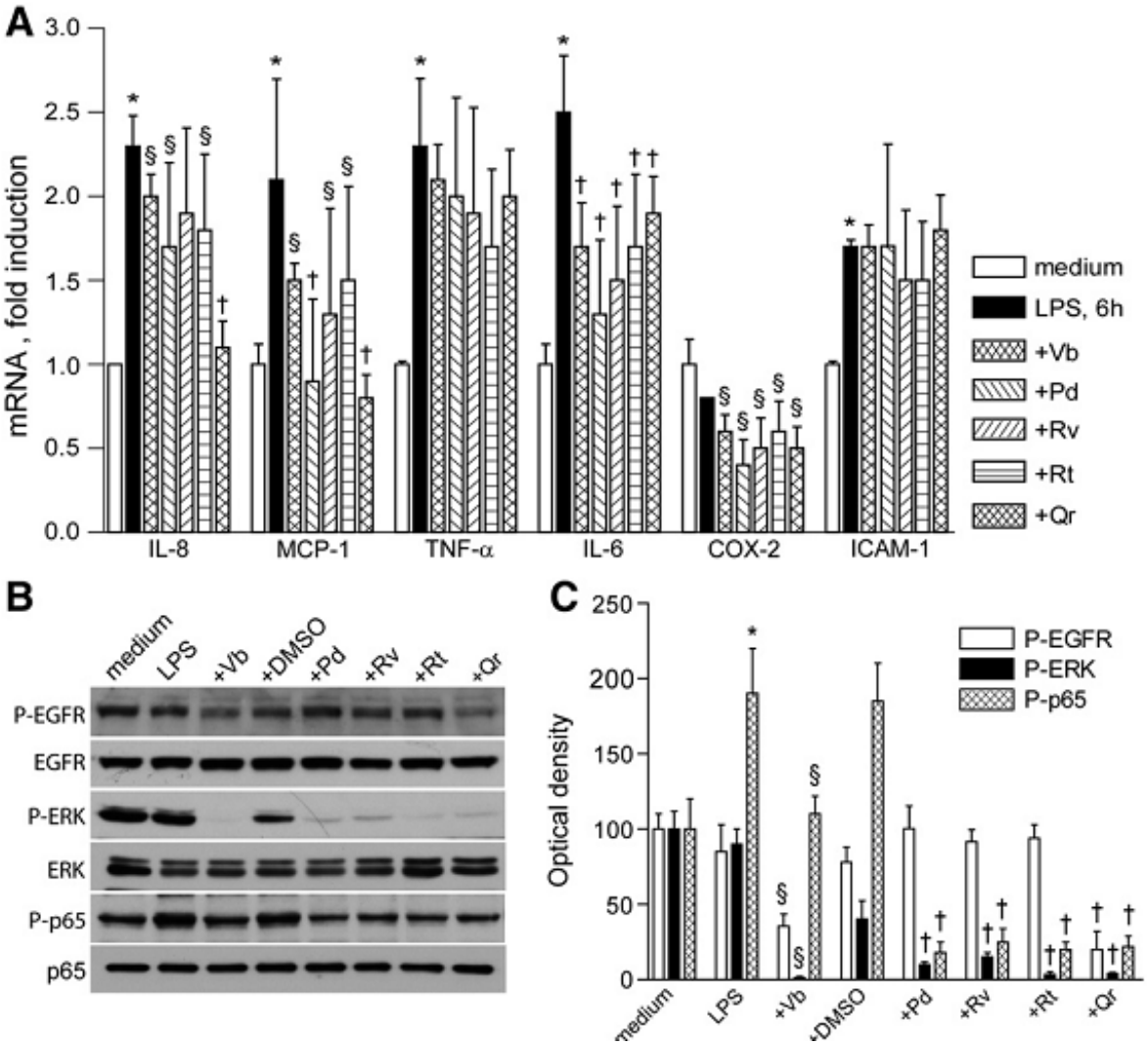


Fig. Effects on pro-inflammatory gene expression and release and protein phosphorylation in normal human epidermal keratinocytes (NHEK). 50 μM verbascoside (Vb), resveratrol (Rv), polydatin (Pd), rutin (Rt), or quercetin (Qr). *P<0.05; §P<0.01 *vs* control.

Source: Toxicol Applied Pharmacol 2011, 255:138–149

Anti-inflammatory effect



*P<0.01 *vs* untreated controls, § P<0.05 and † P<0.01 *vs* LPS.

*P<0.01 *vs* untreated controls, § P<0.01 *vs* LPS, † P<0.01 *vs* 0.25% DMSO+LPS

Fig. Modulation of lipopolysaccharide (LPS)-induced gene expression and NFκB activation, as well as ERK, and EGFR phosphorylation by plant polyphenols.

Source: Toxicol Applied Pharmacol 2011, 255:138–149

Anti-inflammatory effect - Quercetin

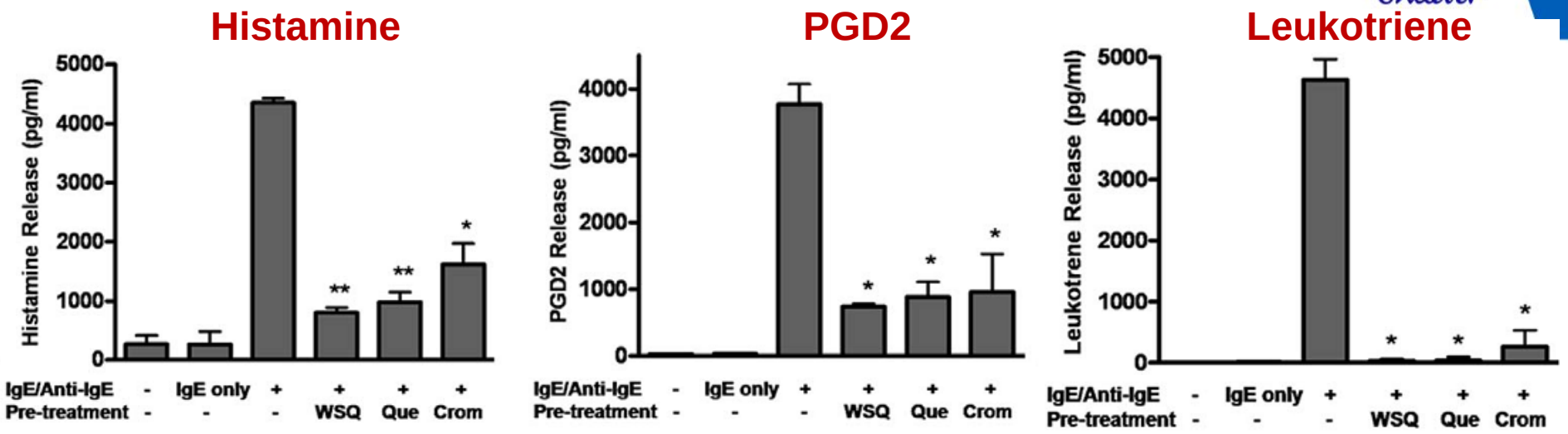


Fig. Quercetin inhibited degranulation of primary human cord blood-derived cultured mast cells (hCBMCs) triggered by IgE/Anti-IgE. * $p<0.05$, ** $p<0.01$. WSQ=water soluble quercetin; Que = quercetin; Crom= cromolyn.

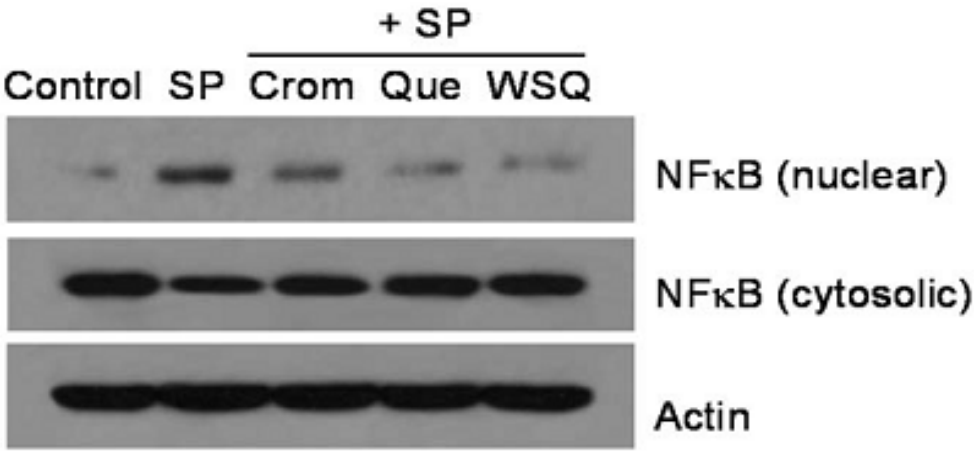
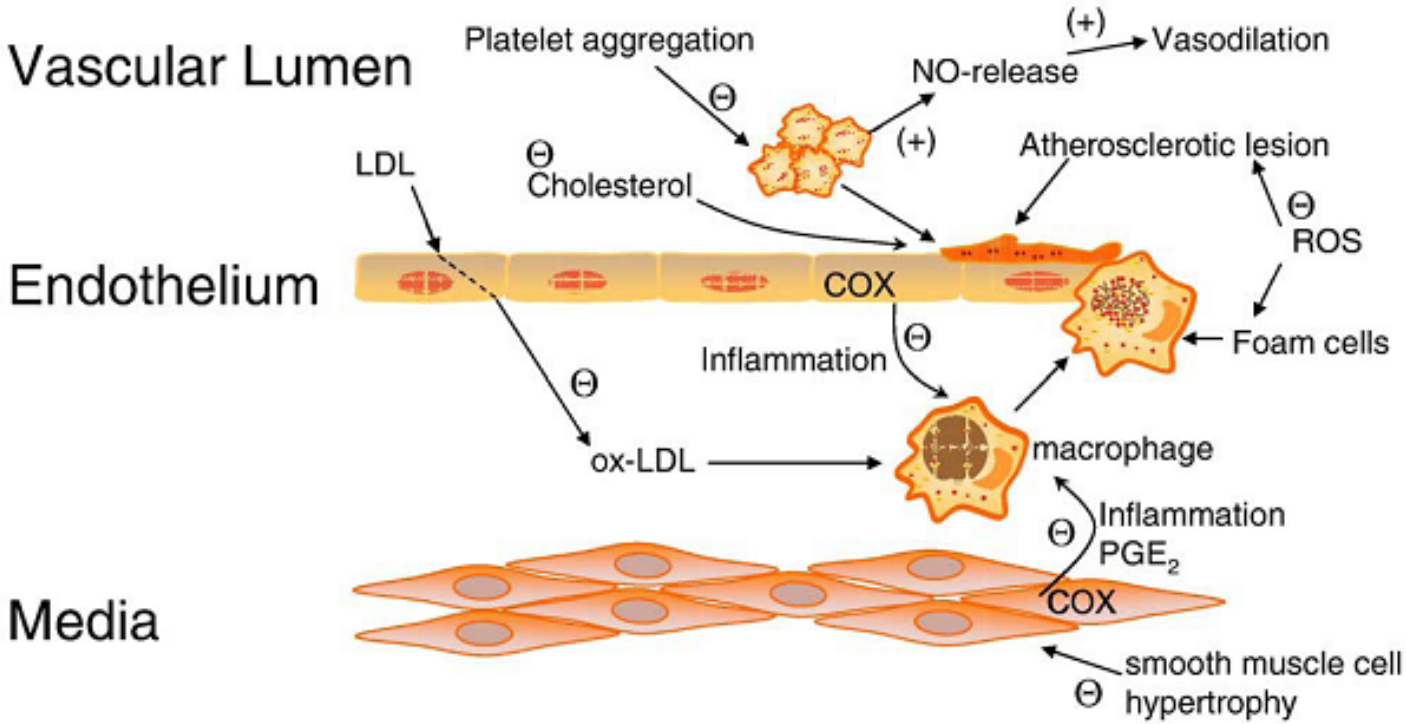


Fig. Quercetin inhibits nuclear translocation of NF-kB induced by Substance P (SP) in LAD2 human mast cells.

Source: PlosOne, 2012, 7: e33805

Cardiovascular protection – grape/wine polyphenols

The cardiovascular protective action of flavonoids on skin blood vessels is complex. Three main components: **blood vessel protection**, **platelet aggregation prevention, and capillary permeability decrease.**

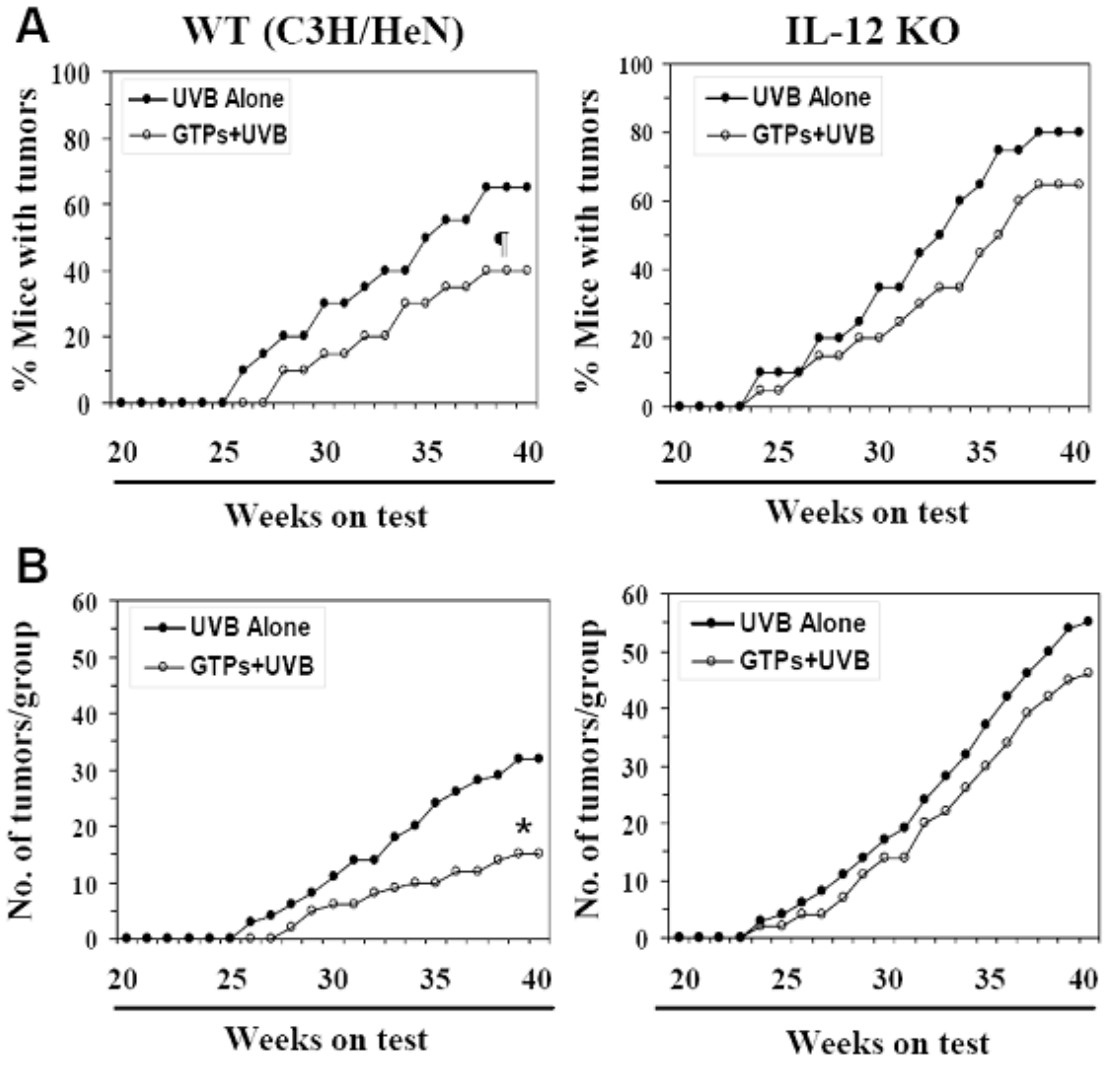


(+) indicates an increase in effect; (−) indicates an inhibitory effect.

Fig. Effects of **grape extract** (skin, seed, juice, resveratrol, etc) on the early steps of atherosclerosis. oxLDL indicates oxidized LDL; PGE2, prostaglandin E2.

Source: Nutri Res 2008, 28: 729–37

Photoprotective effect – Green tea



Source: J Invest Dermatol. 2009, 129: 1258–70.

Fig. Administration of GTPs in drinking water (0.2%, w/v) inhibits UVB-induced skin tumor development in wild-type (WT; C3H/HeN) mice, but does not inhibit it significantly in IL-12 KO mice. Significant inhibition versus UVB alone at the termination of the experiment, *p<0.01, ¶p<0.05.

Photoprotective effect – Green tea (Cont.)

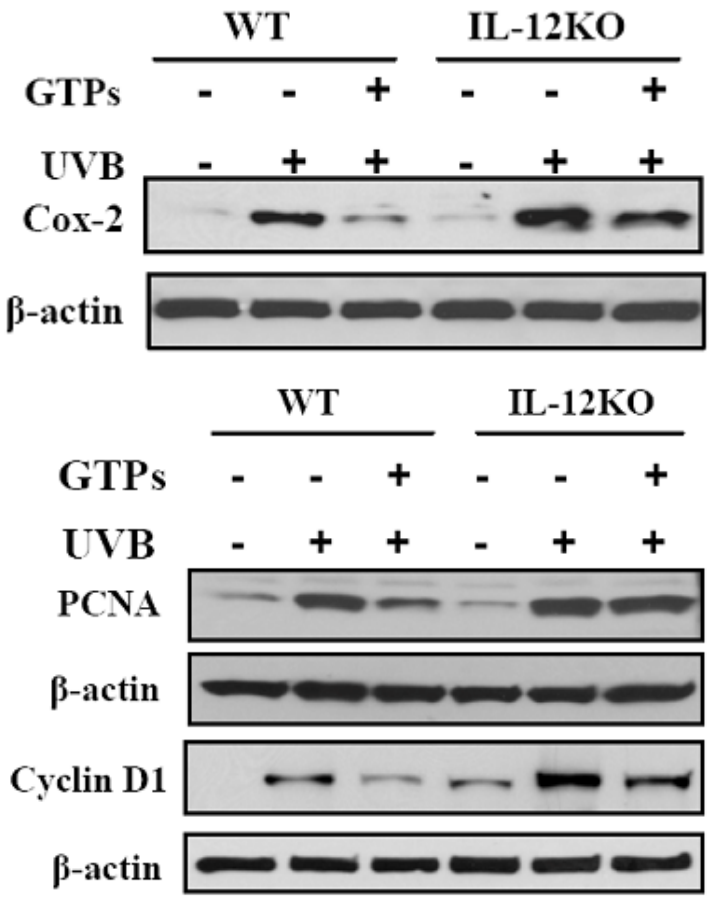


Fig. Administration of GTPs in drinking water inhibits UVB-induced increases in inflammatory responses in the epidermis of WT mouse skin, but is less effective in inhibiting these responses in IL-12 KO mouse skin.

Source: J Invest Dermatol. 2009, 129: 1258–

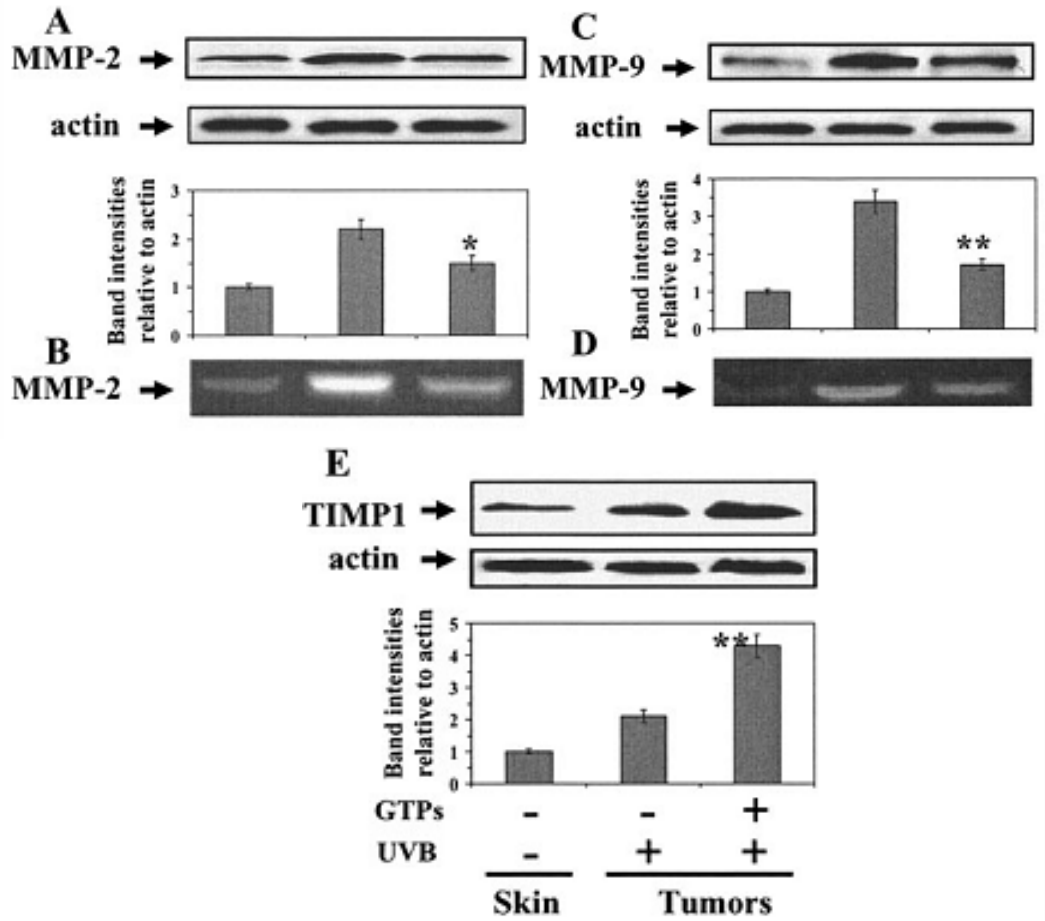


Fig. Oral administration of GTPs to mice inhibits enhanced expression of MMP-2 and MMP-9 in UVB-induced skin tumors while increasing the expression of TIMP1.

Source: J Nutr. 2005, 135: 2871–7.

Photoprotective effect – Apigenin & Luteolin

UVA radiation (15 J/cm²)

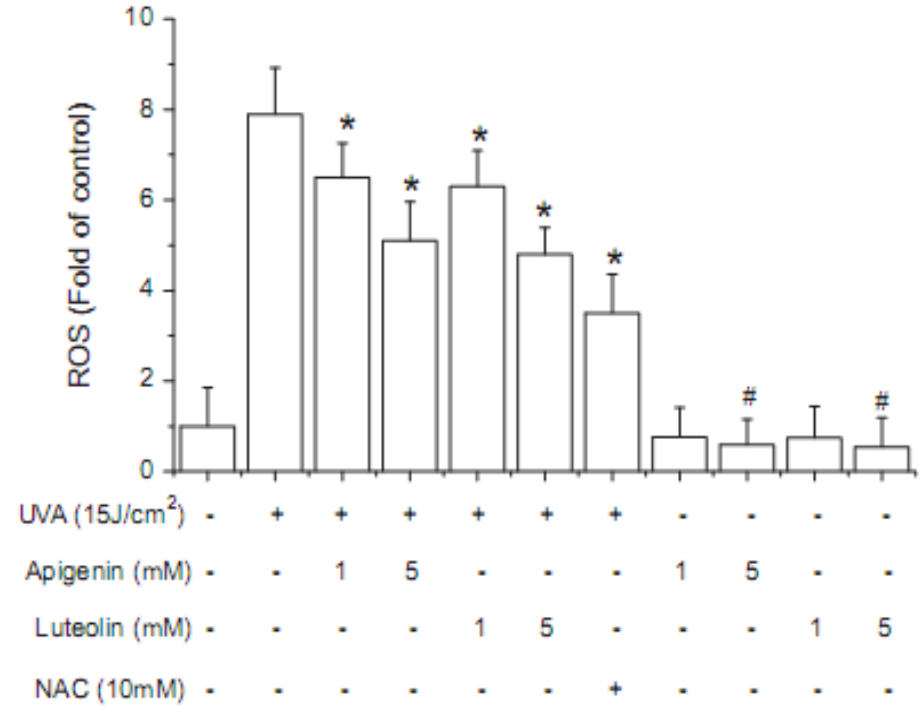
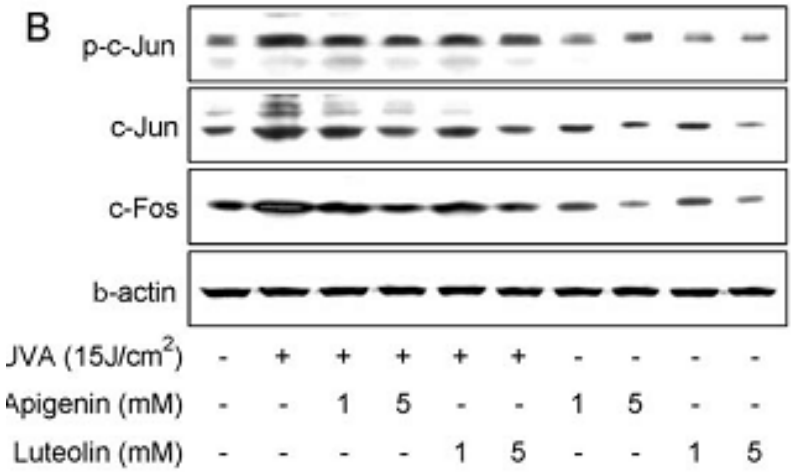


Fig. Effects on intracellular ROS generation in HaCaT cells. *p < 0.01 *vs* UV-treated control.

Source: J Dermatol Sci. 2011, 61: 23–31



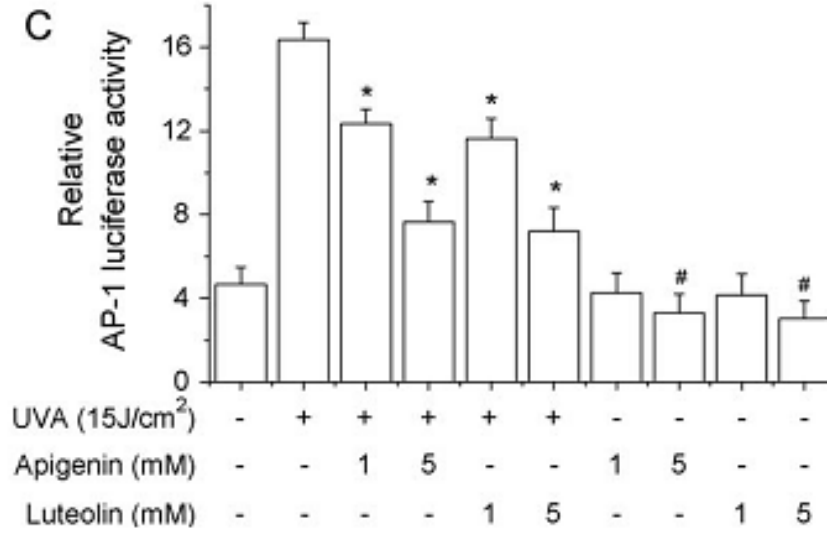


Fig. Effects on the activation of c-Jun and c-Fos transcription factors in HaCaT cells irradiated with UVA. *p < 0.01 *vs* UV-treated control.

Thank you for your attention!
Questions?