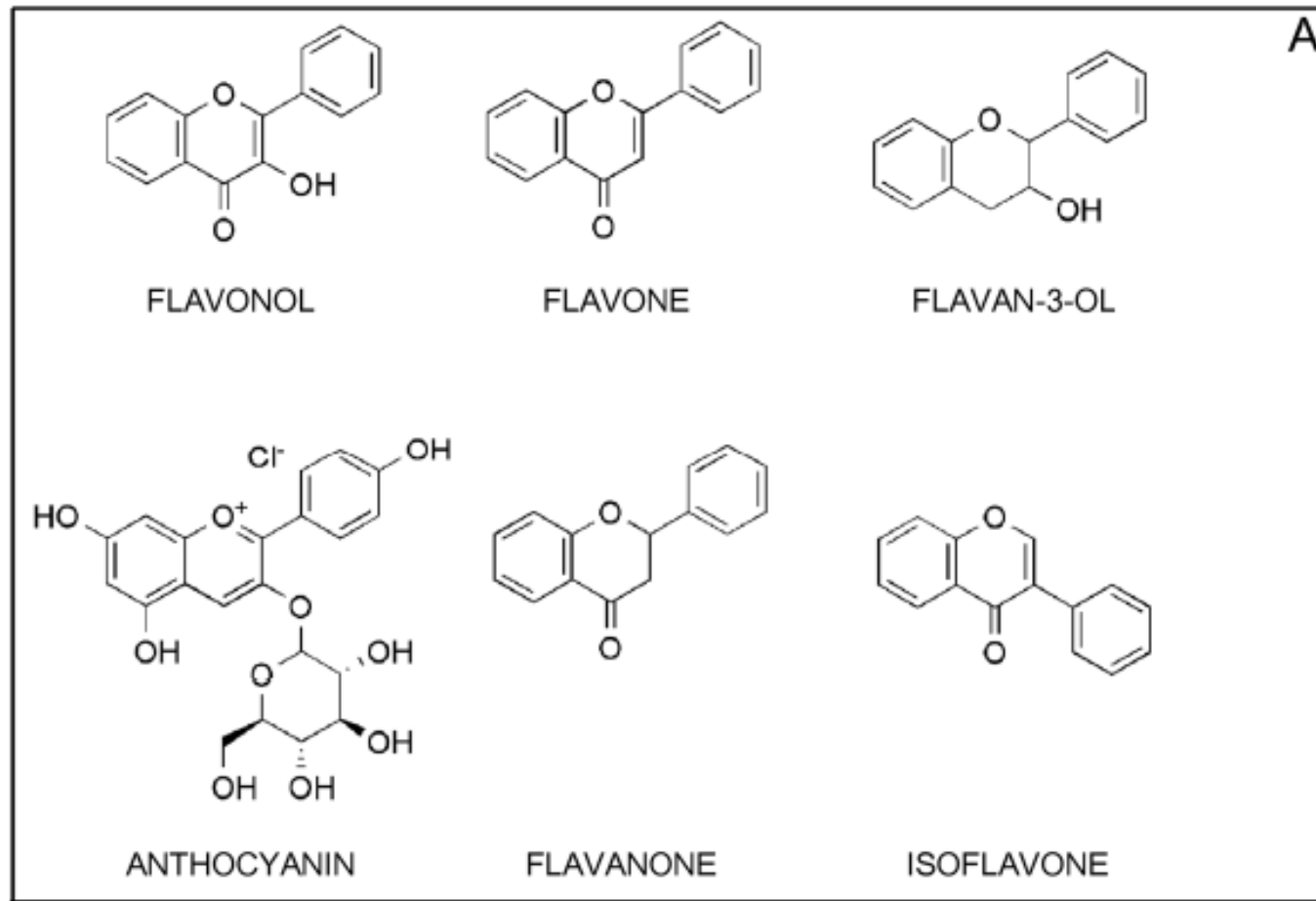


Polyphenols

- Polyphenols are widely distributed in plant-derived foods.
- They comprise a large variety of compounds that have a characteristic structure of at least one aromatic ring bearing one or more hydroxyl groups.
- Polyphenols are classified according to the number of phenol rings that they contain and by the structural elements that bind these rings to one another.
- The main classes of polyphenols are flavonoids, phenolic acids, stilbenes, and lignans



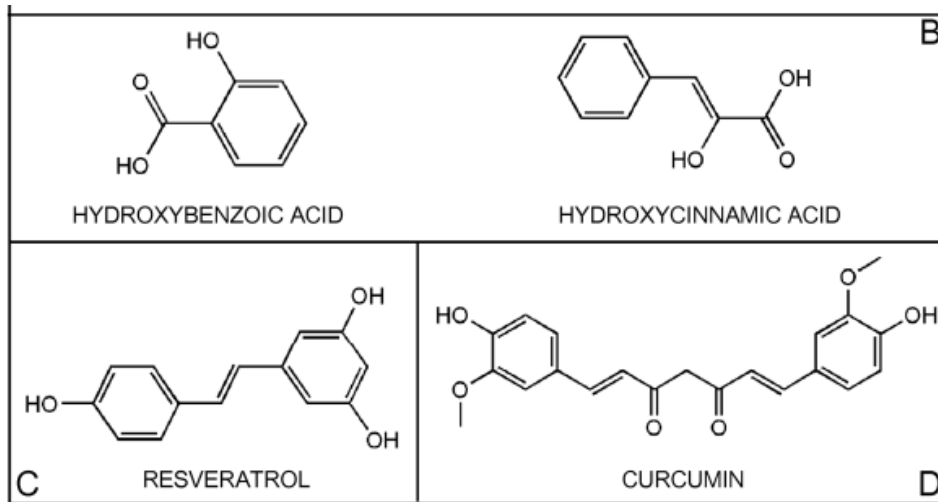
Flavonoids, the most abundant polyphenols in our diet, are formed from phenylalanine through a biosynthetic process involving the shikimic acid and acylpolymalonate pathways. Flavonoids consist of 15 carbon atoms with 2 aromatic rings (A- and B-rings) connected by a 3-carbon bridge that binds with 1 oxygen and 2 carbons of the A-ring, forming a third 6-carbon ring (C-ring). Flavonoids are further classified into subclasses defined by different functional groups and levels of oxidation in the C-ring, and by different connections between the B- and C-rings. Variations between compounds within a subclass consist of different substituents on the A- and B-rings

Flavonoids

- Flavonols are present in plants in glycosylated form. The sugar component, most commonly glucose or rhamnose, is on the 3-position of the C-ring. The main flavonols are quercetin, kaempferol, and myricetin, found mostly in fruits, edible plants, wine, and tea
- Flavones may have a wide range of substitutions, including hydroxylation, methylation, O- and C-alkylation, and glycosylation. Flavones are present in plants mainly as 7-O-glycosides. Their most abundant representatives in foods are apigenin (parsley, celery, onion, garlic, pepper, chamomile tea) and luteolin (thai chili, onion leaves, celery)
- Flavan-3-ols, the most chemically complex subclass of flavonoids, contain a hydroxyl group in the 3-position of the C-ring (Figure 1, Panel A). They exist in monomeric, oligomeric, and polymeric forms and are not glycosylated in foods. The simplest monomers are (+)-catechin and its isomer (–)-epicatechin, whose hydroxylation generates (+)-gallocatechin and (–)-epigallocatechin. (–)-epicatechin-3-O-gallate and (–)-epigallocatechin-3-O-gallate (EGCG) are formed through an additional esterification with gallic acid in the 3-position of the C-ring.

Flavonoids

- Anthocyanins are water-soluble pigments mainly present as glycosides of their aglycone form (anthocyanidin). There are more than 550 anthocyanins in nature. They vary according to the number of hydroxyl groups and degree of methylation in the aglycone molecule, the number and position of sugars linked to the aglycone molecule, and the number and nature of aliphatic or aromatic acids linked to these sugars. The most abundant anthocyanins are cyanidin, pelargonidin, delphinidin, peonidin, petunidin, and malvidin.
- Flavanones are non-planar flavonoids found mainly in citrus fruits, where they occur mainly as mono- and diglycosides or, less frequently, in aglycone form. The most important aglycone flavanones are naringenin and hesperetin. The correspondent glycosylated forms are neohesperidosides such as naringin.
- Isoflavones are classified as phytoestrogens due to structural similarities with estrogens, particularly 17- β -estradiol, that confer pseudohormonal activity. Daidzein, genistein, and glycitein are the most common members of this subclass.



Curcumin (1,7-bis-(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione), a member of the curcuminoid family, is a polyphenol compound found in turmeric, a spice produced from the rhizome of *Curcuma longa*

Phenolic acids are derivatives of benzoic acid and cinnamic acid

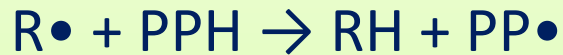
Stilbenes are phytoalexins (C6-C2-C6 structure) produced by plants as a defense against pathogens, disease, injury, and stress conditions. They have a limited presence in our diet and the main member is resveratrol

Lignans are plant-derived compounds whose structural similarities with estrogens classify them as phytoestrogens, similar to isoflavones

Why do plants make substances of benefit to human health, and what are the mechanisms that permit active functions in a xenobiotic environment?



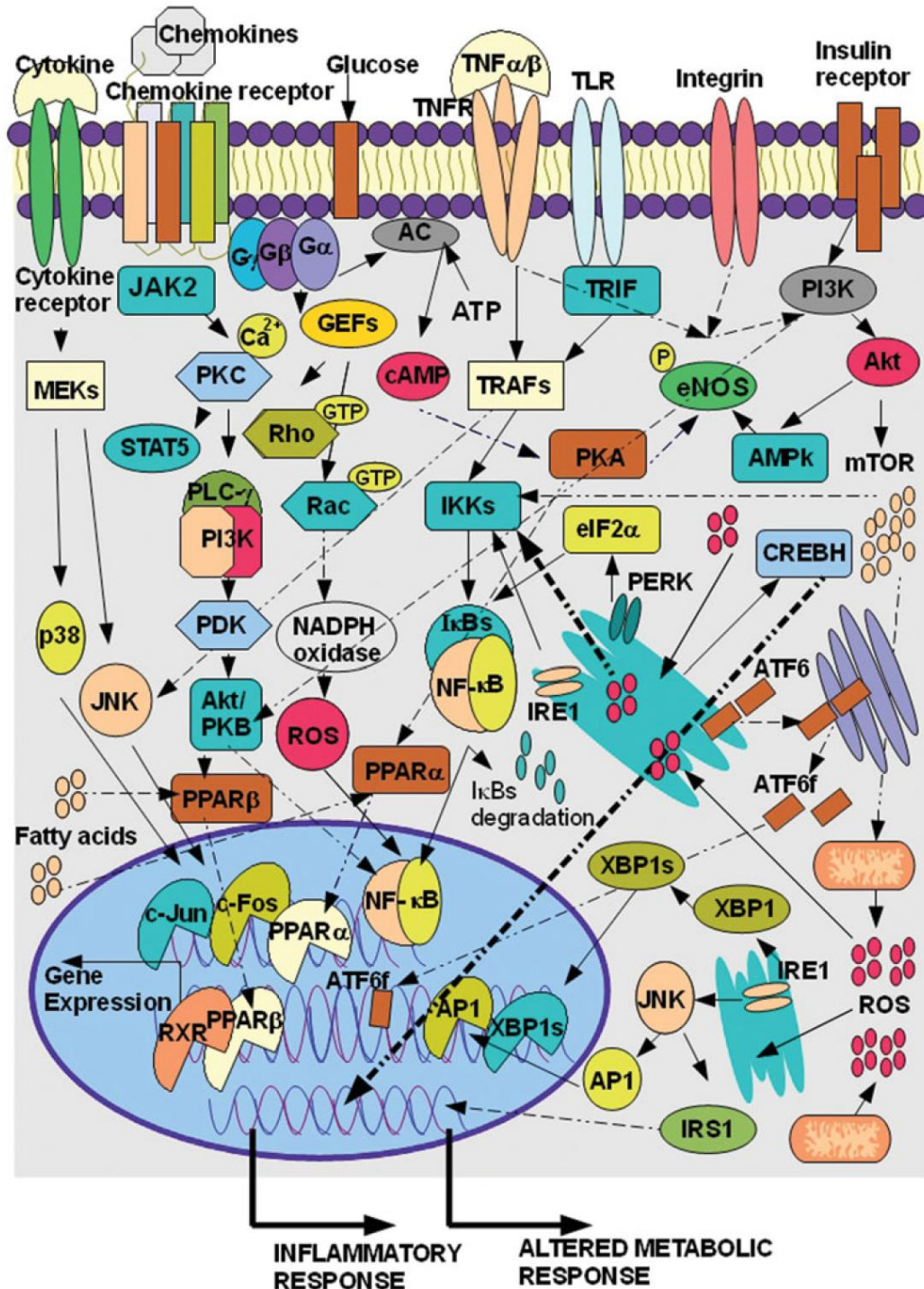
Antiradical, antioxidant , anti-inflammatory activities



Why do plants make substances of benefit to human health, and what are the mechanisms that permit active functions in a xenobiotic environment?

- **Xenohormesis** has recently been suggested as a potential mechanism (hypothesis) to partially explain the effect of plants on animals.
- An environmental stress to a plant leaves a chemical in the form of the plant's polyphenol content, which then provides resistance to stress in humans who eat the plant. This suggests the existence of mechanisms that detect this stress-induced polyphenol content.
- Thus, the stress occurs in the plant, and the beneficiaries are the animals that sense the chemical signals upon ingestion.
- **If xenohormesis is the actual mechanism of the effects of polyphenols, this would indicate that, contrary to what it is generally believed, most benefits from polyphenols do not result from their intrinsic antioxidant properties, but from the evolutionarily adaptive modulation of molecules involved in stress-response pathways.**
- Some of the effects of polyphenols represent relatively simple chemical mechanisms (e.g., antioxidants), but some resemble those produced by signaling molecules or chemical messengers.

Regulation of gene expression



Putative Molecular Targets For Polyphenols

- Influence on the cellular inflammatory and metabolic responses, which may be interpreted as an integration of multiple pathways in response to cellular stress.
- These pathways are extremely complex even when factors being repressed are not depicted to prevent chaotic patterns.
- Multiple targets, multiple signals, and different dimensions!!!!!!

Table 1. Modulation of ErbB receptors, NF- κ B and HH/GLI signaling pathways by polyphenols in cancer cells.

Treatment	<i>In Vitro</i> Model	<i>In Vivo</i> Model	Antitumoral Effects
EGCG	MCF-7 breast cancer cells (5–20 μ M)		↓ ErbB2, ErbB3 phosphorylation ↓ MAPK pathway
	mammary tumor NF639 and SMF cells (0–80 μ g/mL)		↓ Cell proliferation ↓ ErbB2/ <i>neu</i> phosphorylation ↓ NF- κ B, MAPK pathways
	HNSCC (10 μ g/mL), breast cancer cells (30 μ g/mL)		↓ Cell proliferation ↓ EGFR, STAT3, Akt, <i>c-fos</i> activity
	SW837 colon carcinoma cells (30 μ g/mL)		↓ EGFR, ErbB2 and ErbB3 cellular levels
RES	HepG2 liver cancer cells (50–300 μ M)		↓ Cell proliferation ↓ Cyclin D1, Akt, p38 kinase expression ↑ Phospho-ERK1/2 protein levels
	A431 epidermoid carcinoma cells (0–100 μ M)		↓ Cyclin D1, MEK1, ERK1/2 expression
	HT-29 colon cancer cells (25 μ M)		↓ JACK-STAT pathway ↓ iNOS, COX-2 expression
Quercetin	SKBR3 breast cancer cells (100–200 μ M)		↓ ErbB2 tyrosin kinase activity ↓ PI3K, Akt phosphorylation
	HepG2 liver cancer cells (50 μ M)		↓ ERK1/2, Akt phosphorylation ↓ NF- κ B pathway
	A549 lung cancer cells (0–58 μ M)		↓ Cell proliferation ↓ Akt-1 activation ↑ ERK-MEK1/2 phosphorylation
Apigenin	PC-3, LNCaP prostate cancer cells (5–40 μ M)		↓ Cell proliferation ↑ Proportion of cells in G0/G1-phase ↓ Rb, p38 kinase and <i>c-fos</i> phosphorylation
	HNSCC cells (6–100 μ M)		↓ Cell proliferation ↓ EGFR, ErbB2 phosphorylation

Table 1. Modulation of ErbB receptors, NF- κ B and HH/GLI signaling pathways by polyphenols in cancer cells.

Treatment	<i>In Vitro</i> Model	<i>In Vivo</i> Model	Antitumoral Effects
EGCG	A431 epidermoid carcinoma cells (10–40 μ g/mL)		↓ Cell proliferation ↓ NF- κ B/p65 nuclear translocation
Delphinidin	PC-3 prostate cancer cells (30–180 μ M)	Athymic (nu/nu) nude mice bearing prostate cancer tumors (2 mg i.p. thrice weekly)	↓ Tumor growth ↓ I κ B kinase γ , I κ B- α phosphorylation ↓ NF- κ B DNA binding activity
	HCT-116 colon cancer cells (30–240 μ M)		↓ Cell proliferation ↓ I κ B- α phosphorylation ↓ NF- κ B activation
		rats with esophagus tumor (3.8 μ mol/g/day p.o.)	↓ Tumor development ↓ NF- κ B, COX-2 expression
Anthocyanin	CAL-27 oral cancer cells (0–500 μ g/mL)		↓ Cell proliferation, metastasis ↓ NF- κ B, MMPs expression ↓ MAPK pathway
CA, CAPE	HepG2 liver cancer cells (CA 100 μ g/mL; CAPE 5 μ g/mL)	nude mice injected with HepG2 cells (CA + CAPE 5 mg/kg s.c. thrice weekly; CA + CAPE 20 mg/kg/day p.o. for 5 weeks)	↓ Tumor growth ↓ NF- κ B, MMP-9 activity ↓ Liver metastasis
	Cervical cancer cells (5–60 μ M)		↓ I κ B- α phosphorylation ↓ NF- κ B activation
CUR		ICR mice (1–25 μ M)	↓ COX-2 expression ↓ NF- κ B activation ↓ NF- κ B nuclear translocation ↓ ERK1/2 activity

Genistein

- Genistein, a phyto-oestrogen from soybeans acted in breast cancer through **telomerase inhibition** (Li et al., 2009), reversed DNA hypermethylation in a concentration-dependent manner in different cancer cell lines (Fang et al., 2005)
- Dolinoy et al. (2006) described **maternal genistein supplementation (250 mg·kg⁻¹) as protective against obesity in mouse offspring** (Dolinoy et al., 2006). These changes were mediated by modifying the foetal epigenome, with an increase in DNA methylation in the agouti gene (Dolinoy et al., 2006).
- Similarly, DNA methylation levels were increased in liver and muscle tissues in monkeys fed with a diet supplemented with soy components, such as genistein, and this was associated with **increased insulin sensitivity** (homeostasis model assessment index) (Dolinoy et al., 2006; Howard et al., 2011).

Effects on cancer

- Coffee and tea polyphenols also are demethylating agents (Lee and Zhu, 2006), in human breast cancer cell lines where **caffeic acid or chlorogenic acid inhibited DNA methylation** in a concentration-dependent manner
- A constituent of broccoli, **sulforaphane induced cell apoptosis with down-regulation of DNMT1** in human colon cancer cells (Traka et al., 2005)
- **Curcumin induced a decrease in DNA methylation in a leukaemia cell line** (Liu et al., 2009), as it blocked the catalytic thiolate of DNA methyltransferase 1 and inhibited its activity (Link et al., 2010)
- The flavonoid fisetin **inhibited TNF- α and IL-6 expression levels** and suppressed NF-kB transcription activity in cultures of human monocytes (Kim et al., 2012).

Effects on leptin

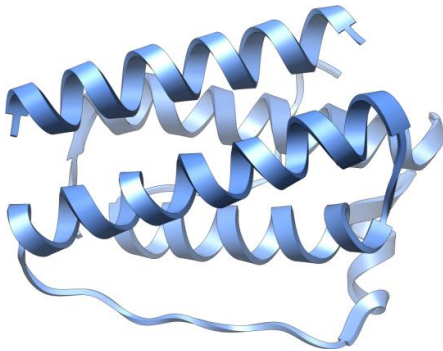
Dietary supplementation with apple extracts (700 mg·kg⁻¹ body weight) rich in the polyphenols chlorogenic acid, phloridzin, quercetin, catechin, epicatechin, procyanidin and rutin in rats fed a high-fat sucrose diet for 8 weeks



Prevention of body weight gain and amelioration of hyperglycaemia, hyperleptinaemia, and insulin resistance

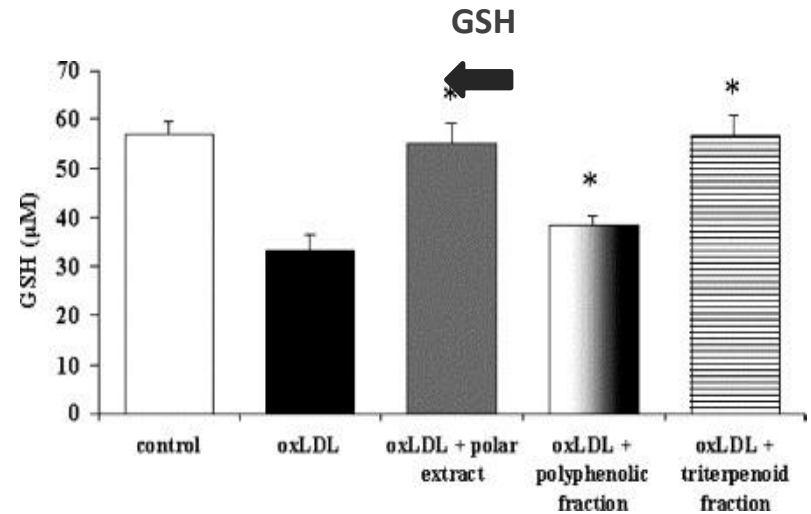
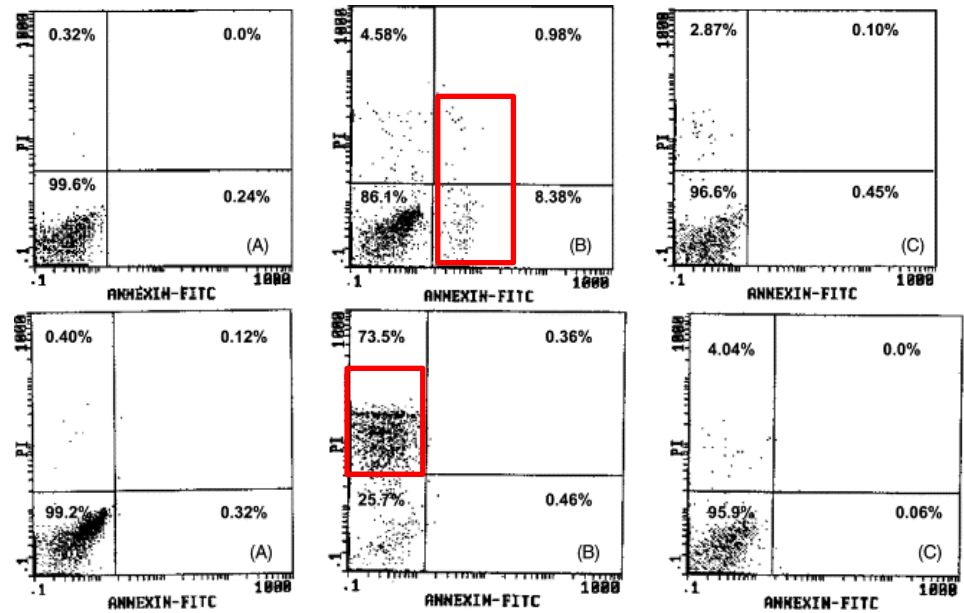
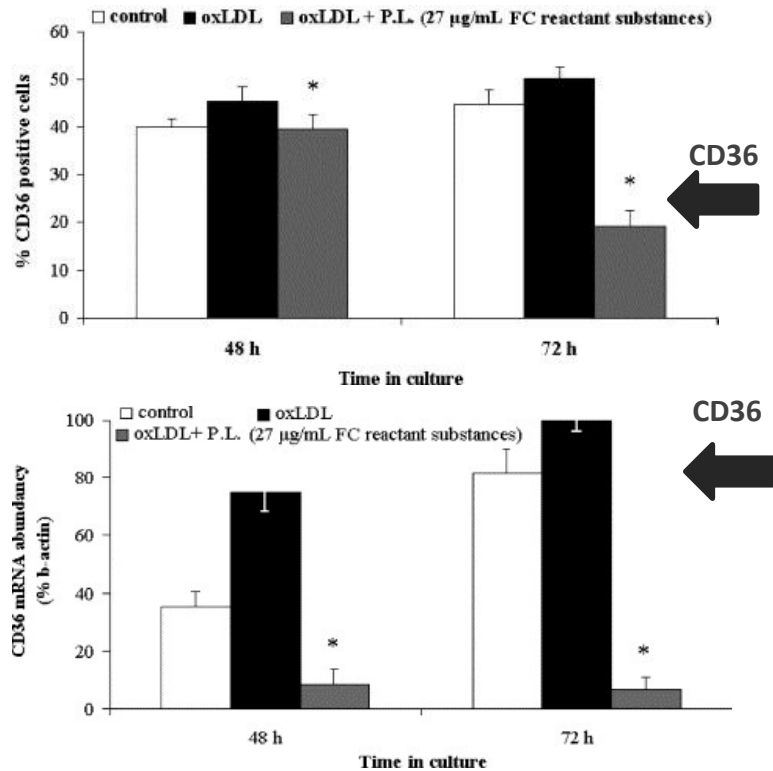


The results were accompanied by decreased methylation of two CpG sites in the leptin promoter of rat epididymal adipocytes (Boque et al., 2013)



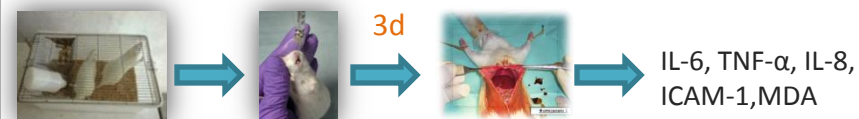
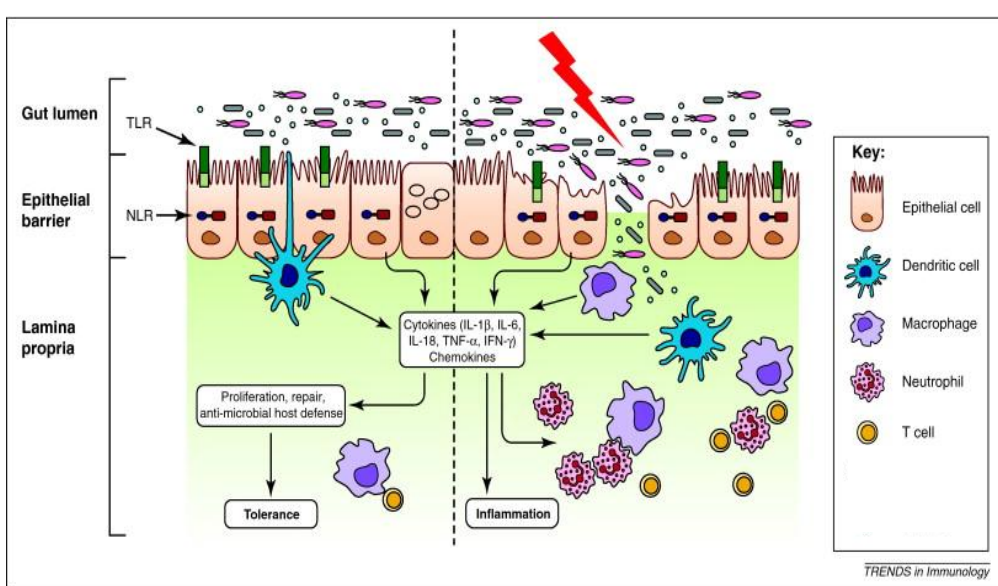
Extract from mastic inhibits

- LDL oxidation in vitro¹
- oxLDL induced cytotoxicity in PBMC²
- oxLDL induced apoptosis/necrosis in PBMC²
- expression of CD36 receptor in Mo/MΦ²
- restores GSH²
- production of proinflammatory proteins in macrophages³
- VCAM-1 and ICAM-1 in human aortic EC⁴

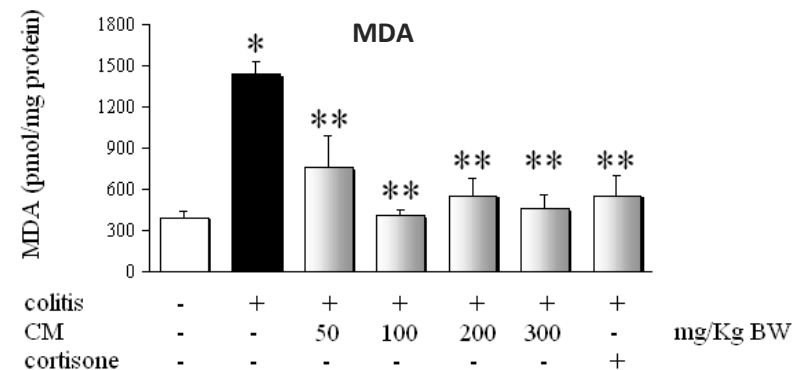
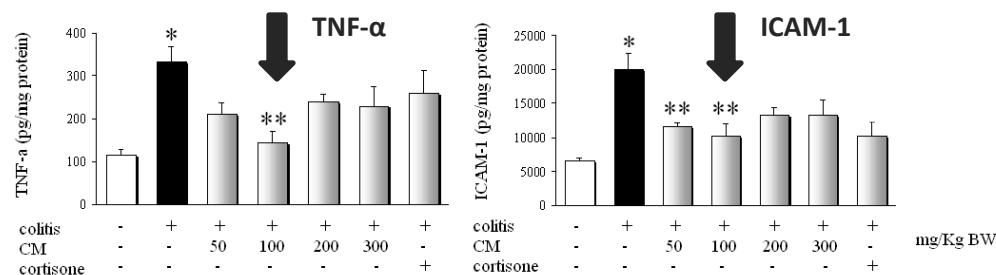
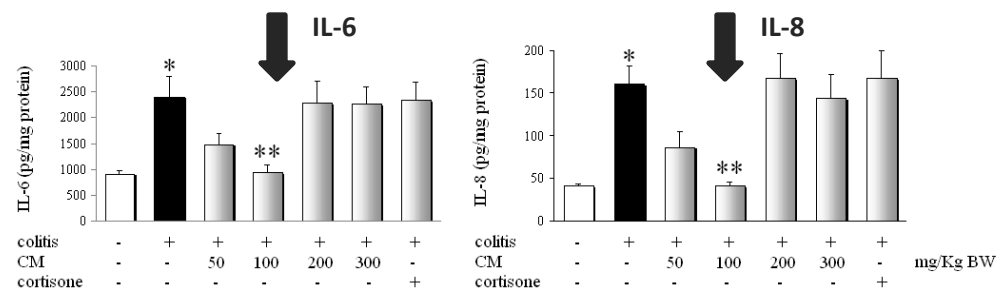
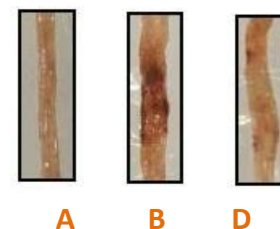
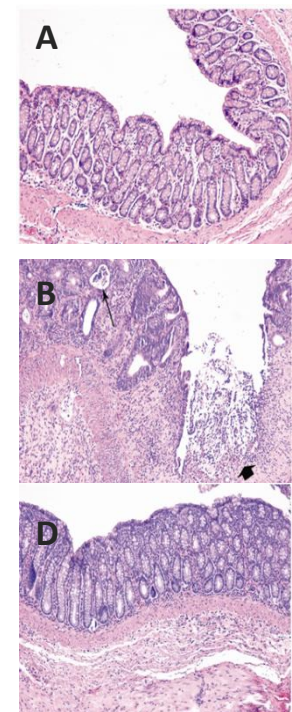


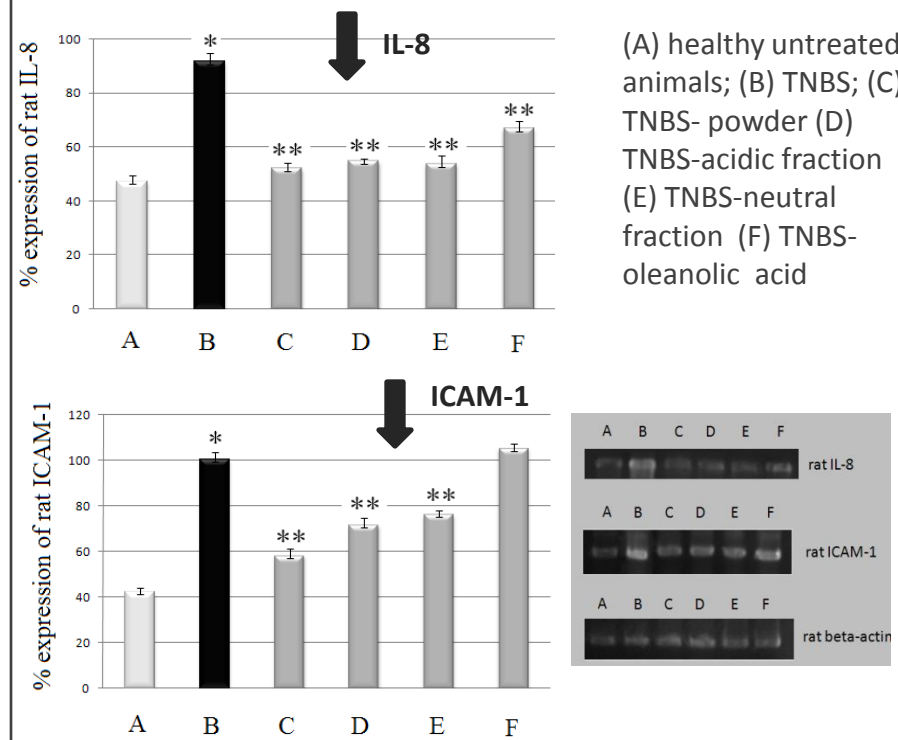
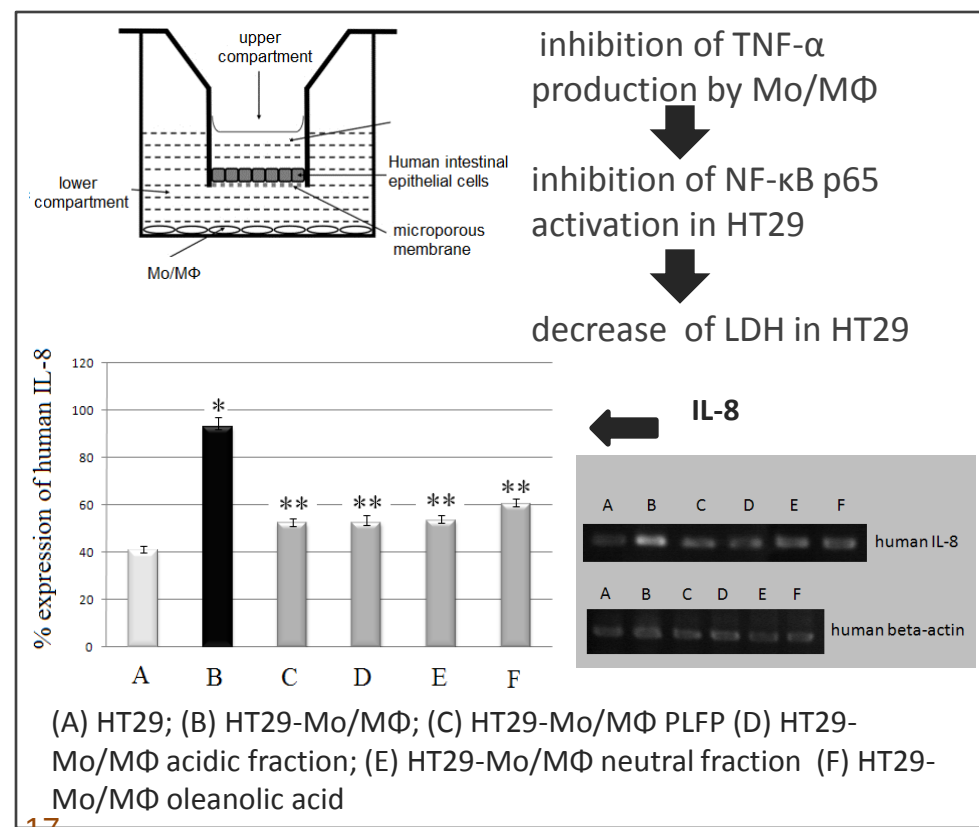
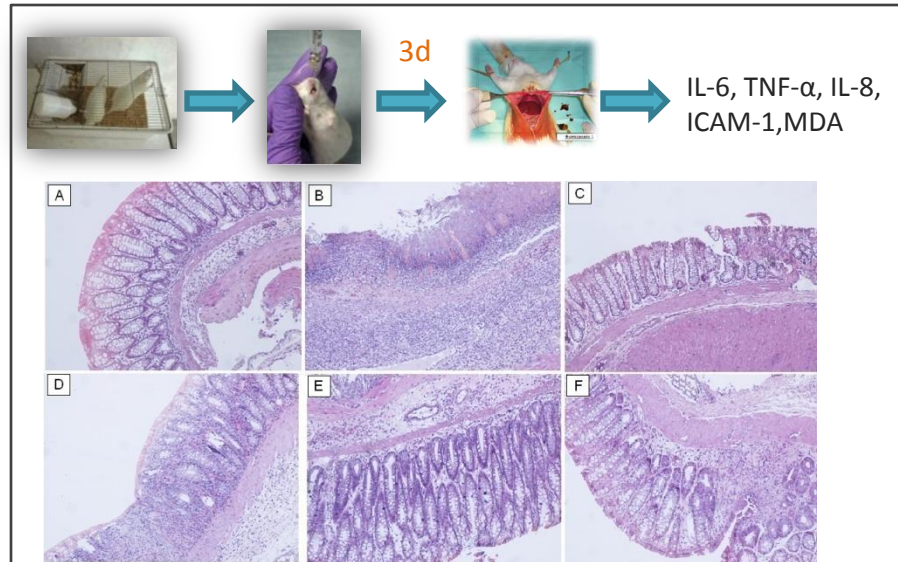
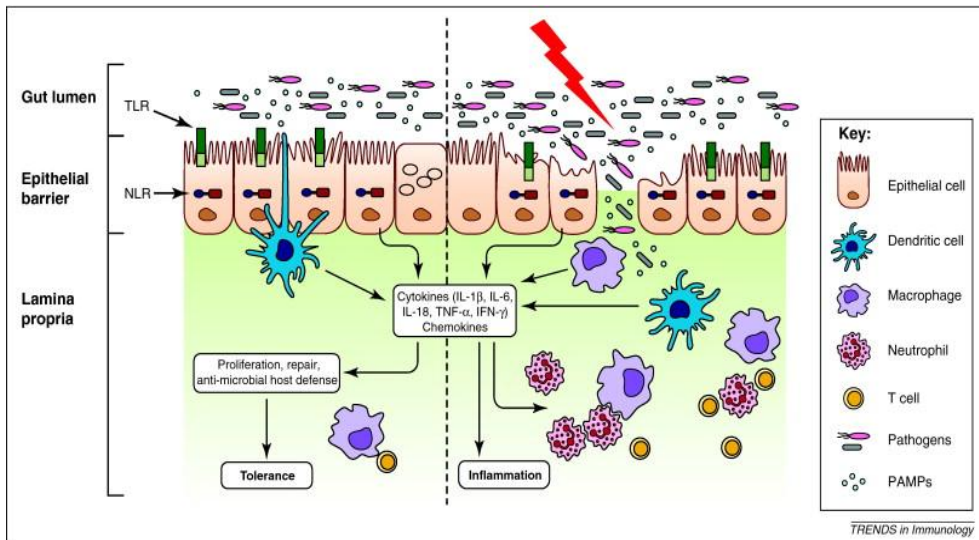
¹ Andrikopoulos et al., 2003, Phytoter Res, 17:501; ² Dedoussis et al., 2004, Atherosclerosis, 174:293;

³ Zhou et al., 2009, In Vivo, 23:583; ⁴ Loizou et al., 2009, Exp Biol Med, 234:553



Groups	3d treatment
A: untreated	0.0 $\pm$ 0.0
B: TNBS	4.7 $\pm$ 0.5*
C: TNBS, 50mg/kg BW	1.4 $\pm$ 0.3**
D: TNBS, 100mg/Kg BW	1.3 $\pm$ 0.1**
E: TNBS, 200mg /Kg BW	2.5 $\pm$ 0.6**
F: TNBS, 300mg/Kg BW	1.7 $\pm$ 0.2**
G: TNBS, cortisone	2.1 $\pm$ 0.0**





A resin with chemopreventive activities

Published by	Research tool	Outcomes
•He et al., 2007a, Acta Pharmacol Sin, 28: 446 •He et al., 2007b, Acta Pharmacol Sin, 28: 567	PC3 cell culture	Cell proliferation suppression, NF-κB activity suppression, maspin mRNA and protein expression induction
He et al., 2006, Cancer, 106: 2547	LNCaP cell culture	Cell proliferation suppression, androgen receptor mRNA and protein levels reduction
Sakagami et al., 2009, In Vivo, 23: 215	HL-60, ML-1 and KG-1 , K562 cell cultures	Cell proliferation suppression, apoptosis induction
Balan et al., 2005, In Vivo, 19: 93	HCT116 cell culture	Cell proliferation suppression, apoptosis induction
Moulos et al., 2009, BMC Med Genomics, 2: 68	Lewis lung carcinoma cell culture	Change in the expression of 925 genes encoding cell proliferation, apoptosis, inflammatory proteins
Dimas et al., 2009, In Vivo, 23: 63	Colon cancer mouse model	Suppression of tumor growth 



PP
extract

NF-κB

COX-2, GSH
IL-8

Inhibition in
growth of
HT29 culture

**“functional” in the
context of
intestinal
homeostasis**



→ Kountouri et al., *in press*

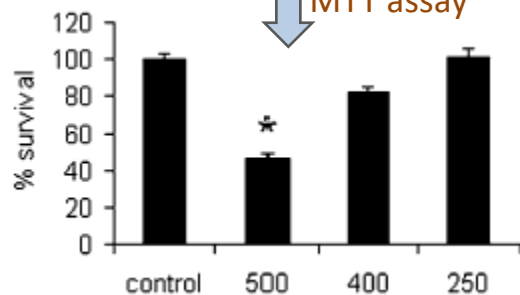


PP
extract

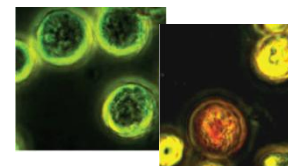
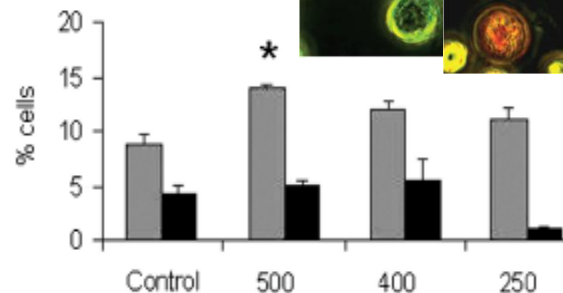
ICAM-1
mRNA

high invasive &
metastatic
potential

ICAM-1



apoptosis



**“functional” in the context of gastric
homeostasis**

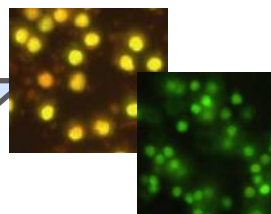
Kaliora et al., 2008, *Nutr Cancer*, 60:792

radical
scavenger

oxLDL
Inhibition

GSH
induction

PBMC
survival



**“functional” in the
context of oxidative
damage**



→ Kaliora et al., 2009,12:1302

Targeting NF- κ B

- NF- κ B is a transcription factor retained inactive in the cytoplasm by its inhibitors, the I κ B proteins (I κ Bs)
- The I κ B proteins bind to NF- κ B, masking its nuclear localization signals and preventing its nuclear translocation
- Activation of the I κ B kinase (IKK) complex promotes phosphorylation of the I κ Bs and their consequent proteasomal degradation. Degradation of I κ Bs promotes NF- κ B nuclear translocation
- Once in the nucleus, NF- κ B activates the transcription of several genes involved in inflammation, cell growth, and invasivity
- Constant activation of NF- κ B in cancer cells is linked to high production of inflammatory mediators such as tumor necrosis factor (TNF), interleukin-1 (IL-1), IL-6, prostaglandin E2 (PGE2), and reactive oxygen species (ROS) within the tumor microenvironment
- Up-regulation of NF- κ B activity is also involved in the development of chemoresistance in tumor cells, which leads to inhibition of apoptosis, increased angiogenesis, and metastatic capability

Phenolic profiles and antioxidant and anticarcinogenic activities of Greek herbal infusions; balancing delight and chemoprevention?

Andriana C. Kaliora^a, Dimitra A.A. Kogiannou^a, Panagiotis Kefalas^b, Issidora S. Papassideri^c, Nick Kalogeropoulos^{a,*}

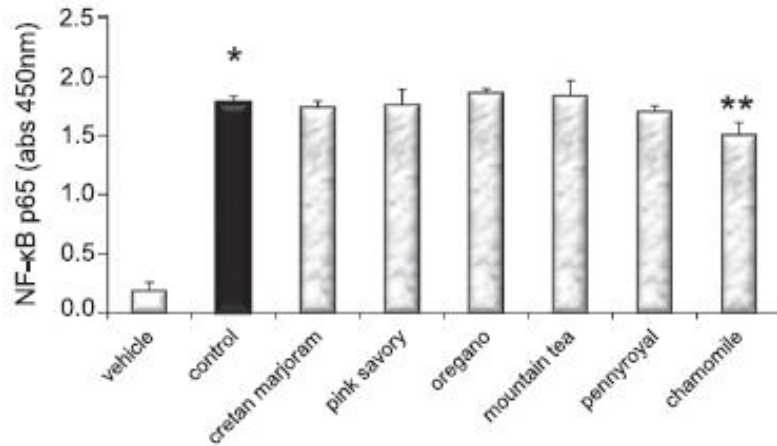
Total phenolic content, antioxidant activity and phenolic profiles of six herbal infusions – namely rosemary, Cretan dittany, St. John's Wort, sage, marjoram and thyme were assayed. Additionally, the infusion anticarcinogenic effect as to their ability to (a) scavenge free radicals, (b) inhibit cell growth, (c) decrease IL-8 levels and (d) regulate p65 subunit in epithelial colon cancer (HT29) and prostate (PC3) cancer cells was investigated.

Herbal infusions; their phenolic profile, antioxidant and anti-inflammatory effects in HT29 and PC3 cells

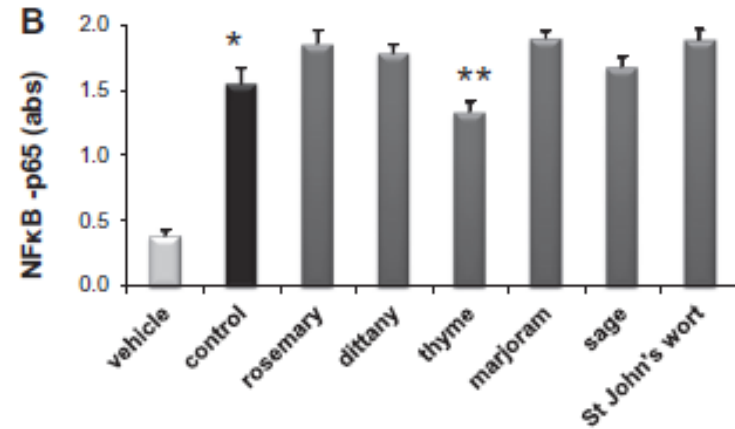
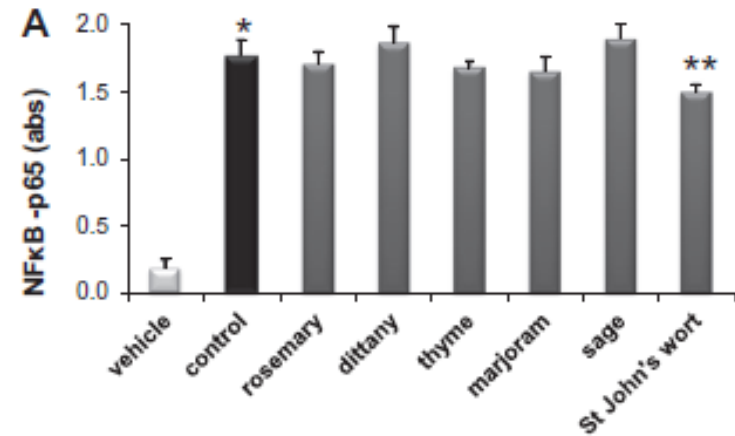
Dimitra A.A. Kogiannou^a, Nick Kalogeropoulos^a, Panagiotis Kefalas^b, Moschos G. Polissiou^c, Andriana C. Kaliora^{a,*}

The phenolic profile of six herbal infusions namely Cretan marjoram, pink savory, oregano, mountain tea, pennyroyal and chamomile by LCDAD–MS and by GC–MS. Further, anticarcinogenic effect as to their ability to (a) scavenge free radicals (b) inhibit proliferation (c) decrease IL-8 levels and (d) regulate nuclear factor-kappa B in epithelial colon cancer (HT29) and prostate (PC3) cancer cells was investigated.

Effect on NF-kappa B



A



B

Simple polyphenols and terpenic acids ($\mu\text{g}/\text{cup}^a$) in the infusions of the aromatic plants studied.

Compounds	Cretan marjoram		Pink savory		Oregano		Mountain tea		Pennyroyal		Chamomile	
	Mean	$\pm\text{SD}$	Mean	$\pm\text{SD}$	Mean	$\pm\text{SD}$	Mean	$\pm\text{SD}$	Mean	$\pm\text{SD}$	Mean	$\pm\text{SD}$
<i>Phenolic acids</i>												
<i>1. Hydrobenzoic acids</i>												
p-Hydroxy-benzoic acid	53.43	4.56	21.03	1.96	56.72	8.39	33.86	1.15	17.69	7.73	18.30	1.22
Vannilic acid	37.37	2.53	30.06	0.83	32.31	2.47	24.85	0.35	45.04	14.14	100.56	10.26
Protocatechuic acid	54.60	6.43	42.90	2.36	169.31	35.74	54.71	6.05	23.33	4.48	588.31	125.88
Syringic acid	99.46	12.50	45.64	2.00	39.08	1.16	37.35	1.48	35.26	9.05	32.23	2.75
Gallic acid	6.76	3.36	–	–	–	–	–	–	–	–	31.97	13.06
p-Hydroxy-phenylacetic acid	8.34	4.15	–	–	–	–	–	–	–	–	–	–
3,4-Dihydroxy-phenylacetic acid	–	–	69.16	3.37	43.84	5.15	–	–	18.28	0.90	–	–
<i>ii Hydroxycinnamic acids</i>												
Cinnamic acid	6.19	0.33	7.28	1.01	–	–	16.65	0.95	14.37	4.93	33.75	3.10
Phloretic acid	–	–	–	–	–	–	0.00	0.00	–	–	–	–
o-Coumaric acid	10.89	5.42	–	–	19.78	9.90	22.48	0.42	29.34	8.37	–	–
p-Coumaric acid	15.17	7.55	–	–	46.23	1.87	56.72	6.56	107.86	5.50	44.09	3.54
Ferulic acid	29.88	0.88	–	–	46.10	2.31	28.83	0.53	–	–	48.62	0.60
Caffeic acid	113.52	9.48	340.81	35.42	895.19	46.41	73.57	14.52	375.42	185.25	263.04	60.42
Sinapic acid	22.45	0.11	–	–	–	–	–	–	24.62	0.23	–	–
Chlorogenic acid	23.46	1.87	–	–	–	–	828.49	87.21	105.35	26.07	4800.34	295.28
<i>Flavonoids</i>												
Chrysin	21.34	1.38	–	–	–	–	43.41	12.32	46.58	1.00	55.78	3.89
Epicatechin	19.15	1.29	19.99	1.35	45.52	6.57	38.43	7.58	22.90	3.18	27.54	0.28
Naringenin	109.33	11.86	65.61	9.52	117.95	40.16	20.69	0.06	–	–	–	–
Catechin	29.85	0.58	34.68	0.65	61.25	3.83	30.55	1.75	32.28	0.86	49.53	0.89
Genistein	–	–	38.95	8.25	76.49	44.34	–	–	–	–	447.86	50.22
Kaempferol	19.44	0.12	–	–	–	–	–	–	–	–	33.37	1.10
Quercetine	22.16	1.18	–	–	39.13	3.42	96.57	16.36	–	–	31.37	0.22
<i>Terpenoid phenols</i>												
Thymol	6046	121.12	34,382	683.07	2545.00	173.95	–	–	1727	56.57	–	–
Carvacrol	26,274	324.87	87,814	794.68	177855.0	803.27	1220	126.57	3755	82.02	9321.50	313.25
<i>Terpenic acids</i>												
Oleanolic acid	14.49	0.27	–	–	29.75	2.22	–	–	13.30	2.52	–	–
Ursolic acid	–	–	–	–	40.10	3.09	–	–	21.99	2.81	–	–
<i>Sums</i>												
Simple polyphenols	33013.65	316.96	122973.95	21.04	181992.6	854.76	2627.68	26.41	6353.76	408.28	15915.15	880.81
Phenolic acids	243.84	10.57	207.20	6.68	341.77	52.85	150.77	6.03	139.60	36.31	838.83	148.90
Hydroxycinnamic acids	197.04	14.94	374.90	109.77	965.08	63.89	1026.75	107.45	630.45	230.35	5107.6	362.94
Flavonoids	217.26	5.07	174.36	41.06	285.79	5.72	229.66	13.32	101.71	3.03	647.39	55.72
Terpenoid phenols	32355.50	286.38	122217.50	136.47	180400.0	977.22	1220.50	126.57	5482.00	138.59	9321.5	313.25
Terpenic acids	14.49	0.27	0.00	0.00	52.08	19.97	–	–	35.24	5.33	–	–

^a 1 cup = 200 mL.

Simple polyphenols and terpenic acids ($\mu\text{g}/\text{cup}^a$) in the infusions of the aromatic plants studied.

Compounds	Rosemary		Cretan dittany		Thyme		Marjoram		St John's Wort		Sage	
	Mean	$\pm\text{SD}$	Mean	$\pm\text{SD}$	Mean	$\pm\text{SD}$	Mean	$\pm\text{SD}$	Mean	$\pm\text{SD}$	Mean	$\pm\text{SD}$
<i>Phenolic acids</i>												
<i>i. Hydroxybenzoic acids</i>												
Vannilic acid	14.8	1.2	11.2	1.6	55.7	3.7	49.4	1.5	59.0	2.4	10.6	1.8
Protocatechuic acid	2.4	0.4	38.9	3.6	31.7	2.4	58.5	1.9	274.0	16.5	22.0	2.9
Syringic acid	5.5	0.4	24.6	2.9	83.0	6.5	88.4	4.5	35.6	3.4	13.0	1.8
Gallic acid	–	–	15.0	2.5	–	–	25.1	2.8	100.6	7.1	–	–
p-Hydroxy-phenylacetic acid	–	–	–	–	–	–	16.5	1.3	–	–	–	–
3,4-Dihydroxy-phenylacetic acid	–	–	73.4	17.3	25.6	0.4	85.7	3.4	–	–	7.0	0.9
<i>ii. Hydroxycinnamic acids</i>												
Cinnamic acid	2.0	0.2	5.8	0.5	8.9	1.4	10.5	2.6	11.8	0.6	3.0	0.3
Phloretic acid	–	–	–	–	–	–	–	–	–	–	2.7	0.4
o-Coumaric acid	–	–	10.1	0.8	33.9	3.9	33.8	2.8	–	–	10.2	1.9
p-Coumaric acid	13.6	0.7	18.6	2.9	–	–	79.1	5.4	77.0	7.1	16.5	2.3
Ferulic acid	9.6	1.1	–	–	37.2	3.7	80.3	2.5	47.8	3.6	17.1	1.7
Caffeic acid	61.3	2.6	67.8	6.8	310.4	12.5	630.1	28.5	183.9	21.1	262.8	70.5
Sinapic acid	5.8	0.9	–	–	26.0	1.6	55.8	4.3	–	–	12.9	0.3
Chlorogenic acid	–	–	37.0	4.3	27.4	3.9	–	–	10.5	3.3	16.4	2.3
Rosmarinic acid	669.2	78.5	7244	322.5	7007.3	103	9674.4	253.8	–	–	8082.7	99.8
<i>Flavonoids</i>												
Chrysin	–	–	28.9	0.8	–	–	68.6	2.2	63.1	8.5	13.0	1.9
Epicatechin	4.8	0.3	36.2	1.9	21.2	1.5	39.5	5.3	29275.4	1240.9	9.4	0.3
Naringenin	–	–	22.0	1.0	33.6	3.2	58.2	4.4	–	–	18.7	5.1
Catechin	8.1	1.2	32.4	6.4	38.2	1.8	61.5	7.5	3448.2	394.5	15.9	1.0
Genistein	–	–	31.4	1.8	29.8	1.6	–	–	–	–	21.3	4.2
Kaempferol	–	–	–	–	–	–	44.7	6.0	165.4	17.9	11.5	1.4
Quercetin	–	–	15.7	2.9	–	–	43.7	5.3	3134.4	298.1	10.9	0.8
<i>Terpenoid phenols</i>												
Thymol	–	–	–	–	80655.6	3184.9	1011.6	74.1	–	–	1859.0	83.2
Carvacrol	362.3	38.9	36416.9	2317.0	182138.0	5651.7	2976.5	125.6	2245.6	202.7	3745.3	290.4
<i>Terpenic acids</i>												
Oleanolic acid	17.7	1.3	–	–	–	–	32.7	2.8	–	–	66.2	5.7
Ursolic acid	12.2	0.7	–	–	–	–	48.2	0.7	–	–	40.6	6.0
<i>Sums</i>												
Total simple polyphenols	1159.4	126.4	44129.9	2697.5	270563.5	8987.7	15191.9	545.7	39132.3	2227.7	14181.9	475.2
Phenolic acids	784.2	56.8	7546.4	365.7	7647.1	143.0	10887.6	315.3	800.2	65.1	8476.9	186.9
Flavonoids	12.9	1.5	166.6	7.3	122.8	5.7	316.2	25.6	36086.5	1240.6	100.7	12.5
Terpenoid phenols	362.3	38.9	36416.9	2317.0	262793.6	3997.9	3988.1	51.5	2245.6	202.7	5604.3	355.6
Terpenic acids	29.9	1.5	–	–	–	–	80.9	3.5	–	–	106.8	11.6

^a 1 cup = 200 mL.

Genes-pp interaction

Association between Maternal *COMT* Gene Polymorphisms and Fetal Neural Tube Defects Risk in a Chinese Population

Jufen Liu, Linlin Wang, Yunting Fu, Zhiwen Li, Yali Zhang, Le Zhang, Lei Jin, Rongwei Ye, and Aiguo Ren*

Maternal tea consumption was reported to increase the risk of fetal neural tube defects (NTDs). Catechol-O-methyltransferase (COMT) may be involved in the metabolism of polyphenolic methylation of tea, thus influence the risk of fetal NTDs.

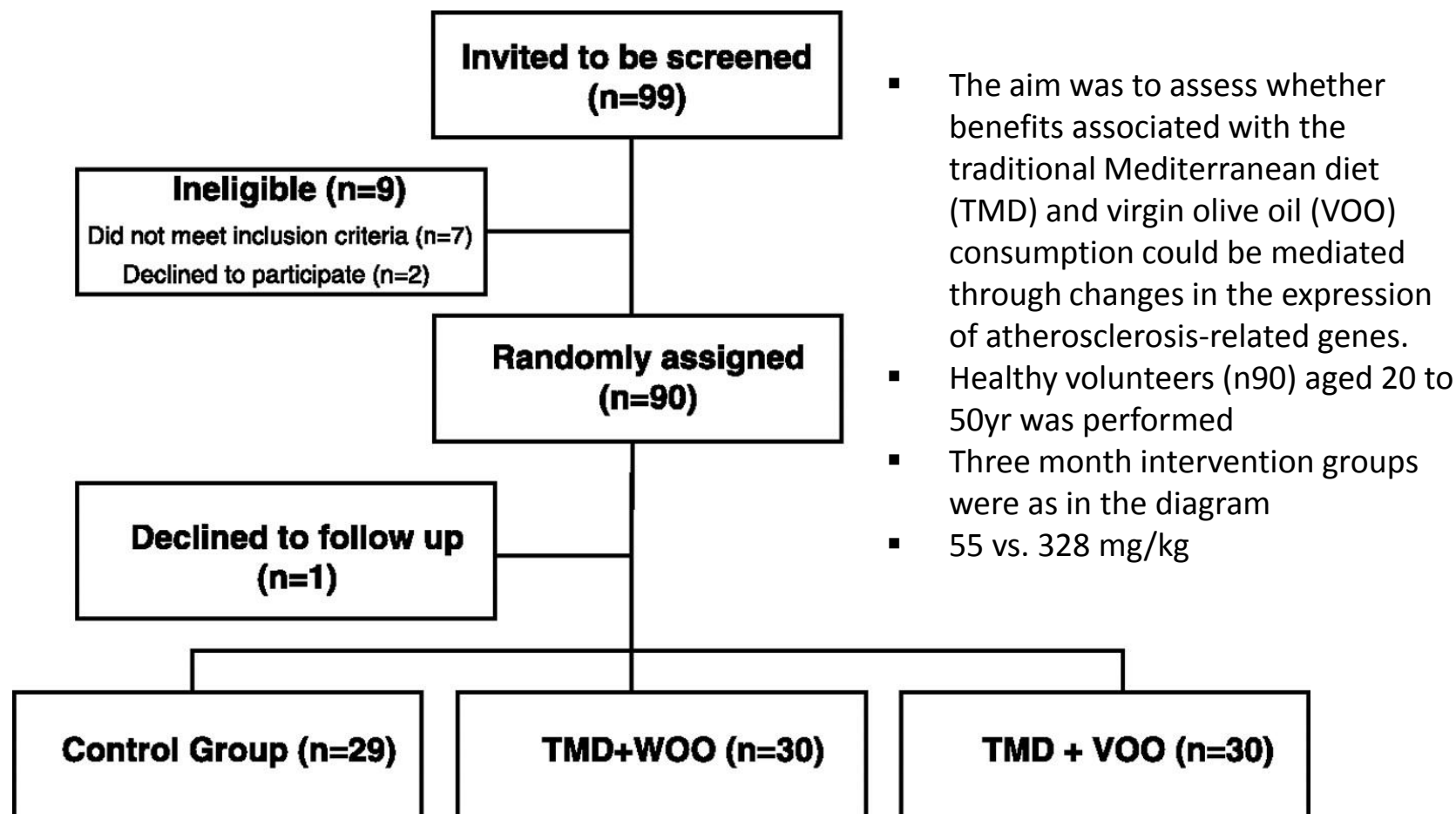
576 fetuses or newborns with NTDs and 594 healthy newborns were included in the case-control study. Information on maternal tea consumption, sociodemographic characteristics, reproductive history, and related behavior was collected through face-to-face interviews. Maternal blood samples were collected to examine polymorphisms in COMT, and the possible interaction of COMT and tea consumption was analyzed.

- Homozygotes of rs737865 showed an elevated risk for total NTDs and for the anencephaly subtype
- The CC genotype of rs4633 was positively associated with the overall risk of NTDs
- Heterozygotes for rs4680 were associated with a decreased risk of spina bifida
- The COMT rs4680 A allele was negatively related with the risk of spina bifida

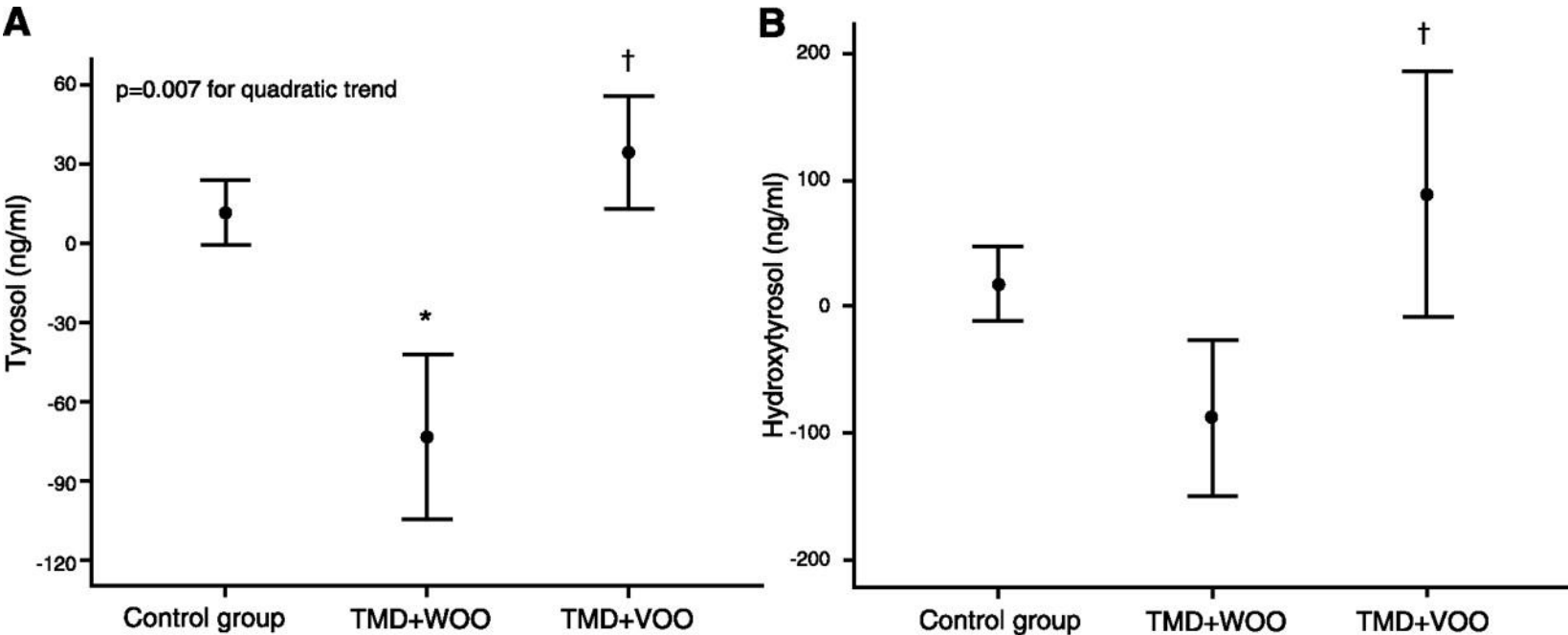


Maternal tea consumption may be associated with an increased risk for fetal NTDs in genetically susceptible subgroups,.....an interaction between tea consumption (1 to 2 cups/day) and the rs4680AA/AG genotype was found in the spina bifida subtype

In vivo nutrigenomic effects of virgin olive oil polyphenols within the frame of the Mediterranean diet: a randomized controlled trial



Changes in urinary tyrosol (A) and hydroxytyrosol (B) after the 3-mo interventions. *P < 0.05 vs. control; †P < 0.05 vs.



Gene expression changes in adrenergic β 2-receptor (ADRB2; A), Rho GTPase activating protein 15 (ARHGAP15; B), INF- γ (IFN γ ; C), and IL-7 receptor (IL7R; D) genes after the 3-mo interventions.

