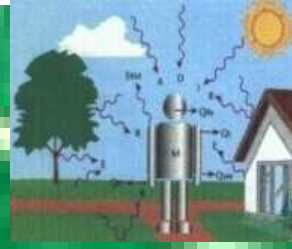
Discover the European Honeyland
Apimondia
Kyiv, Ukraine 2013
29 september - 4 October 2013



Apiproduct propolis and diabetes: Antioxidant and anti-inflammatory properties of propolis protect against diabetes and diabetes-induced pathologies

Pr Badiaa Lyoussi

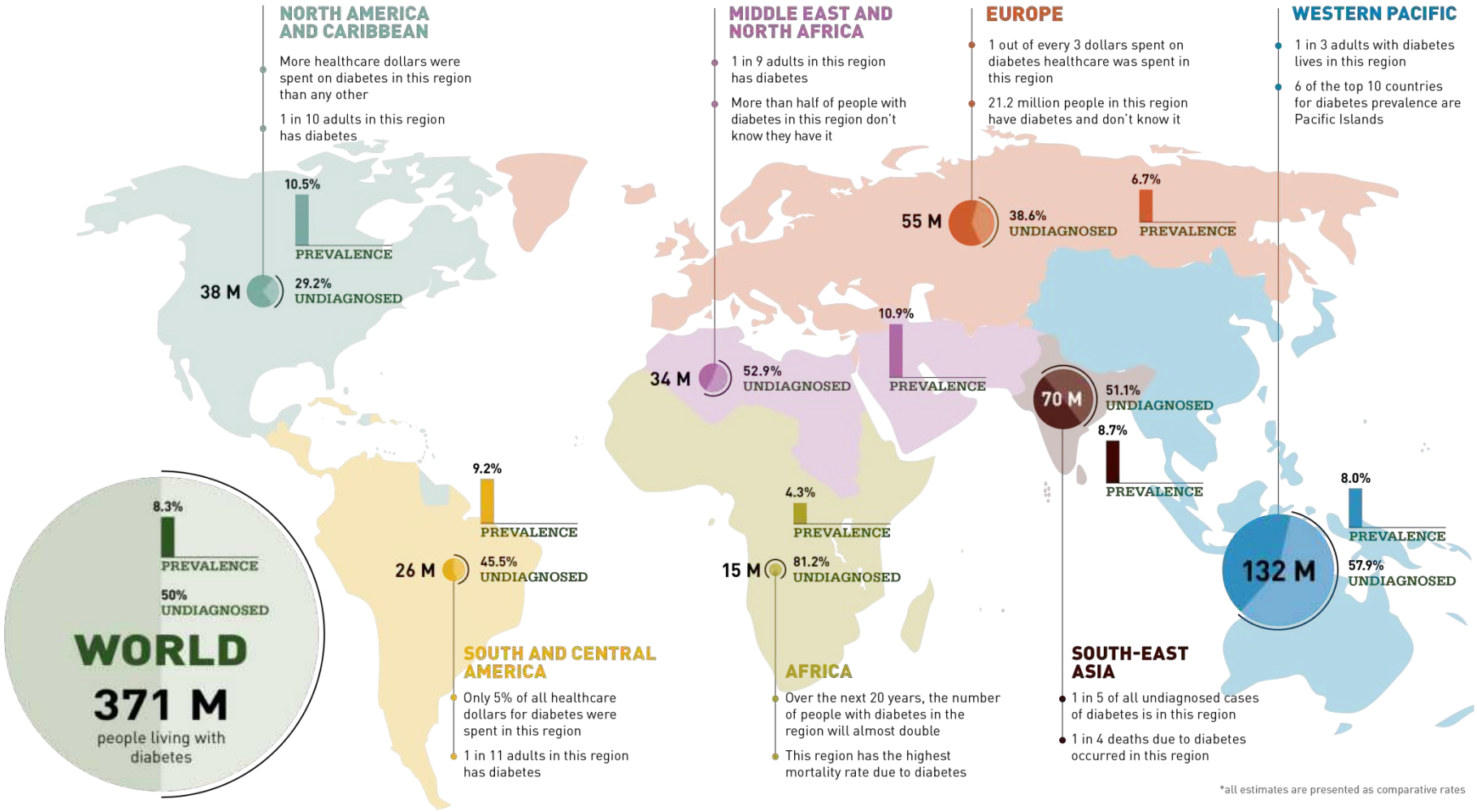
University Sidi Mohamed ben Abdallah, Fez, Morocco

Diabetes: worldwide prevalence and morbidity

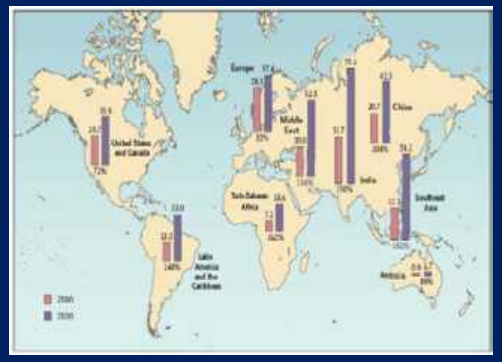
✸ Presently there are 371 million (8.3% of population aged 20-79 yr.) diabetics and estimated to be 438 million by year 2030 (International Diabetic Federation); about 97% have type 2 diabetes mellitus (T_2DM)

✸ 80-85% of T_2DM patients have insulin resistance. Impaired β-cell function occurs in 50% of newly diagnosed T_2DM, and after that, there is a linear reduction in β-cells with time caused by apoptosis

✸ Diabetes account for 60% of lower limb amputations, 44% of new cases of kidney disease, and is the leading cause of blindness among adults; 65% of deaths occur from cardiovascular disease and strokes in diabetics


NORTH AMERICA AND CARIBBEAN
More healthcare dollars were spent on diabetes in this region than any other
1 in 10 adults in this region has diabetes
10.5%
PREVALENCE
38 M
29.2%
UNDIAGNOSED
MIDDLE EAST AND NORTH AFRICA
1 in 9 adults in this region has diabetes
More than half of people with diabetes in this region don't know they have it
34 M
52.9%
UNDIAGNOSED
10.9%
PREVALENCE
EUROPE
1 out of every 3 dollars spent on diabetes healthcare was spent in this region
21.2 million people in this region have diabetes and don't know it
55 M
38.6%
UNDIAGNOSED
6.7%
PREVALENCE
WESTERN PACIFIC
1 in 3 adults with diabetes lives in this region
6 of the top 10 countries for diabetes prevalence are Pacific Islands
70 M
51.1%
UNDIAGNOSED
8.7%
PREVALENCE
132 M
8.0%
PREVALENCE
57.9%
UNDIAGNOSED
9.2%
PREVALENCE
26 M
45.5%
UNDIAGNOSED
SOUTH AND CENTRAL AMERICA
Only 5% of all healthcare dollars for diabetes were spent in this region
1 in 11 adults in this region has diabetes
4.3%
PREVALENCE
15 M
81.2%
UNDIAGNOSED
AFRICA
Over the next 20 years, the number of people with diabetes in the region will almost double
This region has the highest mortality rate due to diabetes
SOUTH-EAST ASIA
1 in 5 of all undiagnosed cases of diabetes is in this region
1 in 4 deaths due to diabetes occurred in this region
8.3%
PREVALENCE
50%
UNDIAGNOSED
WORLD
371 M
people living with diabetes
*all estimates are presented as comparative rates

T_2DM - Major public health problem



Prevalent and increasing

171 millions in 2000

366 millions in 2030 ?

6.6 % adult population in Morocco

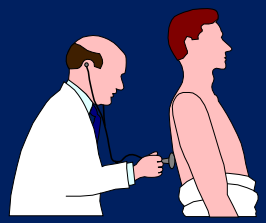
6.7 % adult population in Europe

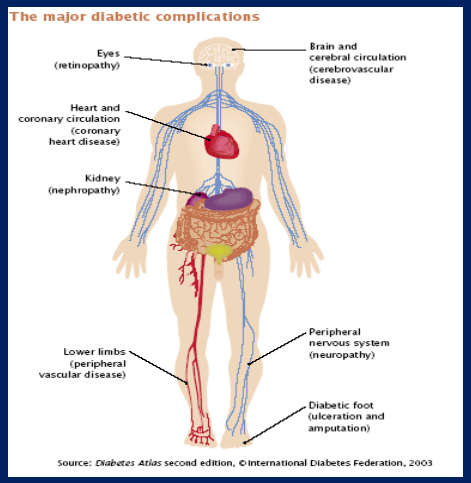
Significant cost

+ $200 billion

(ADA)

T_2DM





Treatments

Not curative

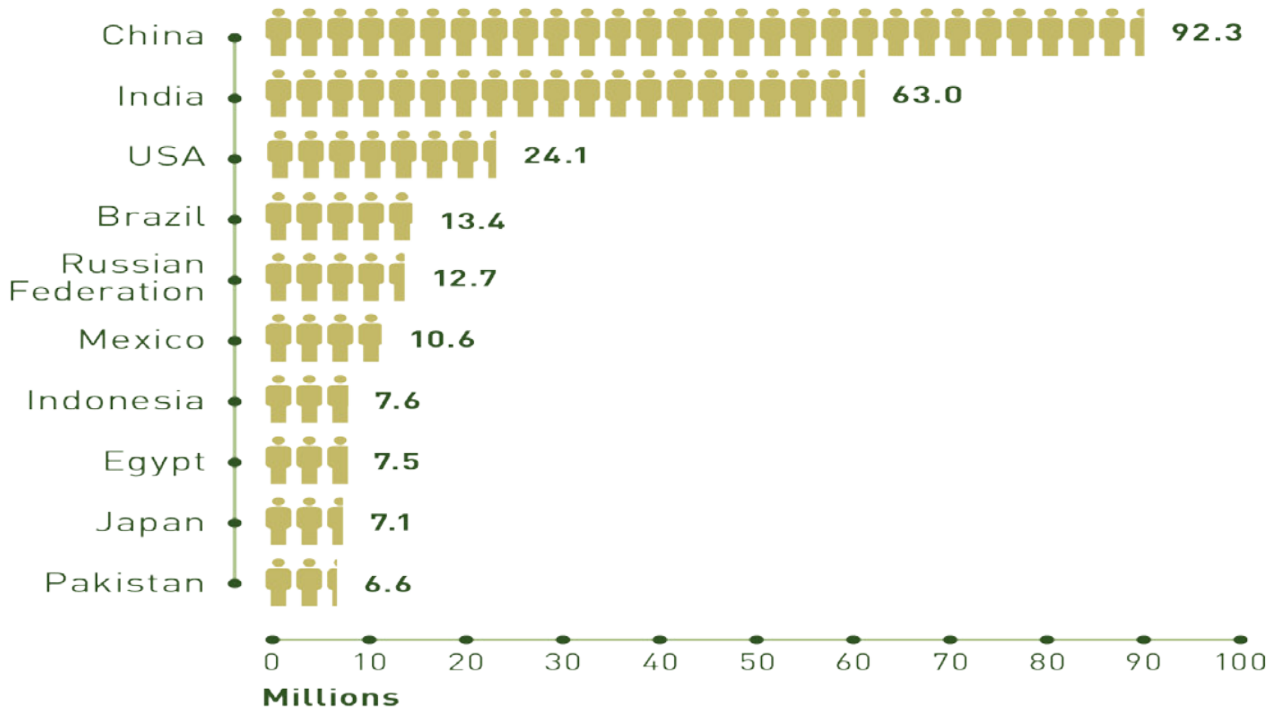
Oral antidiabetics, insulin, Diet ,,,

Complications micro- and macro-vascular

Blindness, kidney failure,
Lower limb amputations
cardiovascular disease ,,,

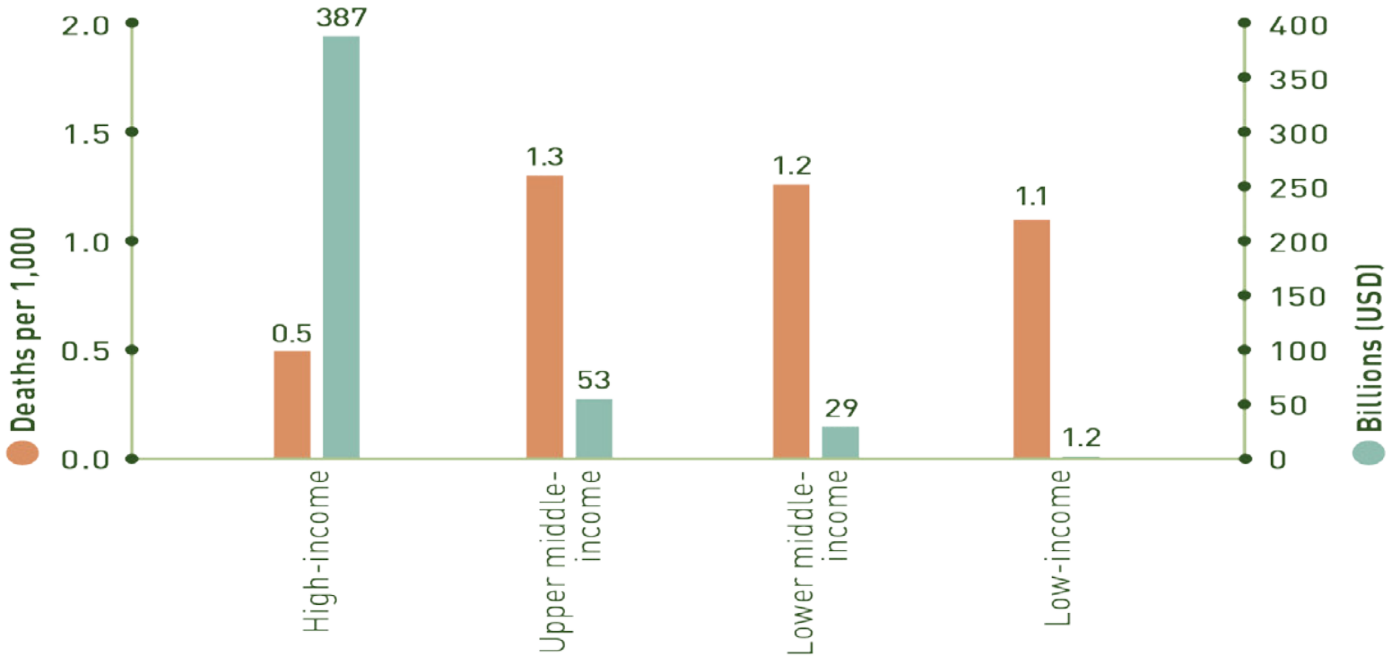
More than **371 million** people have diabetes.

TOP 10 COUNTRIES/TERRITORIES FOR PEOPLE WITH DIABETES (20-79 YEARS)



4.8 million people **died** and **471 billion USD** were **spent** due to diabetes in 2012.

HEALTHCARE EXPENDITURES AND DEATHS PER 1,000 DUE TO DIABETES BY INCOME GROUP

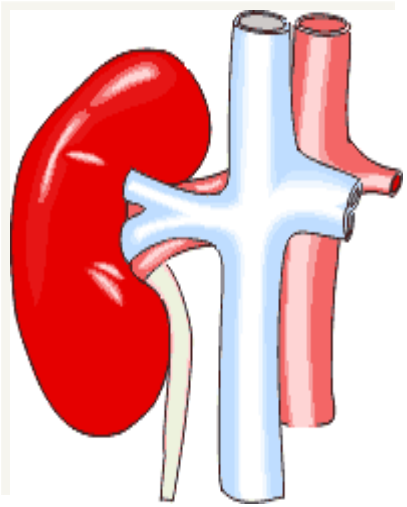


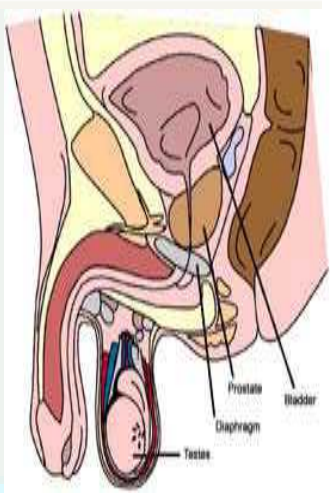
Risk factors

Risk factors associated with type 2 diabetes include:

- Obesity
- Improper diet and physical inactivity
- Increasing age
- Insulin resistance
- Family history of diabetes
- Ethnicity

Microvascular complications of diabetes



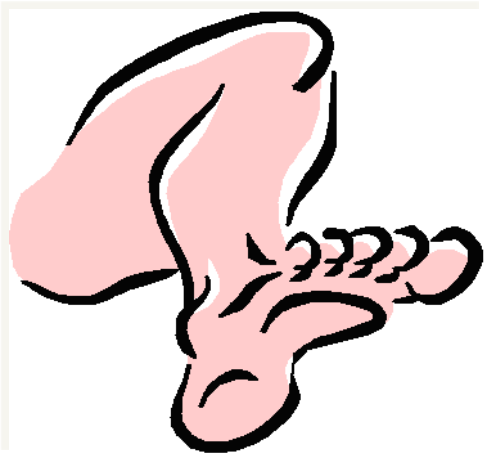


Nephropathy **Retinopathy** **Neuropathy**

Macro-vascular complications of diabetes

Coronary artery disease
Myocardial infarction

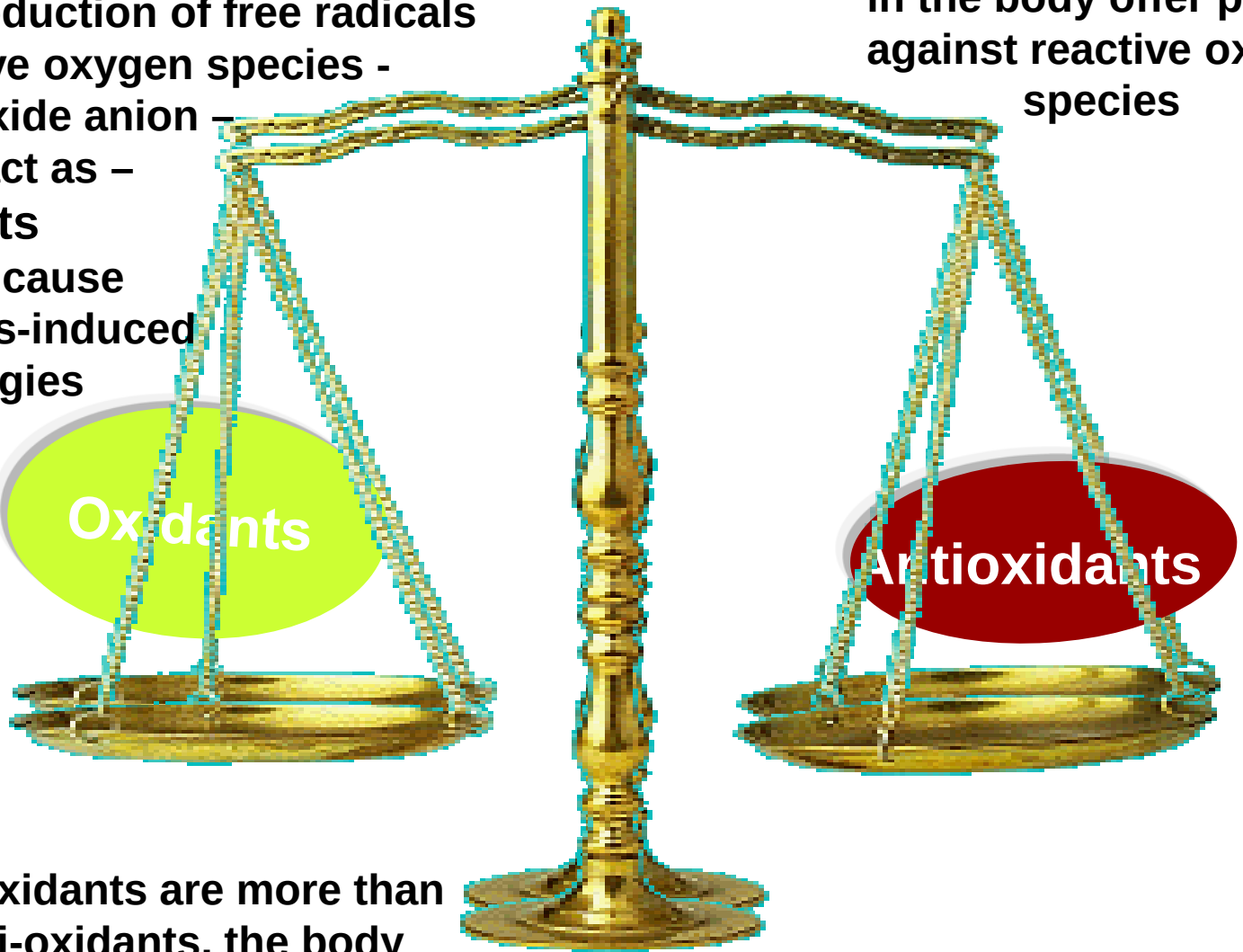
Cerebrovascular accidents



Arteriopathy

Diabetes mellitus promotes overproduction of free radicals - reactive oxygen species - superoxide anion – which act as – **oxidants** – these cause diabetes-induced pathologies

The anti-oxidants present in the body offer protection against reactive oxygen species



If the oxidants are more than the anti-oxidants, the body faces oxidative stress

OXIDATIVE STRESS

Endogenous Pro-Oxidants and Antioxidants

Oxidants

ROS: $\bullet O_2$, H_2O_2, $\bullet OH$, $ONOO^-$

NADPH oxidase
Xanthine oxidase
Myeloperoxidase
Uncoupled NOS
Mitochondrial electron transport
Heme oxygenase
Cytochrome P450
Lipoxygenase
Cyclooxygenase

Antioxidants

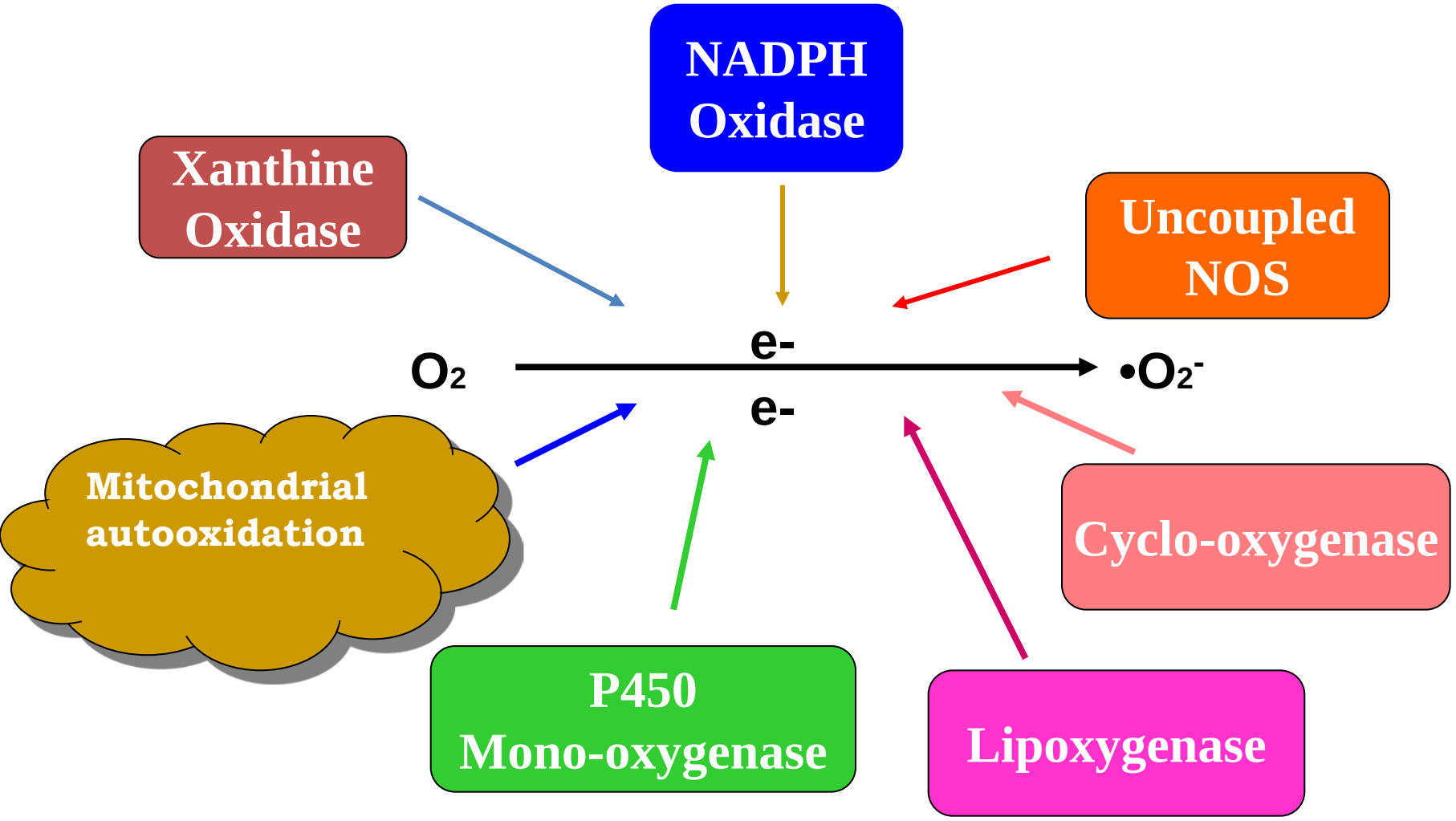
Enzymes

Superoxide dismutase (SOD)
Glutathione peroxidase
Catalase
Thioredoxin Reductase

Non-enzymes

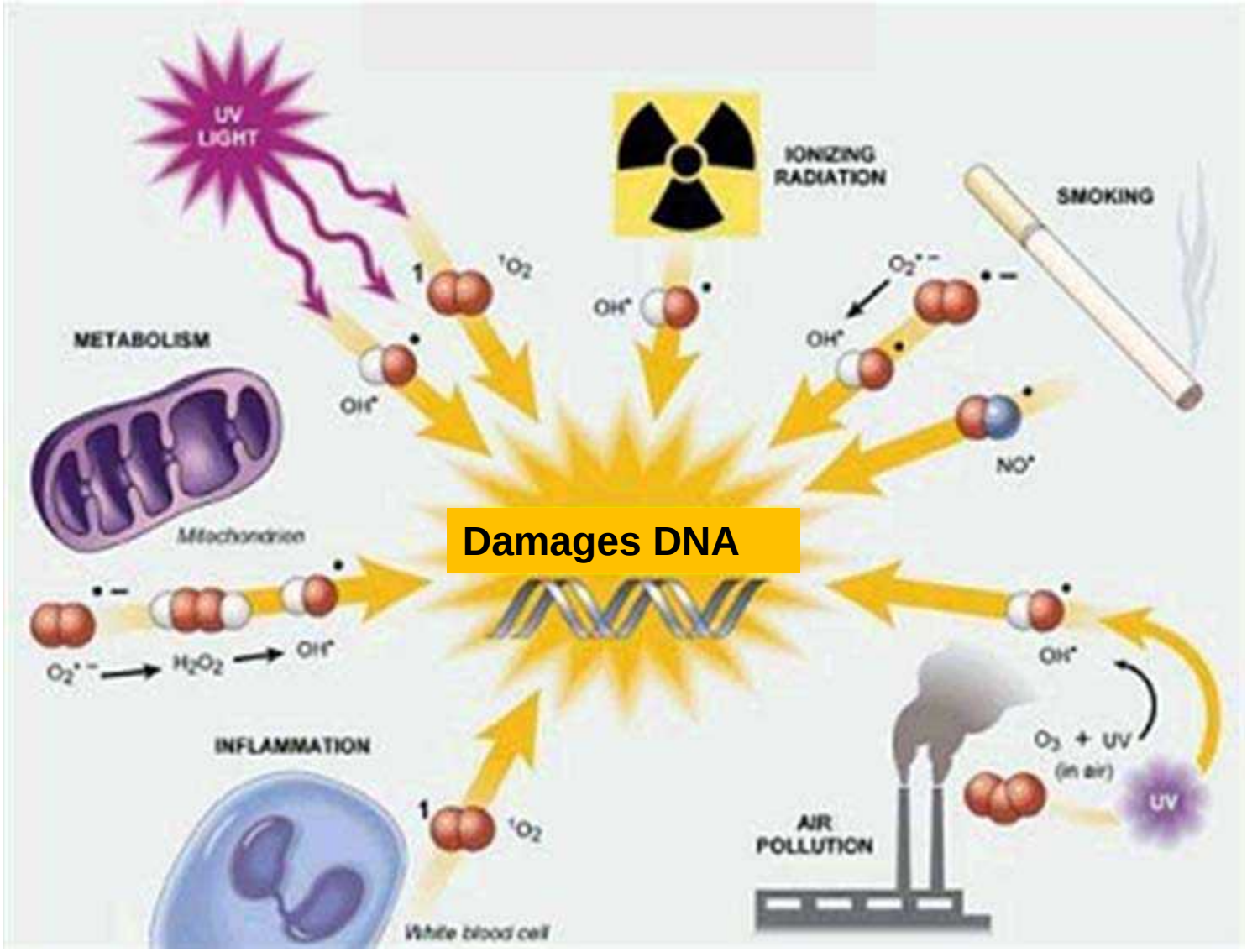
Vitamins A, C and E
Thiols
Flavonoids
Other polyphenols

Many Cellular Enzymes Catalyze the Generation of Superoxide anion from Molecular Oxygen



Free radical sources

BIOLOGICAL



ENVIRONMENTAL

Formation of Propolis

Propolis is formed from plant resins secreted by the buds and bark of certain trees
It is collected by bees, thanks to its antenna (location) and mandible.
These substances are brought back to the hive in the form of drops.
They are partially modified by bee secretions (mainly wax and salivary secretions)

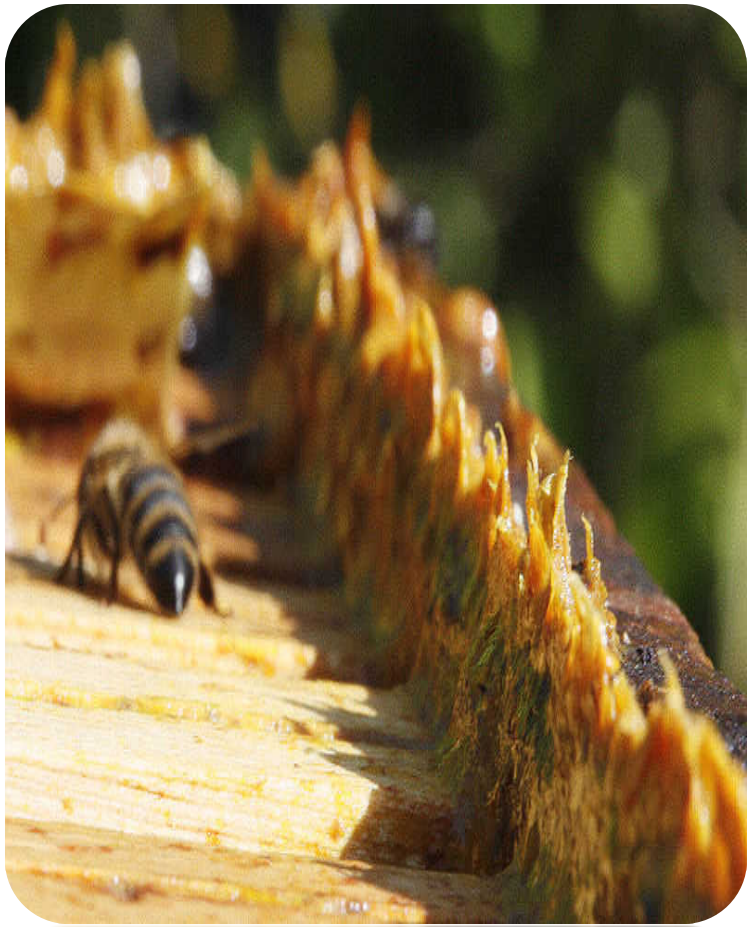
300 grams per hive per year

Propolis, an apiproduct used by the honeybees as a sealant, has been rediscovered as a medicinal agent, reported to be of benefit in the treatment of allergies, bruises, burns, ulcers, sunburn, wounds, tumors, fatigue, sore throat, nasal congestion, respiratory ailments, flu, colds, acne, skin disorders, and shingles. Propolis consists of plant resins, balsams, wax, bee pollen and essential oils. The composition of propolis (of different colors) depends on the phytogeographical location, seasonal collection time, and botanical source. It is reported to contain more than 300 natural compounds such as polyphenols, phenolic aldehydes, stilbenes, sesquiterpene-quinones, coumarins, chalcones, flavones, flavonols, flavonoids (galangin, chrysin, caffeic acid phenethyl ester, pinocembrin), amino acids, steroids, and inorganic compounds

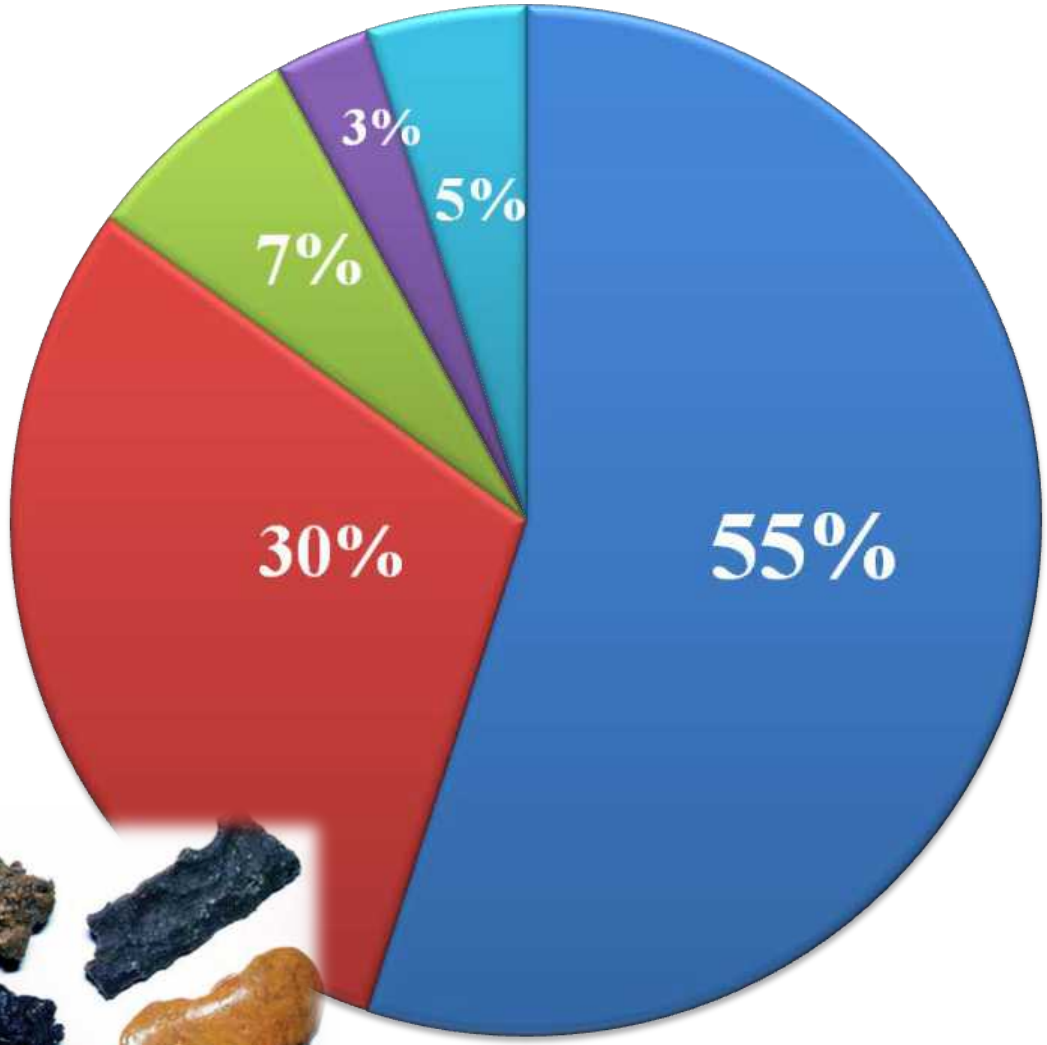




Propolis is reported to have anti-angiogenic, antihypercholesterolemic, antihypertensive, anti-inflammatory, antimicrobial, antioxidant, anti-parasitic, anti-septic, anti-tumor, antiulcer, anti-viral, immune-stimulatory properties, and hepato-, cardio-, and neuro-protective activity. Diabetes and pathologies associated with it are mainly due to inflammation and oxidative stress, as a result of elevated levels of reactive oxygen species (ROS), which cause lipid peroxidation and protein oxidation.

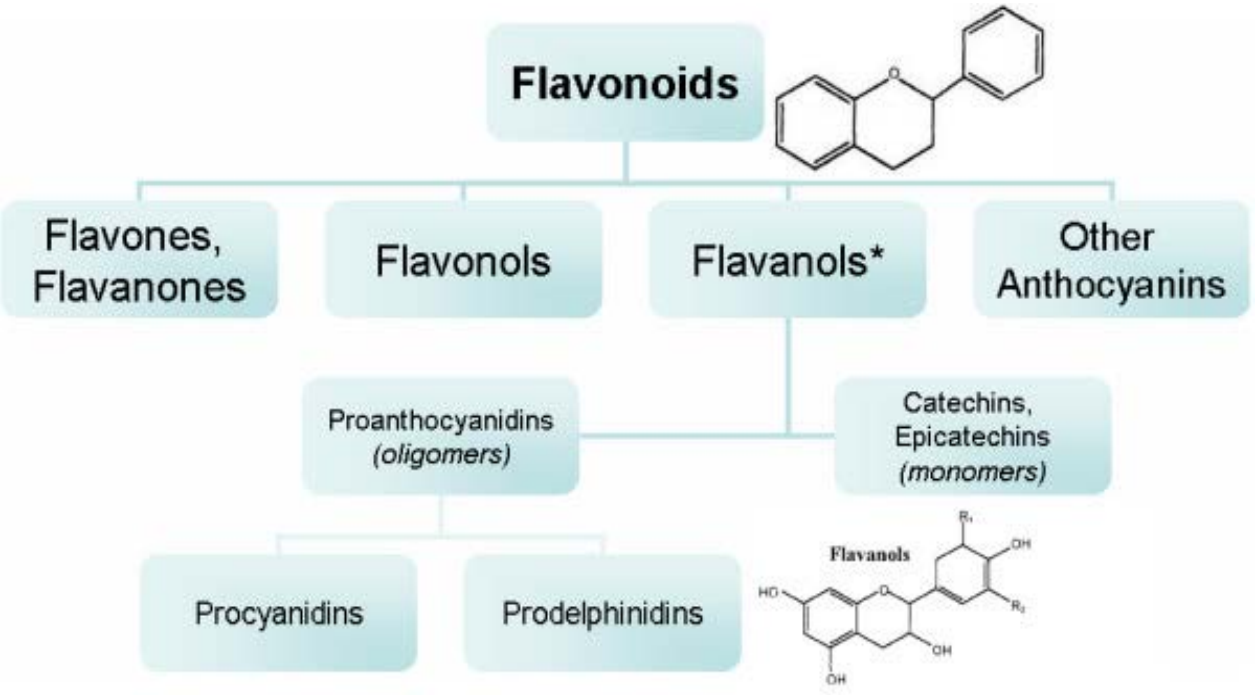


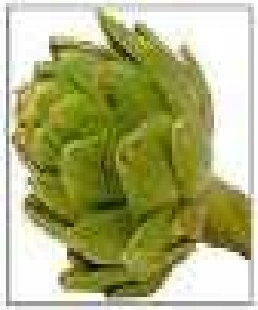
Chemical Composition of propolis



- Resins and balms مركبات صمغية وبلسم
- Wax شمع النحل
- Essential Oils الزيوت الأساسية
- Pollen حبوب اللقاح
- Others أخرى

The anti-oxidant, oxygen radical scavanging activity of propolis (and its extracts) is mainly due to the presence of phenolics and flavonoids





Artichoke
(Silymarin)

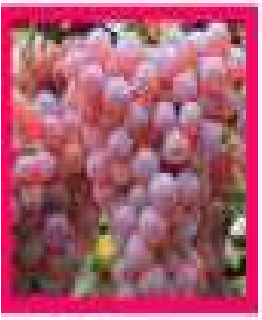
Oleander
(Oleanderin)

Tomato
(Lycopene)

Garlic
(Diallyl sulfide, ajoene, S-allyl cysteine, allicin)

Carrots
(β-carotenes)

Tea
(Catechins)



Red grapes
(Resveratrol)

Red chilli
(Capsaicin)

Turmeric
(Curcumin)

Cloves
(Eugenol & isoeugenol)

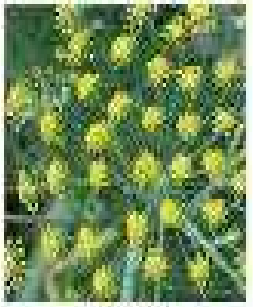
Honey-bee propolis
CAPE

Cruciferous vegetables
(Sulforaphane)

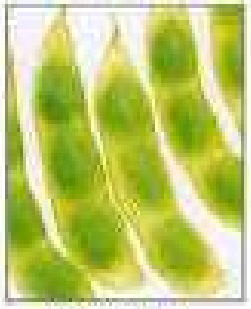
Pomegranate
(Ellagic acid)

Ginger
(6-Gingerol)

Basil
(Ursolic acid)



Fennel,
(Anethol)

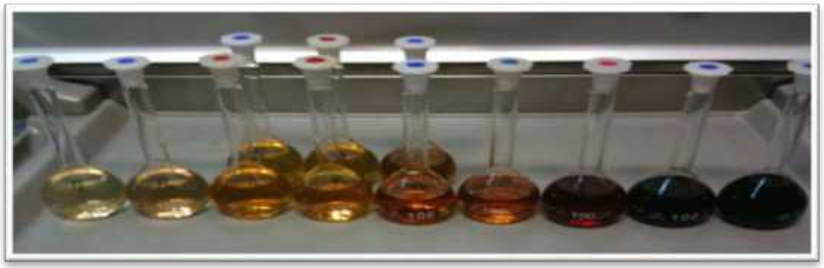


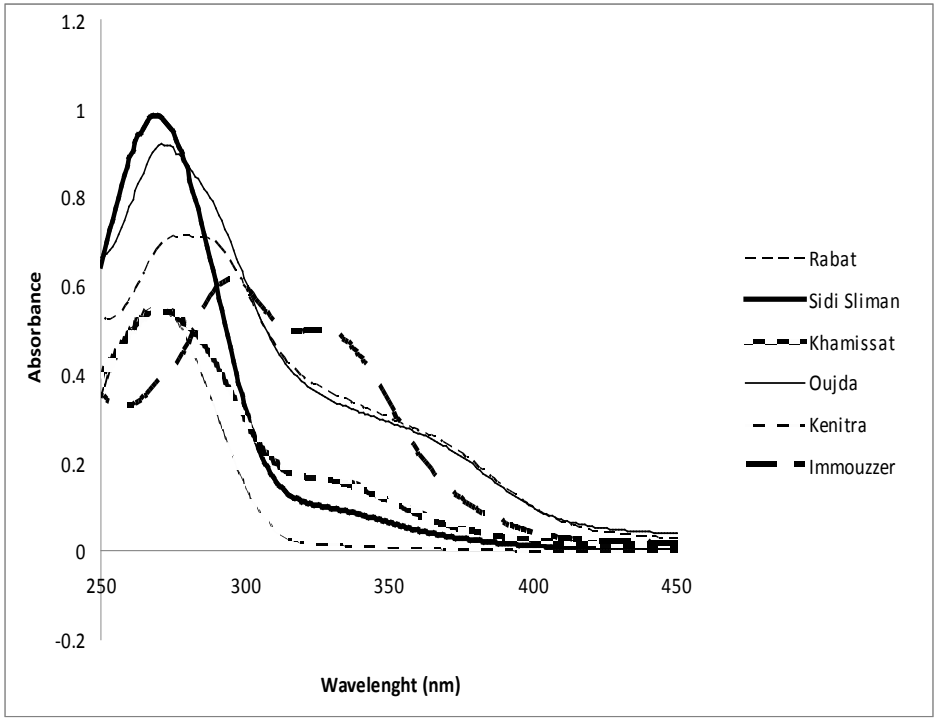
Soybean
(Genistein)

Aloe
(Emodin)

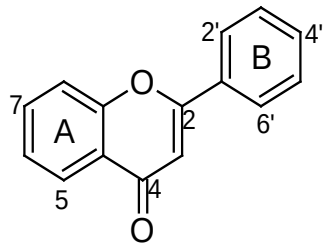
RESINS, BALMS AND WAX FROM PROPOLIS SAMPLES

PROPOLIS	% WAX	% RESINS	% BALMS
Moulay Bouslham	87.70	3.25	0.86
Sidi Ifni	57.15	2.09	0.09
Bhalil	16.69	20.80	0.21
Zawiyat Chikh	46.34	19.70	0.79
Rabat	2.79	51.77	0.46
Sidi Sliman	75.55	5.17	1.69
Khamissat	16.24	41.12	1.80
Araich	68.08	20.42	0.27
Oujda	1.80	47.89	0.43
Kenitra	67.77	20.15	9.66
Imouzar	16.34	38.98	1.94

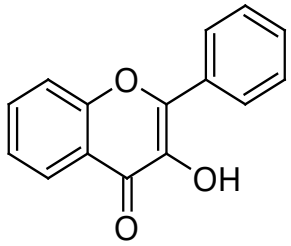




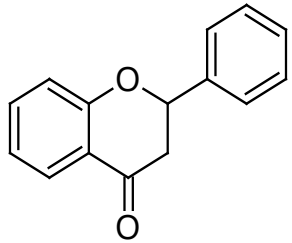
Absorption spectra of the ethanolic propolis extracts from diverse locations of Morocco. Different dilutions are made: Sidi sliman (40), Kenitra (160), Immouzzer, Oujda and Rabat (320), Khamissat (640).



Flavone



Flavonol



Flavanone

General structure of some subgroups of flavonoids

Phenol and flavonoid content in samples of propolis from diverse regions of Morocco obtained by maceration

Sample	Phenol (mg/g)	Flavonoid (mg/g)
Moulay Bouslham	5.98±1.12^{f}	1.75±1.39^{d}
Sidi ifni	6.82±1.12^{f}	1.80±1.39^{d}
Bhalil	12.86±1.12^{e}	3.25±1.39^{d}
Zawiat chikh	5.34±1.12^{fg}	1.87±1.39^{d}
Rabat	53.51±1.12^{c}	33.31±1.39^{a}
Sidi sliman	1.45±1.12^{gh}	0.30±1.39^{d}
Khamissat	65.67±1.12^{b}	12.78±1.39^{c}
Larache	6.00±1.12^{f}	2.05±1.39^{d}
Kenitra	0.74±1.12^{i}	0.20±1.39^{d}
Oujda	44.73±1.12^{d}	34.27±1.39^{a}
Immouzzer	91.22±1.12^{a}	26.30±1.39^{b}
Taza	7.83±1.12^{f}	1.68±1.39^{d}
Taounat	5.89±1.12^{f}	0.93±1.39^{d}
Sefrou	6.211±1.120^{f}	1.05±1.39^{d}

Results are shown as the mean ± SD (n=3). In the same column, values with the same letter are not significantly different (P<0.05).

Miguel, Lyoussi, *Food Science Biotechnology, in press*

IC_{50} values (mg/ml) found for the extracts of propolis from diverse locations of Morocco and obtained by maceration. For ORAC method, IC_{50} values are given as Trolox Equivalent (TE)

Sample	ABTS (mg/ml)[1]	DPPH (mg/ml)[1]	Hydroxyl (mg/ml) [1]	ORAC μmol TE/g[1]
Moulay Bouslham	0.279±0.016^{c}	0.523±0.031^{cd}	1.398±0.008^{b}	1106.423±78.151^{e}
Sidi ifni	0.236±0.016^{cd}	0.384±0.031^{e}	0.719±0.008^{e}	1570.866±78.151^{c}
Bhalil	0.297±0.016^{e}	0.239±0.031^{f}	1.111±0.008^{d}	1404.360±78.151^{bcd}
Zawiat chikh	0.366±0.016^{b}	0.409±0.031^{e}	1.441±0.008^{a}	1198.169±78.151^{cde}
Rabat	0.136±0.016^{e}	0.008±0.031^{g}	0.104±0.008^{k}	1455.039±78.151^{bc}
Sidi sliman	1.009±0.016^{a}	1.125±0.031^{b}	-	1353.256±78.151^{abcd}
Khamissat	0.0126±0.016^{f}	0.025±0.031^{g}	0.059±0.008^{l}	2012.152±78.151^{a}
Larache	0.408±0.016^{b}	0.559±0.031^{c}	1.191±0.008^{c}	1278.603±78.151^{cde}
Kenitra	-	1.813±0.031^{a}	0.540±0.008^{i}	1291.157±78.151^{cde}
Oujda	0.022±0.016^{f}	0.025±0.031^{g}	0.398±0.008^{j}	1143.483±78.151^{de}
Immouzzer	0.009±0.016^{f}	0.019±0.031^{g}	0.078±0.008^{l}	1865.506±78.151^{b}
Taza	0.209±0.016^{d}	0.294±0.031^{f}	0.577±0.008^{h}	ND
Taounat	0.297±0.016^{c}	0.459±0.031^{e}	0.651±0.008^{g}	ND
Sefrou	0.296±0.016^{c}	1.086±0.031^{b}	0.677±0.008^{f}	ND

Miguel, Lyoussi, *Food Science Biotechnology, in press*

Pearson correlation coefficients among compounds/antioxidant activities,compounds/acetylcholinesterase inhibition, compounds/lipoxygenase inhibition

	Phenols	Flavonoids
DPPH	-0.623**	-0.592**
ABTS	-0.609**	-0.535**
Hydroxyl	-0.743**	-0.647**
TBARS	-0.640**	-0.774**
ORAC	+0.676**	+0.218NS
Lipoxygenase	-0.752**	-0.743**
Acetylcholinesterase	-0.873**	-0.866**

Pearson Correlation significance levels: NS: not significant.
-: Assay not performed
** significant at $P < 0.01$.

Miguel, Lyoussi, *Food Science Biotechnology, in press*

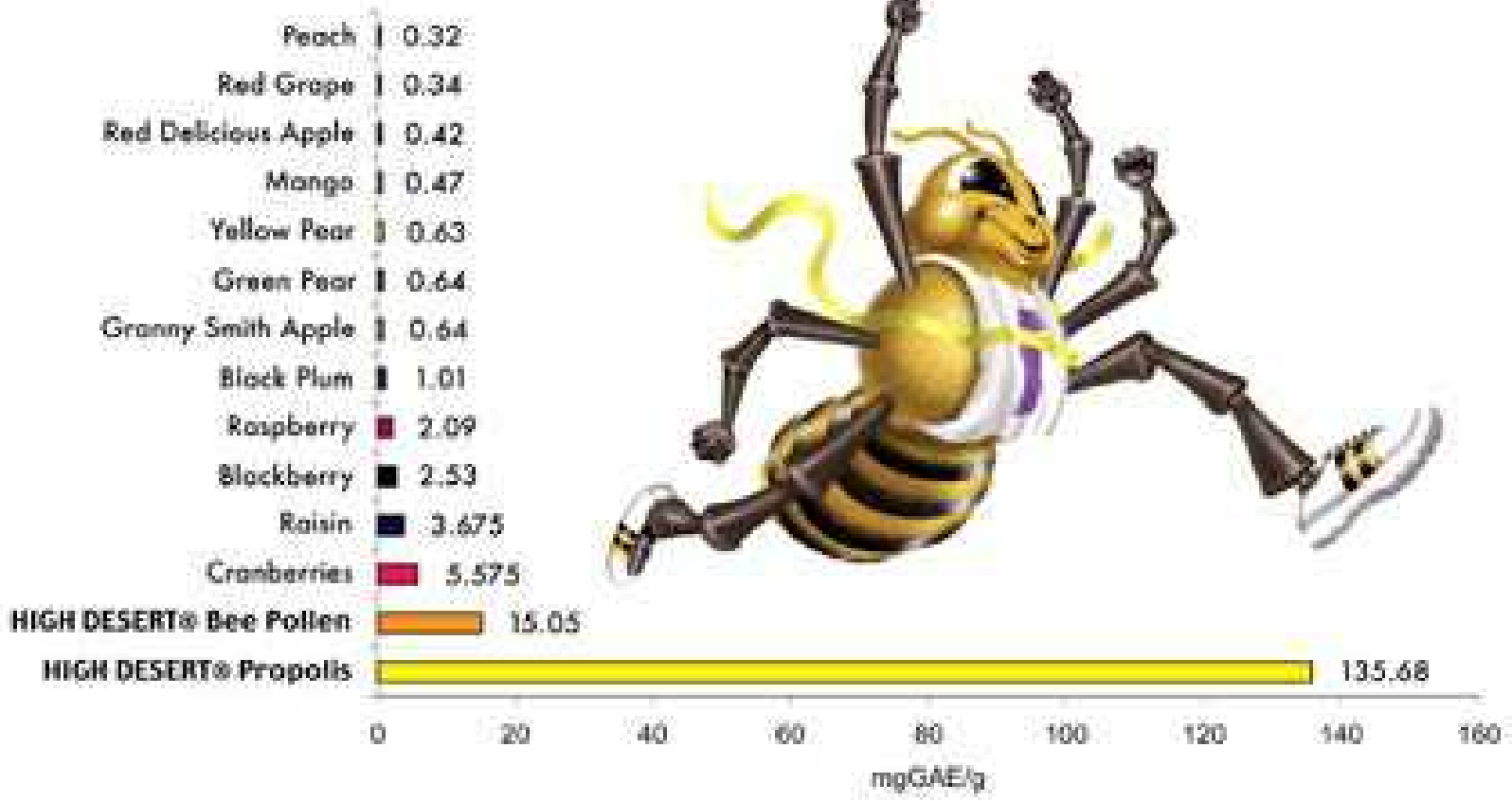
IC_{50} values (mg/ml) found for the extracts of propolis from diverse locations of Morocco and obtained by maceration

Sample	TBARS	Lipoxygenase	Acetylcholinesterase
Moulay Bouslham	0.685 ± 0.023^{ab}	1.968 ± 0.016^{e}	-
Sidi ifni	0.572 ± 0.023^{d}	1.206 ± 0.016^{f}	-
Bhalil	0.144 ± 0.023^{e}	0.217 ± 0.016^{h}	0.569 ± 0.006^{b}
Zawiat chikh	0.312 ± 0.023^{d}	2.182 ± 0.016^{c}	0.743 ± 0.006^{a}
	0.014 ± 0.023^{f}	0.149 ± 0.016^{i}	0.089 ± 0.006^{c}
Sidi sliman	-	-	-
Khamissat	0.249 ± 0.023^{d}	0.248 ± 0.016^{h}	0.087 ± 0.006^{c}
Larache	0.609 ± 0.023^{bc}	1.995 ± 0.016^{e}	0.559 ± 0.006^{b}
Kenitra	-	-	-
	0.051 ± 0.023^{f}	0.272 ± 0.016^{h}	0.043 ± 0.006^{d}
Immouzzer	0.241 ± 0.023^{d}	0.380 ± 0.016^{g}	0.085 ± 0.006^{c}
Taza	-	2.092 ± 0.016^{d}	-
Taounat	0.699 ± 0.023^{a}	2.521 ± 0.016^{a}	-
Sefrou	0.657 ± 0.023^{ab}	2.461 ± 0.016^{b}	-
BHT	0.097 ± 0.023^{ef}	ND	ND
NDGA	ND	0.020 ± 0.016^{j}	ND
Galantamine	ND	ND	0.003 ± 0.006^{e}

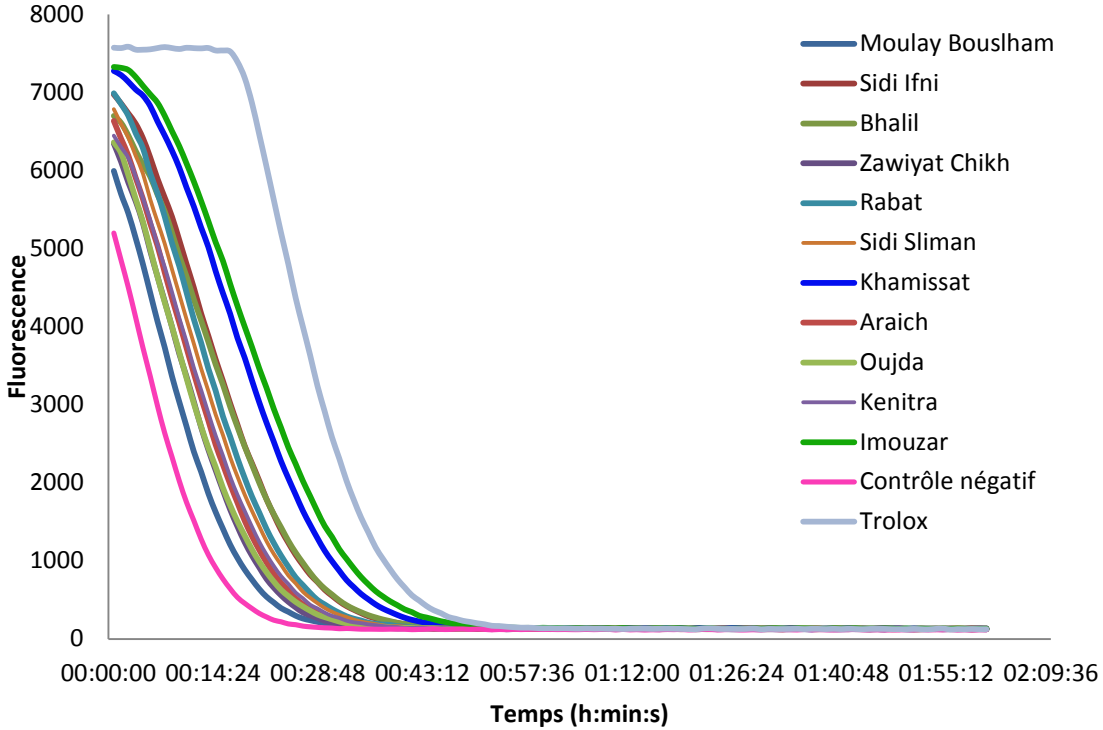
Results are shown as the mean ± SD (n=3). In the same column, values with the same letter are not significantly different (P<0.05).
-: the concentrations assayed did not permit to determine IC_{50} values
ND: Not determined

Miguel, Lyoussi, *Food Science Biotechnology, in press*

Total Polyphenol Content



Oxygen Radical Absorbance Capacity (ORAC)



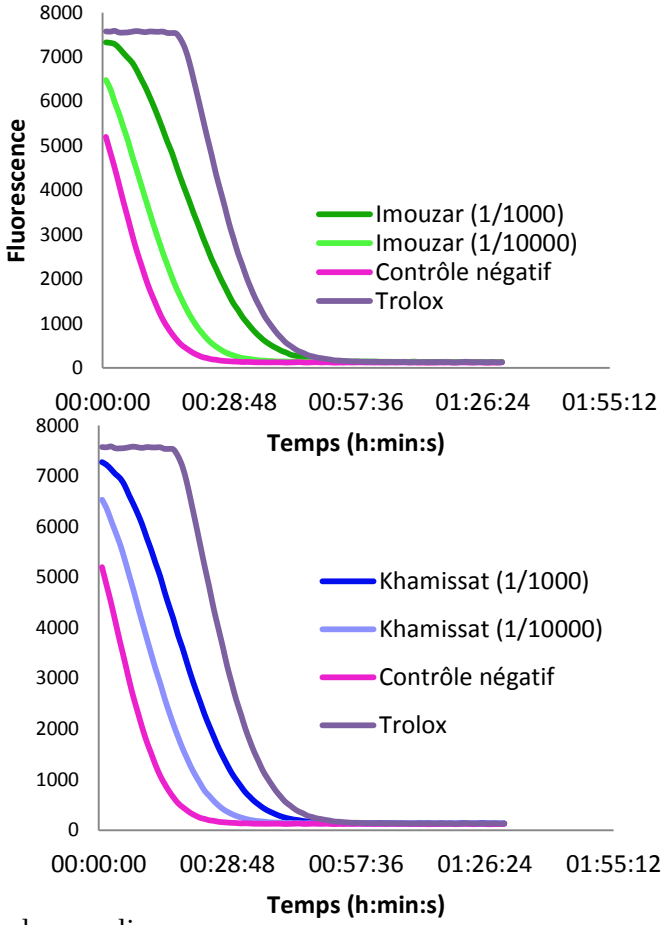


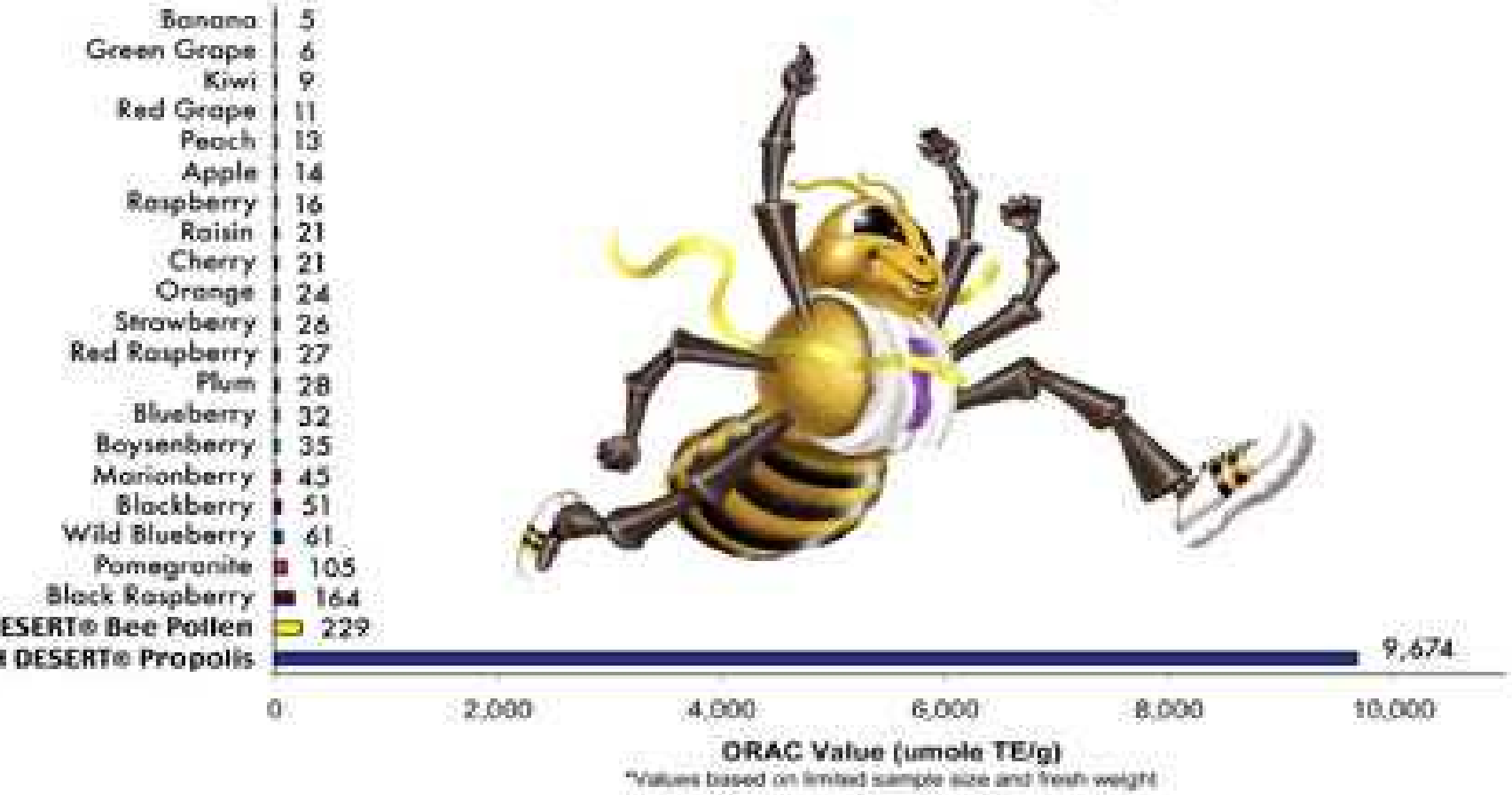
Figure : Graphes de l'ORAC des échantillons de propolis.

Tableau : µEq Trolox/mg de l'ORAC des échantillons de propolis.

Propolis	Moulay Bouslham	Sidi ifni	Bhalil	Zawiat chikh	Rabat	Sidi sliman	Khamissat	Araich	Oujda	Kenitra	Imouzar mermoucha
µEq Trolox/mg propolis±SD	1,106 ± 0,004	1,374 ± 0,032	1,436 ± 0,259	1,198 ± 0,009	1,459 ± 0,025	1,277 ± 0,021	2,014 ± 0,008	1,279 ± 0,003	1,182 ± 0,097	1,202 ± 0,035	2,052 ± 0,008

ORAC (Oxygen Radical Absorbance Capacity) Chart

Whole Food Antioxidant Activity



*Values based on limited sample size and fresh weight

ANTI-INFLAMMATORY ACTIVITY

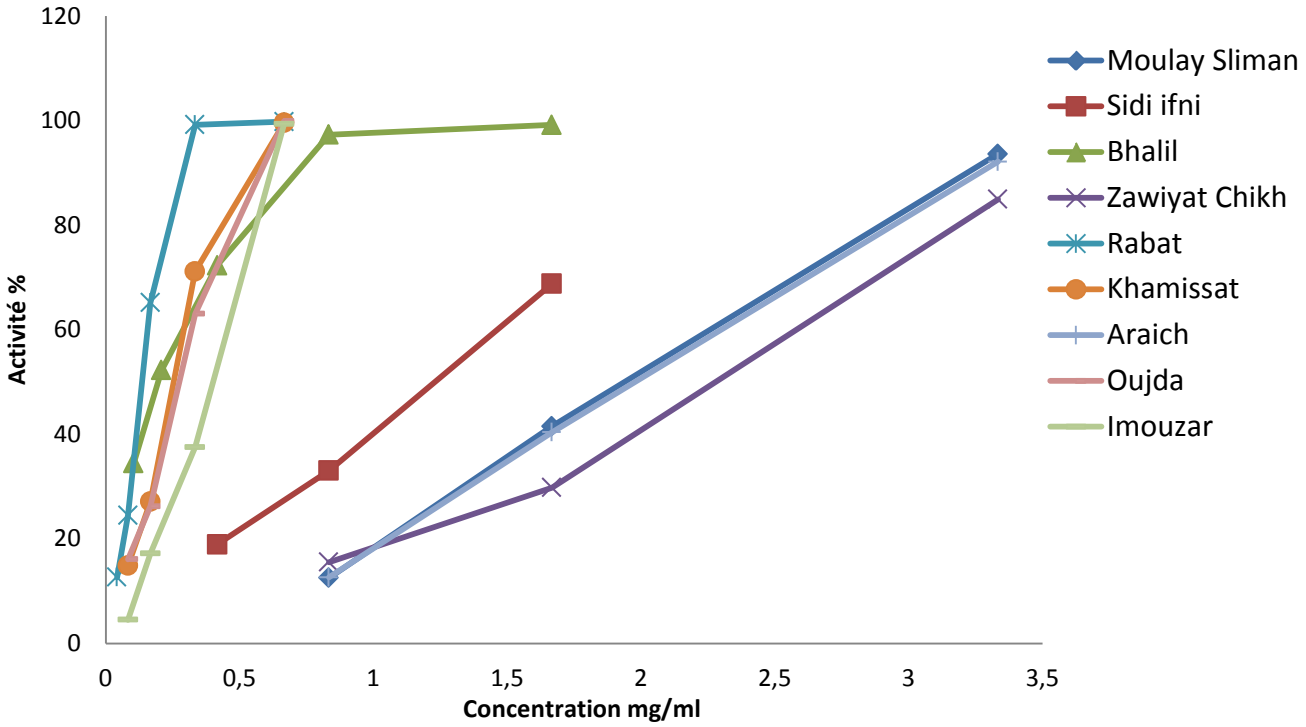
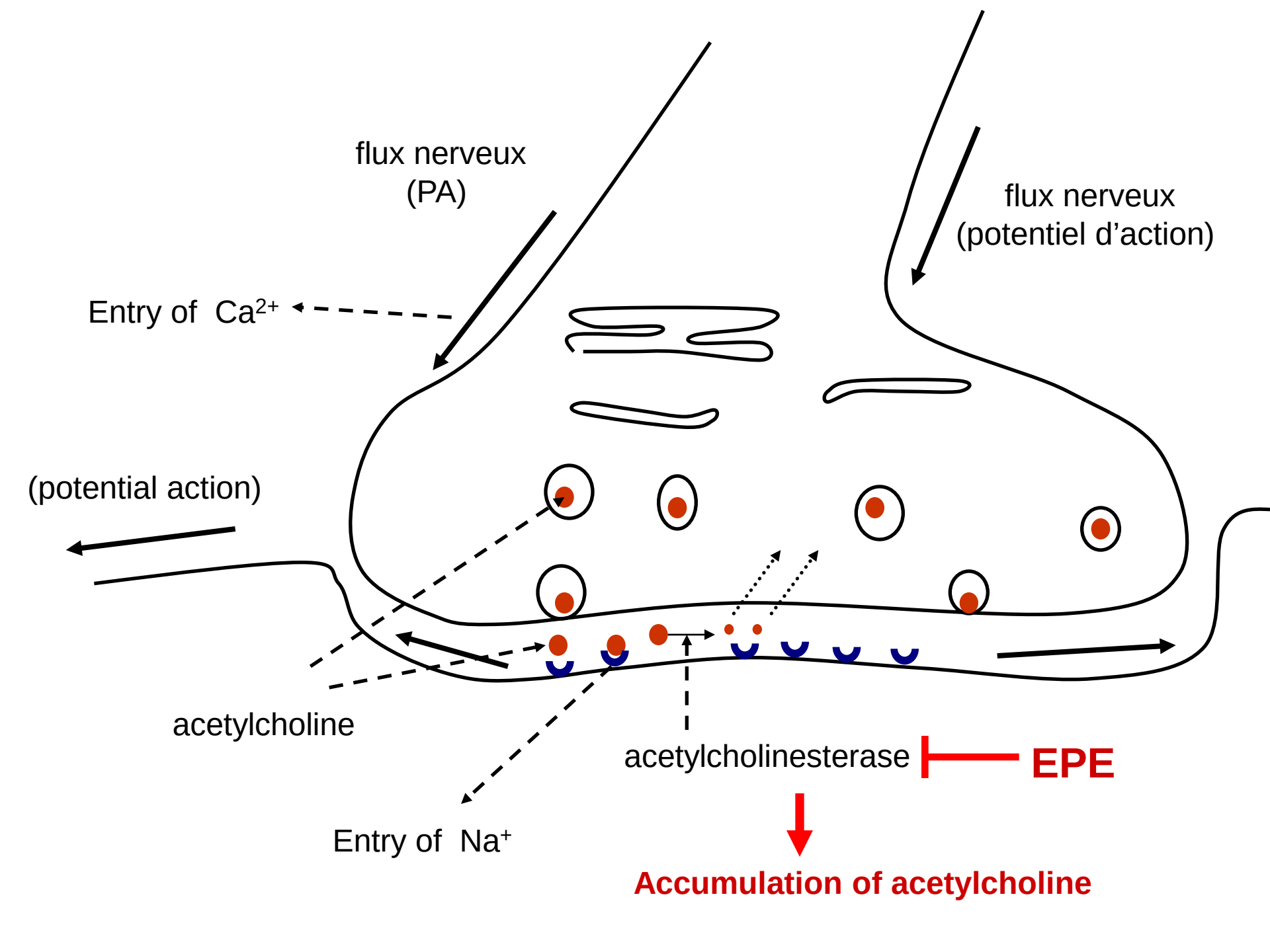


Figure : Inhibitory activity of lipoxygenase from propolis samples

Propolis	Moulay Bouslham	Sidi ifni	Bhalil	Zawiat chikh	Rabat	Sidi sliman	Khamissat	Araich	Oujda	Kenitra	Imouzar mermoucha
IC_{50} (mg/ml ± SD)	1,968 ± 0,025	1,213 ± 0,016	0,217 ± 0,008	2,174 ± 0,011	0,134 ± 0,005	-	0,247 ± 0,003	1,994 ± 0,008	0,271 ± 0,003	-	0,380 ± 0,009


flux nerveux
(PA)
flux nerveux
(potentiel d'action)
Entry of Ca2+
(potential action)
acetylcholine
acetylcholinesterase
EPE
Entry of Na+
Accumulation of acetylcholine

ANTI-ACETYLCHOLINESTERASE ACTIVITY

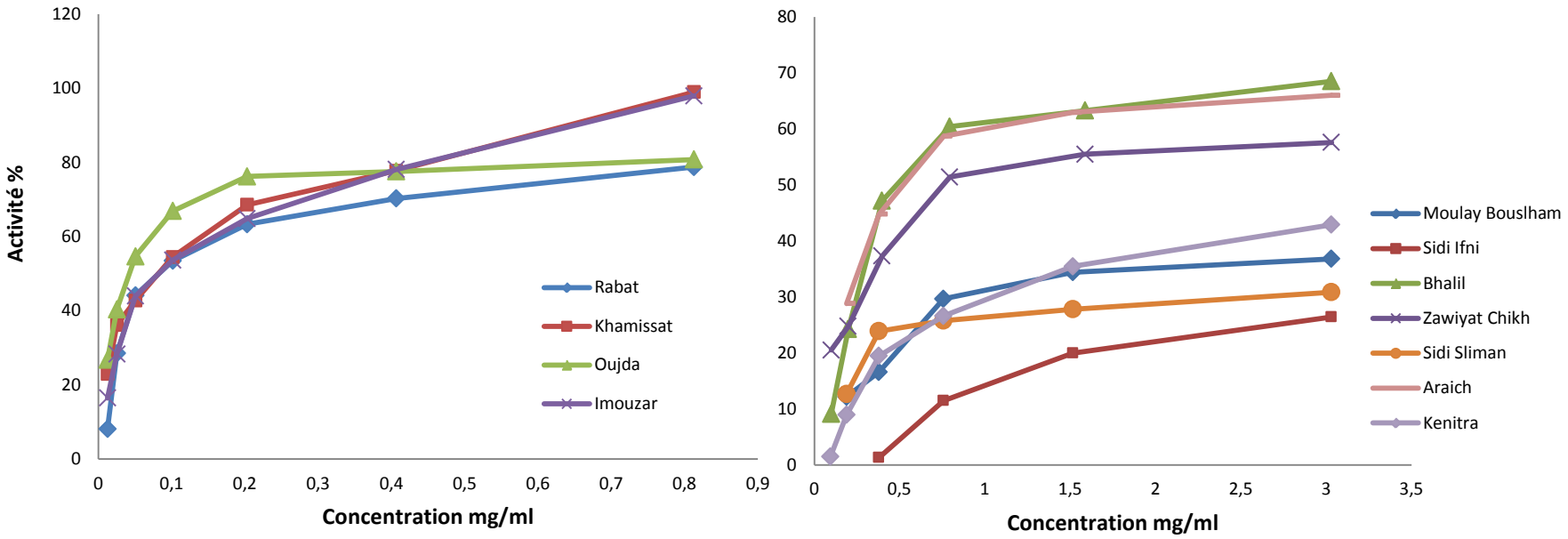
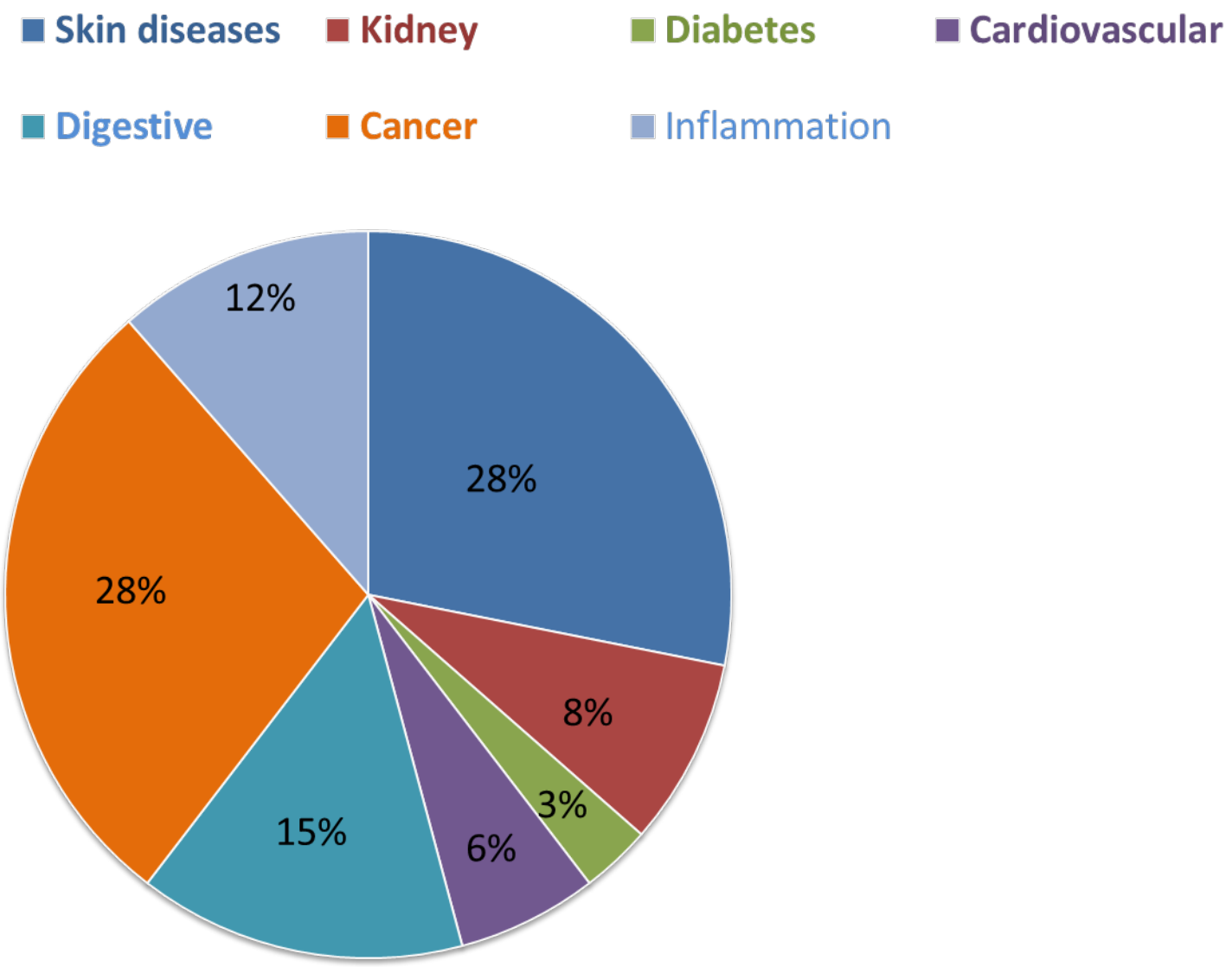


Tableau : IC_{50} de l'activité anti-AChE des échantillons de propolis.

Propolis	Moulay Bouslham	Sidi ifni	Bhalil	Zawiat chikh	Rabat	Sidi sliman	Khamissat	Araich	Oujda	Kenitra	Imouzar
IC_{50} (mg/ml ± SD)	-	-	0,569 ± 0,002	0,743 ± 0,021	0,088 ± 0,009	-	0,082 ± 0,005	0,559 ± 0,015	0,042 ± 0,0001	-	0,087 ± 0,008

Propolis and Pathologies



Propolis - A Novel Antidiabetic Agent

Effect of propolis on glycemic control (glucose, fructosamine and glycosylated hemoglobin)

The measurements of blood glucose, fructosamine and glycosylated hemoglobin are commonly employed to assess the extent of glycemic control in diabetes mellitus Unlike fasting blood glucose, fructosamine and glycosylated hemoglobin measure glycemic control over a period of two to three weeks and eight to twelve weeks, respectively

Therapeutic Uses of Propolis

Effect of propolis on glucose-regulating hormones and pancreas

The antidiabetic effect of propolis was via inhibition of gene expression and enzyme activity of glucose-6-phosphatase (Kang LJ, et al., Phytother Res 2010;24:1554)

Therapeutic Uses of Propolis

Antidiabetic effect of propolis: Potential mechanisms of action based on the free radical scavenging constituents and anti-oxidant effect of propolis

An ethanol extract of propolis – contained phenolic acids and flavonoids (caffeic acid, ferulic acid, and luteolin) – able to have reducing power and ability to scavenge free radicals and metal ions – and block intracellular oxidation in *Saccharomyces cerevisiae*
Mavri A, et al. Chemistry & Biodiversity 2012;9:1545-1558

Antioxidant activity was proportional to amount of phenols, flavones and flavonols in aqueous extracts of propolis (Isla MI et al., J Med Food 2009; 12:1334; Gregoris E et al., Food Chem Toxicol 2010;48:76; Miguel MG et al., Food Chem Toxicol 2010;48:3418)

Anti-oxidants/free-radical scavengers, anti-apoptotics in propolis

- **Antioxidants and free-radical scavengers** [flavones, flavonols, flavanones and dihydroflavonols, and total phenolics (caffeic acid, p-coumaric acid, ferulic acid, and caffeic acid phenethyl ester)]

- **Anti-oxidants and anti-apoptotics** [pinocembrin]

Propolis and Diabetes

- Water extract of propolis prevented streptozotosin-induced β-cell destruction by inhibiting 1L-1β generation and NO synthase activity (Matsushige K et al., Phytomedicine 1996;3:203)
- Water and ethanol extract of propolis controlled glycemia and reversed lipid abnormalities in streptozotocin-induced diabetic rats (by inhibition of lipid peroxidation and free radical scavenging) (Fuliang HU et al., Pharmacol Res 2005;51:147)
- It was suggested that the antioxidant effect of propolis might ameliorate oxidative stress and delay the development of nephropathy in diabetes mellitis (Abo-Salem OM et al., Pakistan J Pharm Sci 2009;22:205)
- Ethanol extract of propolis improved the biochemical and histopathological findings in a rat model of experimental pancreatitis (by inhibiting inflammatory cytokines and oxidative stress) (Buyukberber M et al., Turkish J Gastroenterol 2009;20:122)

Propolis and Diabetes

- Propolis-treatment reduced HbA1c in streptozotocin-diabetic rats, and increased serum superoxide dismutase and hepatorenal glutathione peroxidase, decreased malonaldehyde and NO synthetase (NOS), as well as serum alanine transaminase, aspartate transaminase and microalbuminuria - demonstrating hepatorenal protection (Zhu W et al., Human & Exp Toxicol 2011;30:1246)

- The antidiabetic effect of propolis was shown as it inhibited the expression and enzyme activity of glucose-6-phosphatase by a non-antioxidative mechanism (Kang LJ et al., Phytother Res 2010;24:1554)

- Propolis decreased plasma insulin and insulin resistance (HOMA index) in Otsuka Long-Evans Tokushima Fatty rats, a non-insulin-dependent type 2 diabetic model (Zamami Y et al., Yakugaku Zasshi 2010;130:833)

-

Propolis and Diabetes

☸ Ethanol extract of propolis prevented streptozotosin-induced alteration in body weight, serum glucose, lipids, lipoproteins, NO, reduced, catalase and pancreatic MDA & superoxide dismutase in rats (El-Sayed el-SM et al., Pakistan J Pharm Sci 2009;22:168) Abo-Salem OM. Aly HA. Mansour AM.

☸ The antidiabetic effect of propolis was shown as it inhibited the expression and enzyme activity of glucose-6-phosphatase by a non-antioxidative mechanism (Kang LJ et al., Phytother Res 2010;24:1554)

☸ Propolis decreased plasma insulin and insulin resistance (HOMA index) in Otsuka Long-Evans Tokushima Fatty rats, a non-insulin-dependent type 2 diabetic model (Zamami Y et al., Yakugaku Zasshi 2010;130:833)

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Propolis and Diabetes type 2

Diabetes type 2

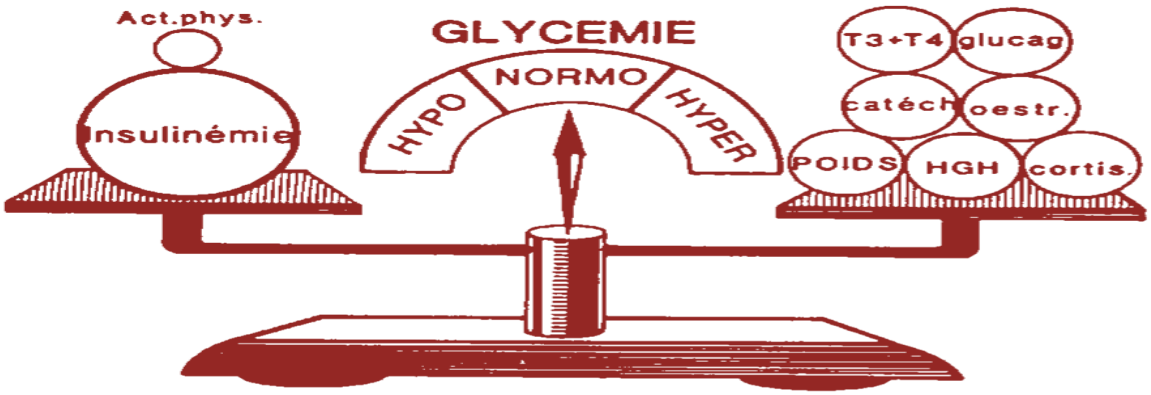
- Zamami Y, Fujiwara H, Hosoda M, Hino H, Hirai K, Okamoto K, Jin X, Takatori S, Doi-Takaki S, Kawasaki H. Ameliorative effect of propolis on insulin resistance in Otsuka Long-Evans Tokushima Fatty (OLETF) rats. Yakugaku Zasshi 2010;130:833-840.

- Yajing Li. Effects of Encapsulated Propolis on Blood Glycemic Control, Lipid Metabolism, and Insulin Resistance in Type 2 Diabetes Mellitus Rats. Evidence-Based Complementary and Alternative Medicine 2012

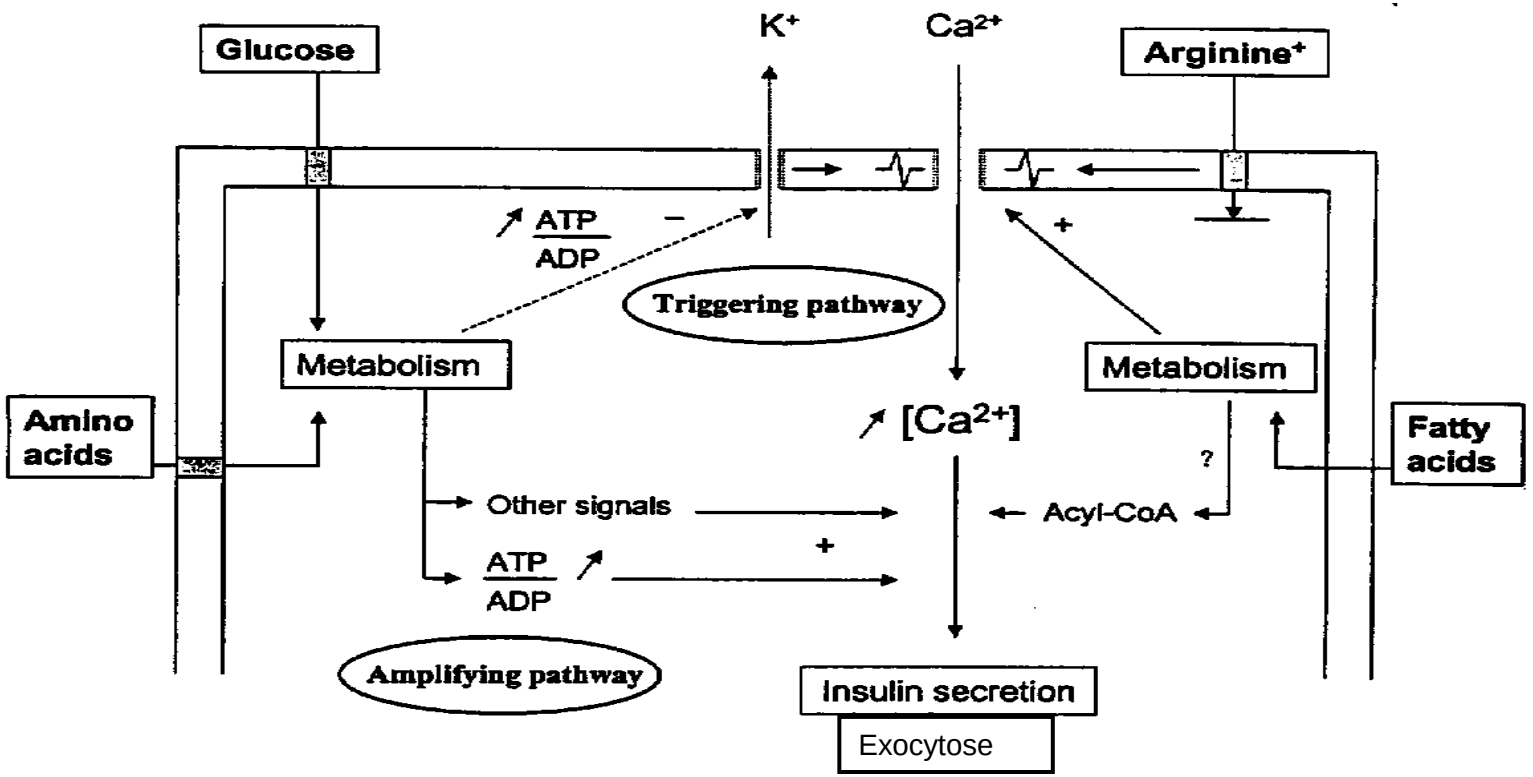
Propolis components and Diabetes

☸ Caffeic acid phenethyl ester (present in propolis) reduced the oxidative stress in streptozotocin-induced diabetic rats (Okutan H et al., Clin Biochem 2005;38:191)

☸ Chrysin (present in propolis) significantly inhibited the release of nitric oxide and proinflammatory cytokines such as tumor necrosis factor-α and interleukin-1, as well as expressions of inducible NO synthase and cyclooxygenase-2, and induction of nuclear factor-kB, the signaling molecules involved in inflammation (Ha SK et al., Neurosci Lett 2010;485:143)

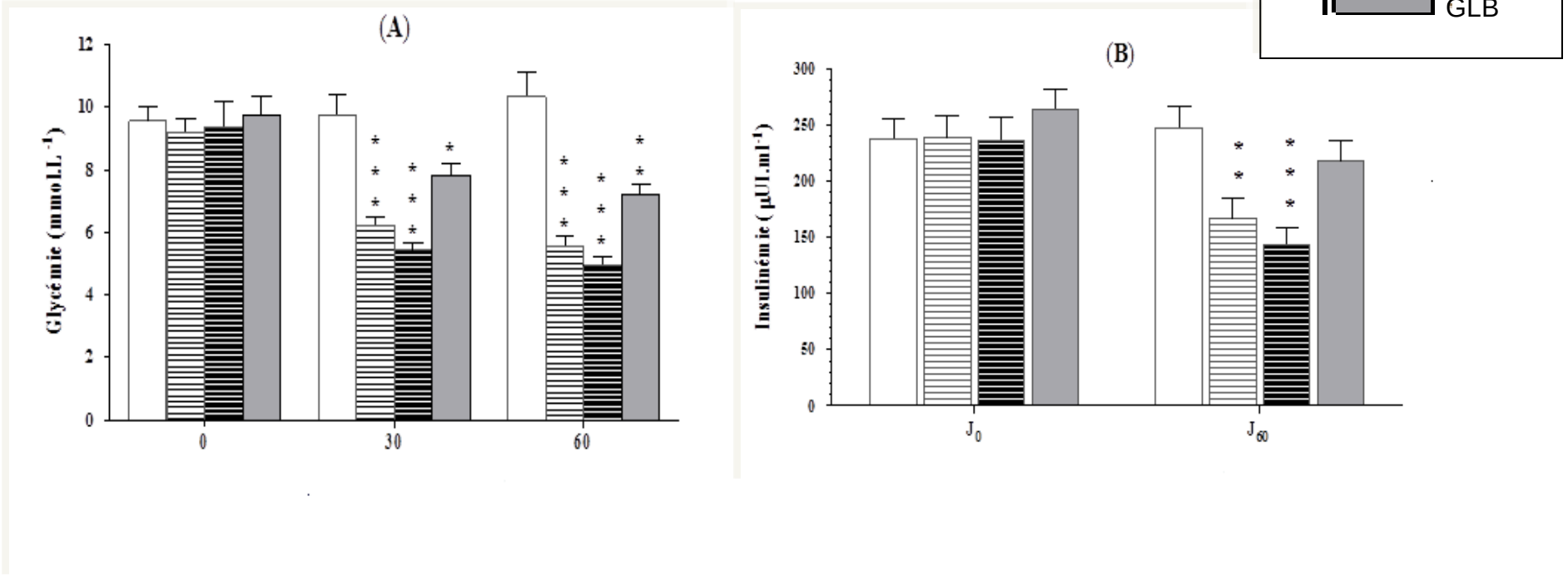


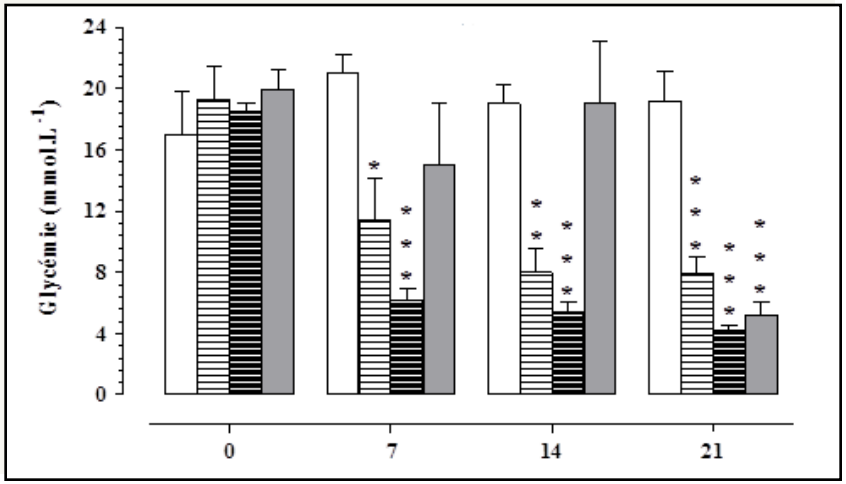
Glucose as physiological regulator of insulin secretion

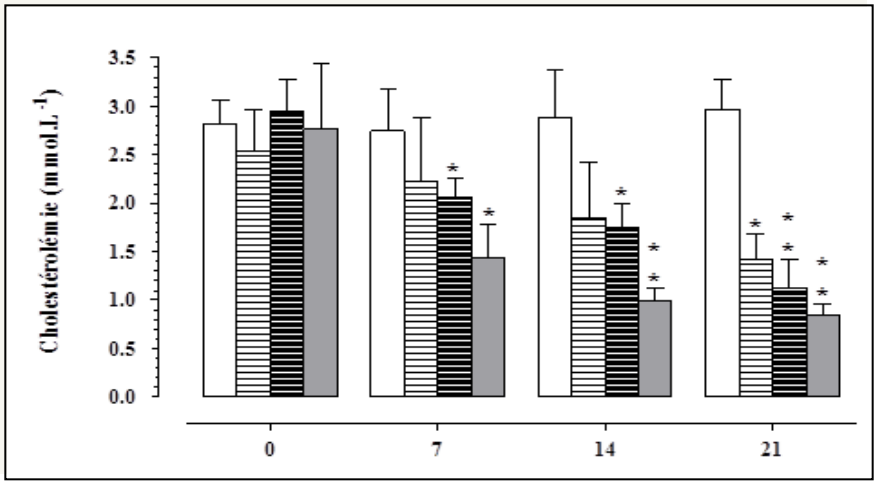


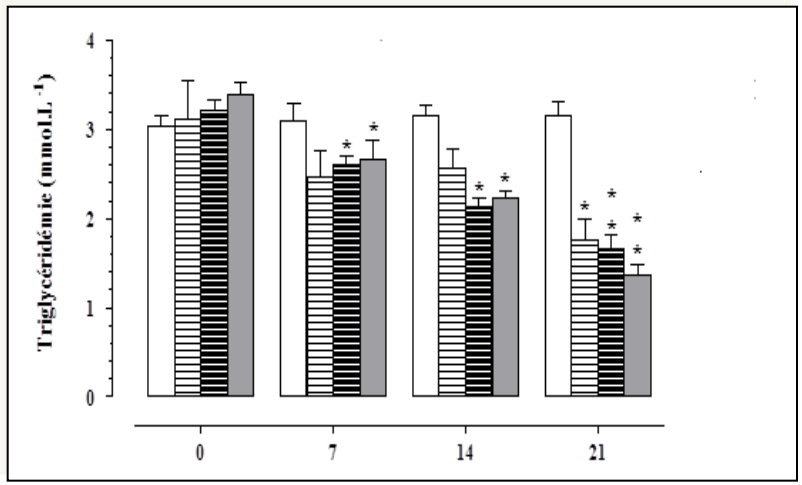
Antidiabetic activity of Moroccan propolis

When given orally at a dose of 10 mg/100 g BW, to streptozotocin (STZ)-induced type 1 diabetic rats, it significantly decreased glycemia and plasma insulin



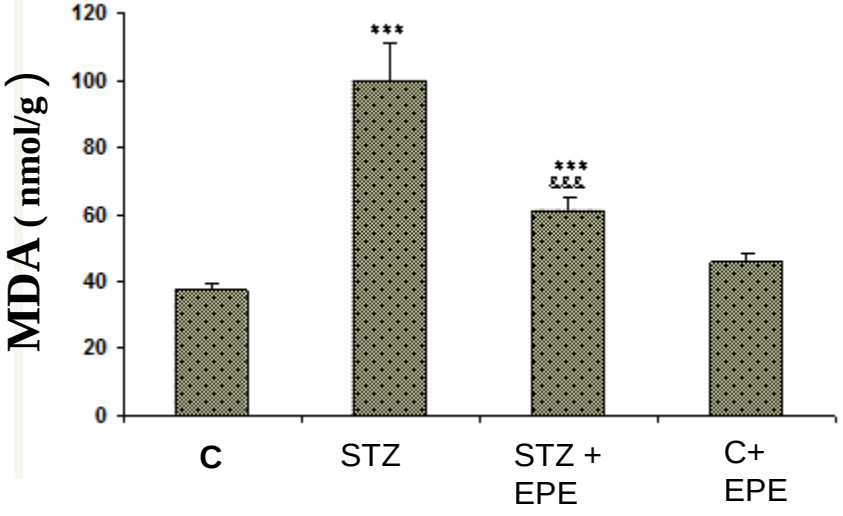


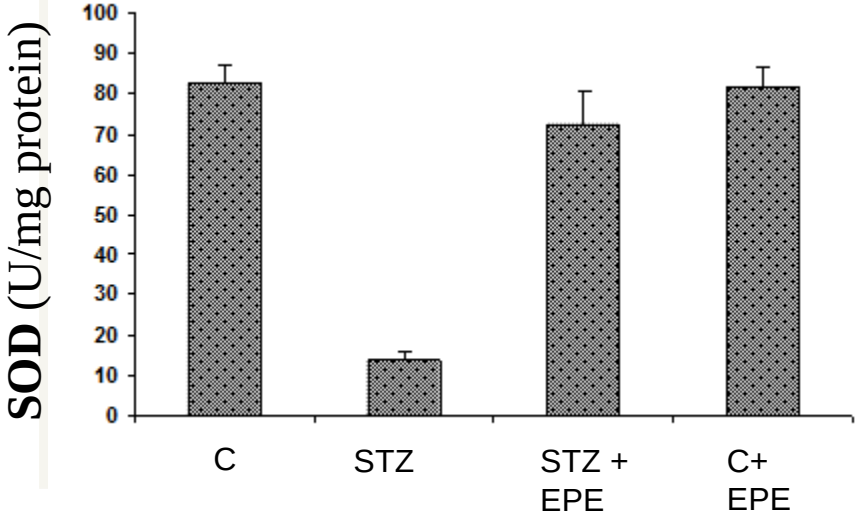


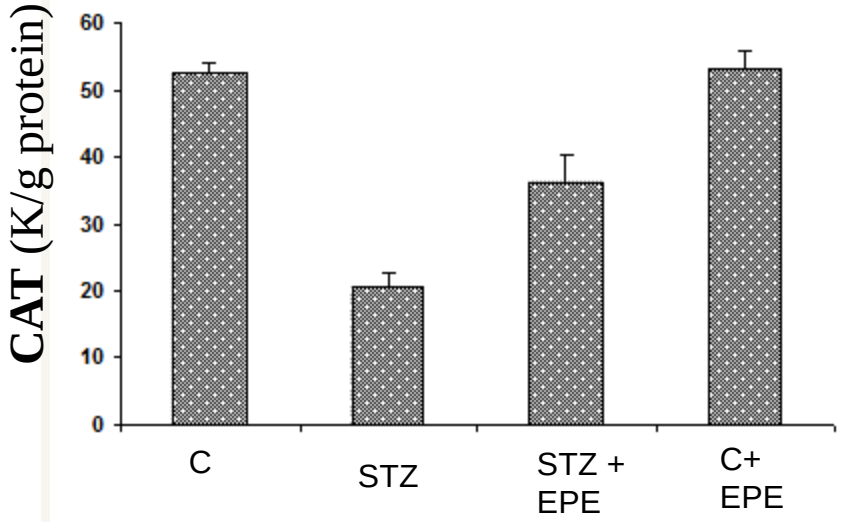


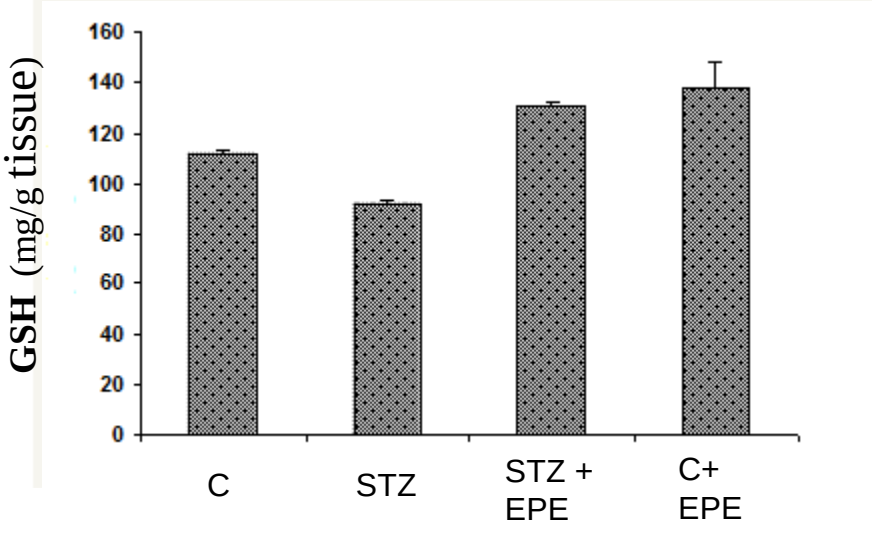
Moroccan Propolis given orally to streptozotocin (STZ)-induced type 1 diabetic rats significantly decreased glycemia, total cholesterol and triglyceride levels

The protective role of propolis against the reactive oxygen species-induced damages in diabetic rats and nephrotoxicity models gives hope that it may have a similar protective action in humans. Experimental diabetes study in rodents suggests that propolis (or compounds isolated from propolis) may be useful in human diabetes





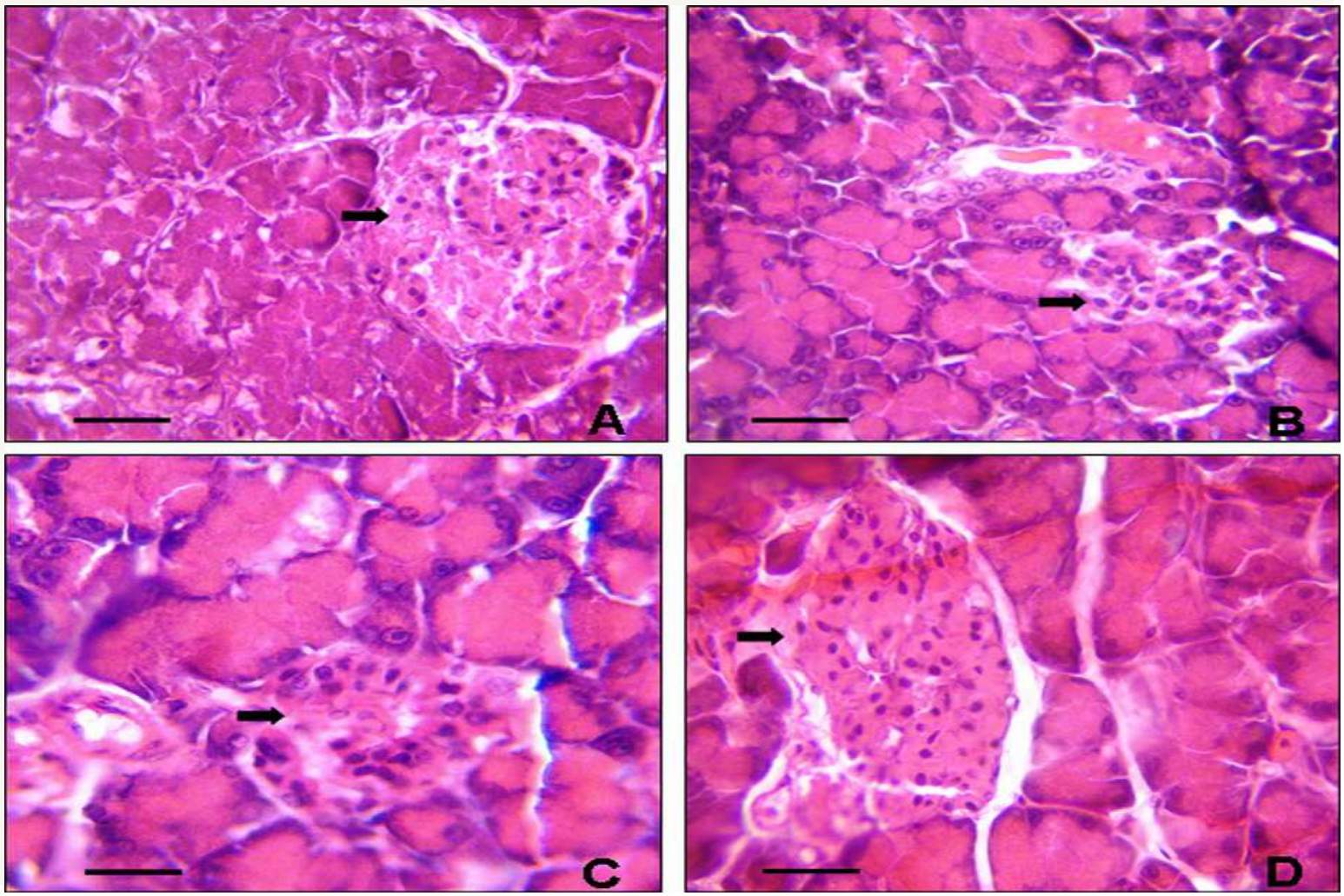




MDA, GSH levels and antioxidant enzymes activities (SOD, CAT) in the pancreas tissue of adult rats : Controls and Diabetic Groups)

	C	C + EPE	STZ	STZ + EPE
MDA (nmol/g tissue)	37.2 ± 1.9	45.6 ± 2.5	100.03 ± 10.7*	60.9 ± 4.2*
GSH (mg/g tissue)	111.8 ± 1.6	137.81 ± 10.1*	91.97 ± 1.29*	130.7 ± 1.9*
SOD (U/mg prot)	82.6 ± 4.4	81.76 ± 5.10	13.7 ± 2.3*	72.2 ± 8.3
CAT (µmol/min/mg prot)	52.6 ± 1.4	53.06 ± 2.82	20.3 ± 2.3*	36.2 ± 4.1*

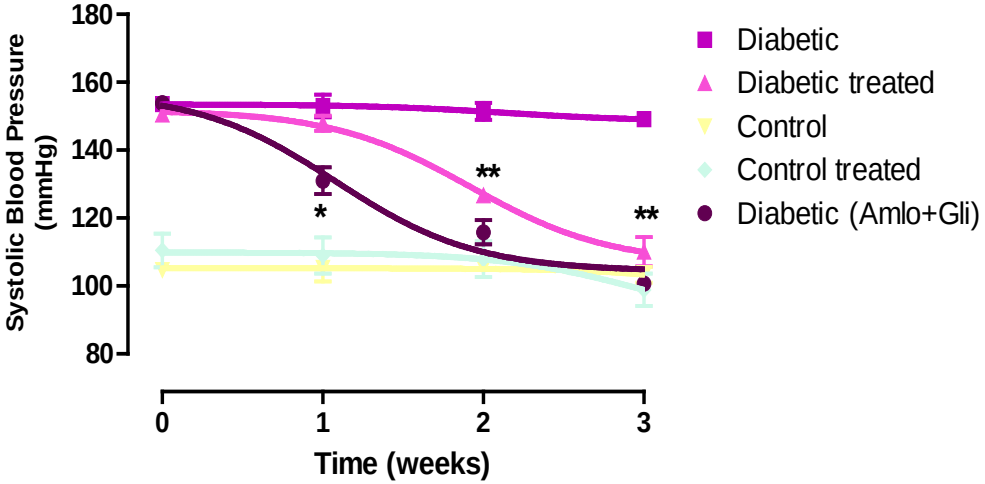
EPE alleviates streptozotocin –induced oxidative stress and cell damage in rat pancreas

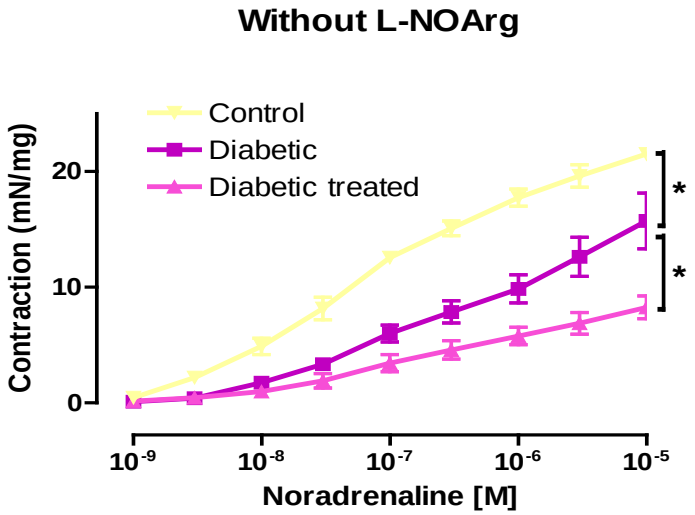


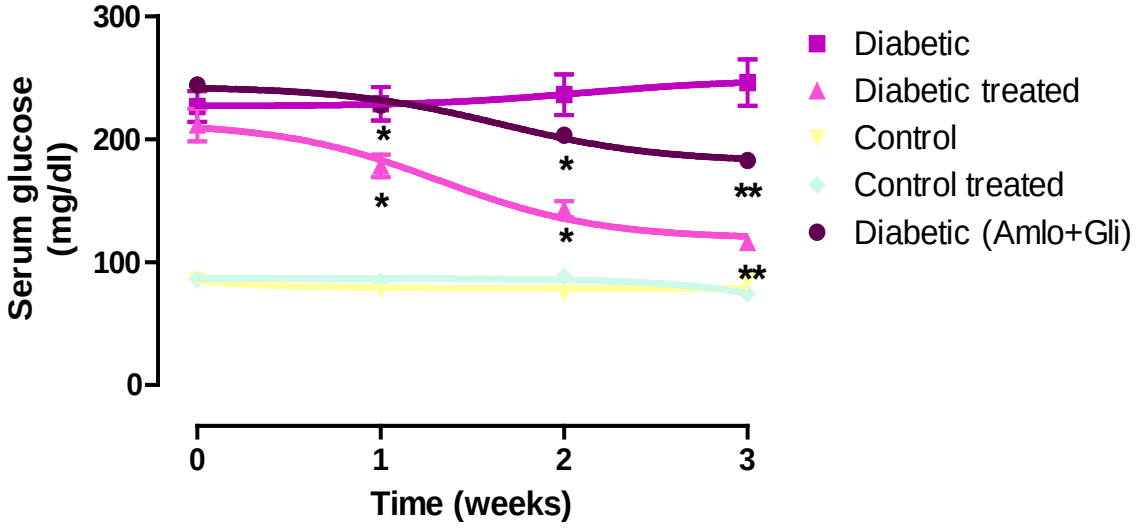
Histological section of pancreas in adult rats

A : Control, B: Diabetic, C: Diabetic + EPE, D: Control + EPE

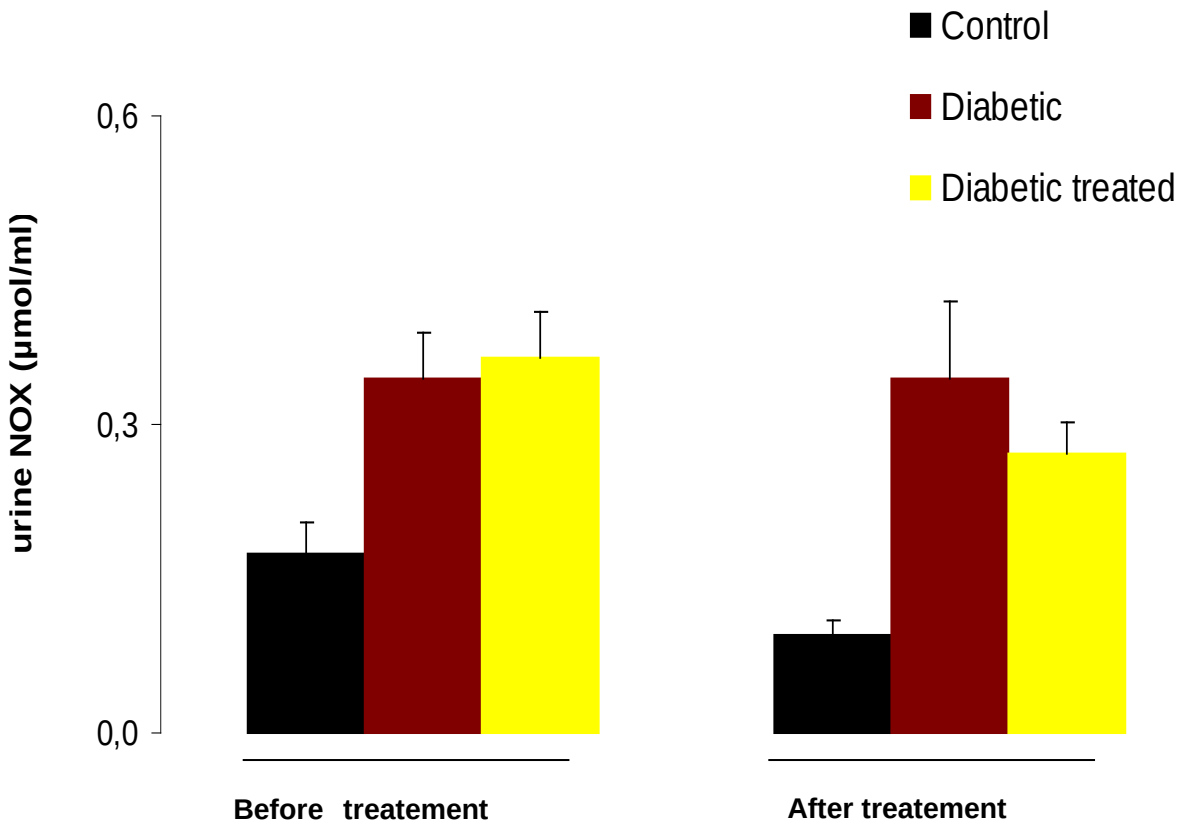
Antidiabetic & Hypotensive effects of EPE in *Meriones Shawi* rats : animal model of diabetes type 2







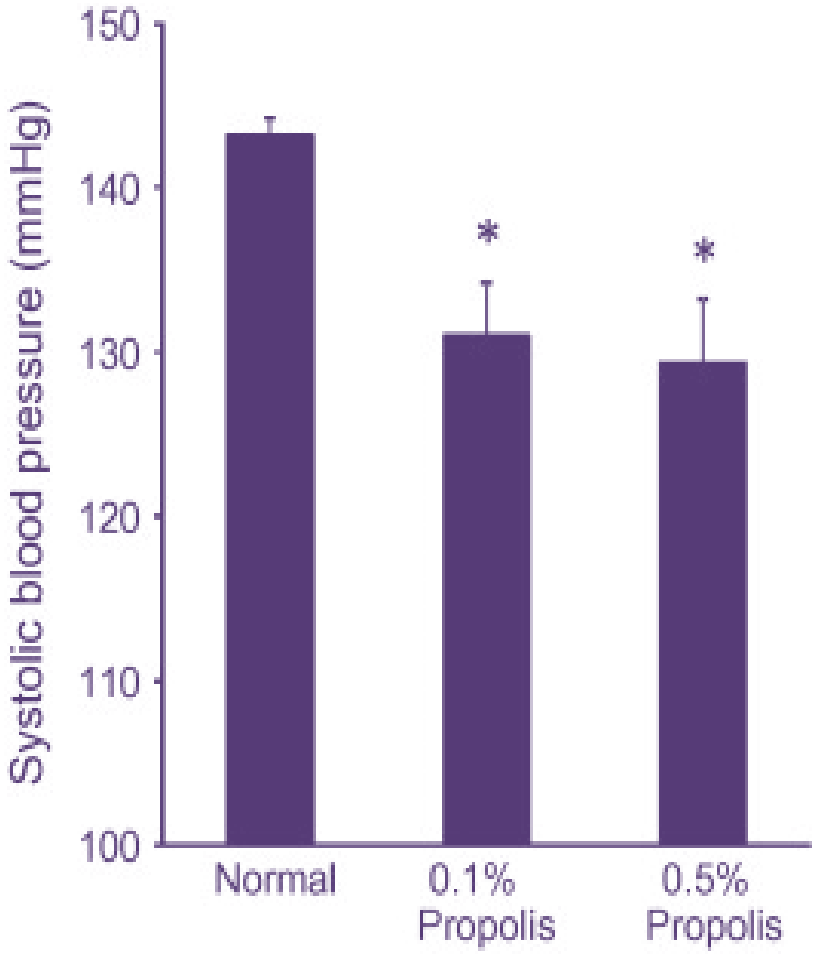
NOX ($NO_2^-+NO_3^-$) Effect of EPE



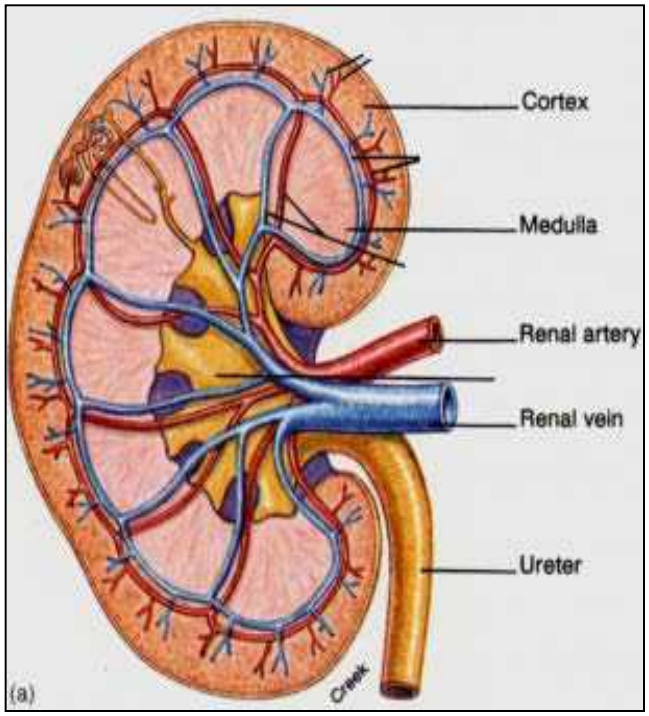
Improvement of Insulin Resistance, Blood Pressure and Interstitial pH in Early Developmental Stage of Insulin Resistance in OLETF Rats by Intake of Propolis Extracts

These data suggests that dietary propolis improves insulin sensitivity and blood pressures in the early stage of the process in development of insulin resistance, which may be mediated by suppression of metabolic acidosis.

Wataru Aoi
Biochem Biophys res commun
2013



Propolis - Detoxifying Effect



Kidney: a vital organ but vulnerable to toxicants

Nephrotoxic chemicals

- **Drugs (antibiotics, analgesics) - Solvents (halogenated hydrocarbons, ethylene glycol)**
- **Pesticides (paraquat) - Mycotoxins (ochratoxin A) - Metals (Pb, Cd, Hg, Al, Cr, U, As, etc.)**

Hemodynamic and renal parameters in control and nephrotoxic (NTOX) rats

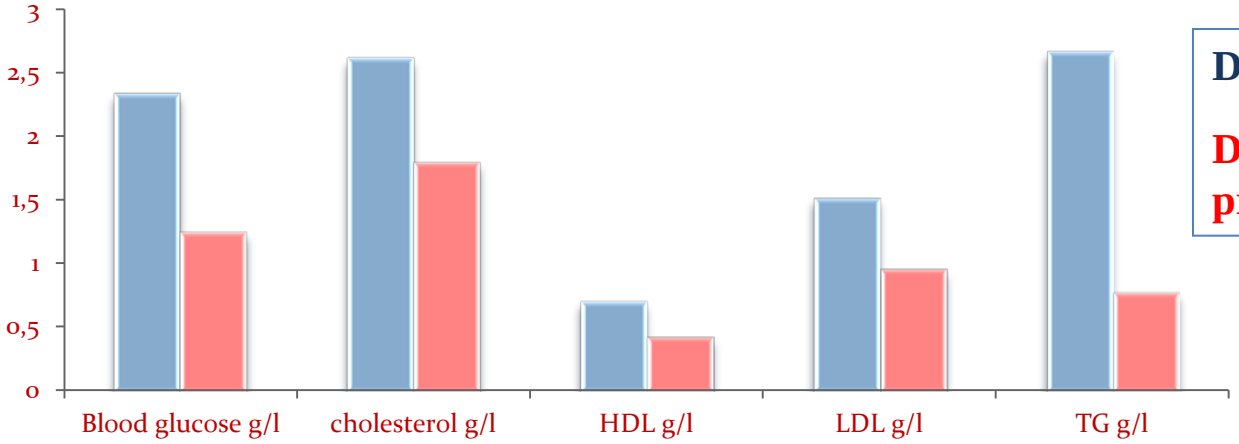
	CONT (n = 8)	NTOX (n = 8)	NTOX + EPE (n = 8)
Hct (%)	44.5 ± 0.5	39.1 ± 1*	42.5 ± 0.3
PAM (mmHg)	116 ± 3	145 ± 6*	118 ± 5
DFG (ml/min)	3.62 ± 0.26	2.14 ± 0.36*	3.35 ± 0.37
UV (µl/min)	23 ± 4	12 ± 2*	20 ± 6
$U_{Na}^{+}V$ (µEq/min)	3.89 ± 0.08	1.88 ± 0.01	2.90 ± 0.05
$U_{K}^{+}V$ (µEq/min/min)	2.56 ± 0.2	1.29 ± 0.12	2.36 ± 0.4
Osm (mOsm/Kg H_2O)	1451 ± 81	1012 ± 131	1247 ± 75

Thiobarbituric acid reactive substances levels (MDA= malondialdehyde) and antioxidant enzyme activity in control and nephrotoxic (NTOX) rats

	CONT	NTOX	NTOX + AEP
MDA (nM/mg protein)	0.32 ± 0.05	0.48 ± 0.07*	0.35 ± 0.04
SOD (U/mg protein)	9.7 ± 0.03	2.7 ± 0.08*	9.9± 0.05
GSH-Px (nM NADPH/min/mg protein)	14.2 ± 0.2	20.1 ± 1.3*	15.2 ± 0.4
CAT (K/g protein)	85.2 ± 1.8	112 ± 2*	93.2 ± 1.5

Effects of oral administration of PE extract on plasma concentration of sodium, potassium (mmol/L), and glomerular filtration rate (ml/min) in samples before (Ti) and after (Tf) treatment

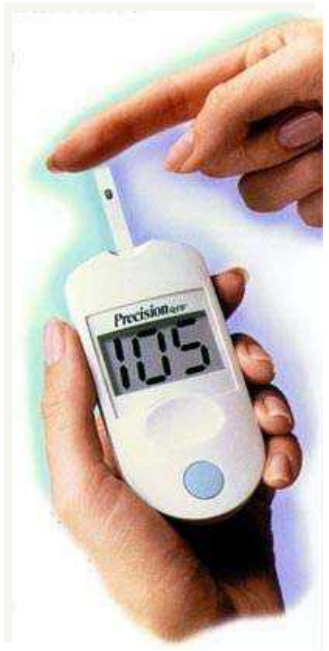
Treatment	Sodium		Potassium		Glomerular filtration rate	
	T_i	T_f	T_i	T_f	T_i	T_f
Control (NaCl 0.9%)	**142±2.1**	**143±1.9**	**4.3±0.5**	**4.4±0.4**	**0.19±0.07**	**0.24±0.1**
PE extract (200 mg/kg)	**145±1.4**	**143±2.9**	**4.2±0.3**	**4.1±0.8**	**0.24±0.05**	**1.31±0.2***
Furosemide (0.5mg/kg)	**146±1.9**	**144±2.5**	**4.1±0.4**	**2.9±0.4 ***	**0.22±0.02**	**1.56±0.2***



Diabetics

Diabetics treated with propolis

Parameter	Diabetics	Treated Diabetics
HbA1C	**8.7 %**	**6.5%**



Preliminary data in diabetic subjects, demonstrating beneficial effects of propolis to control and prevent diabetes, and suggesting that propolis (or compounds isolated from propolis) may be useful in human diabetes

Artepillin C, a constituant of propolis and a PPAR ligand, enhances adipocyte differentiation, improves insulin sensitivity in type 2 diabetes

Thiazolidinedines

↓

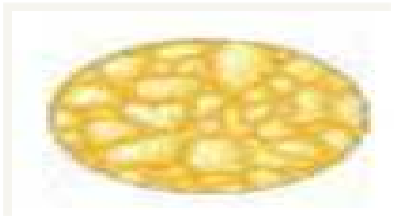
PPAR – ɣ activation

↓ Blood glucose
- improved lipids
- Anti-inflammatory Effects

↓ Endothelial function

? Direct effects

Direct effects on Adipose tissue



↓ Lipolysis
↑ Fat synthesis

↓

↓ FFA

Cytokines

— ↑ Adiponectin

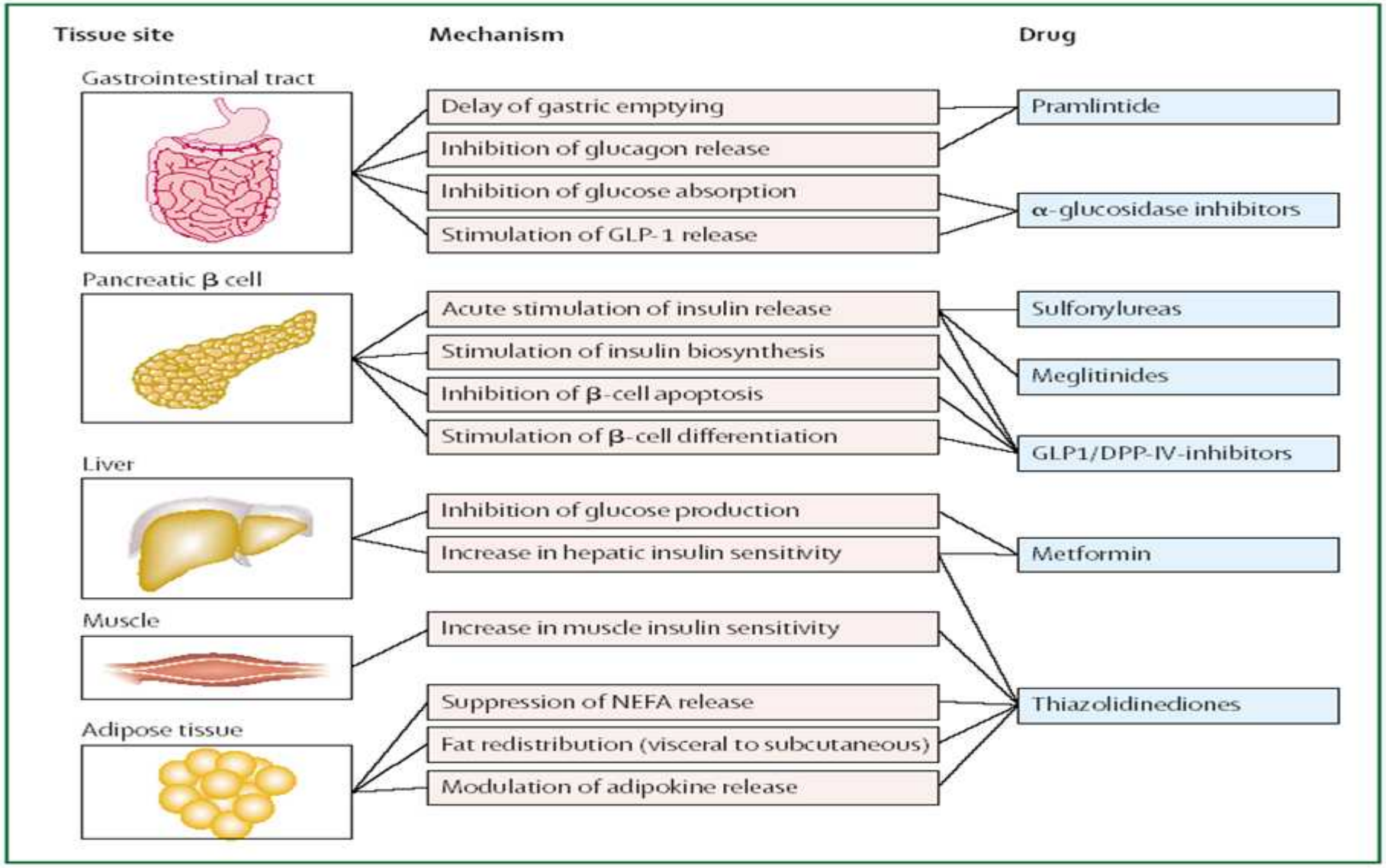
— ↓ TNF α, IL-6

Liver

Skeletical muscle

Pancreas

Pharmacological treatment of hyperglycemia according to target



Hypothetical mechanism(s) of hypoglycemic action of propolis

- Insulin –like / insulin – mimetic activity
- Insulinotropic effect
- Decrease in insulin resistance/insulin sensitization / enhancement of peripheral glucose utilization
- Induction of insulin-like glucose transport into adipocytes
- PPAR-γ agonist (glitazone-like) activity:
- Dual-PPAR-α/γagonist activity
- Increase in binding of GLP-1 to its receptor

Acknowledgments

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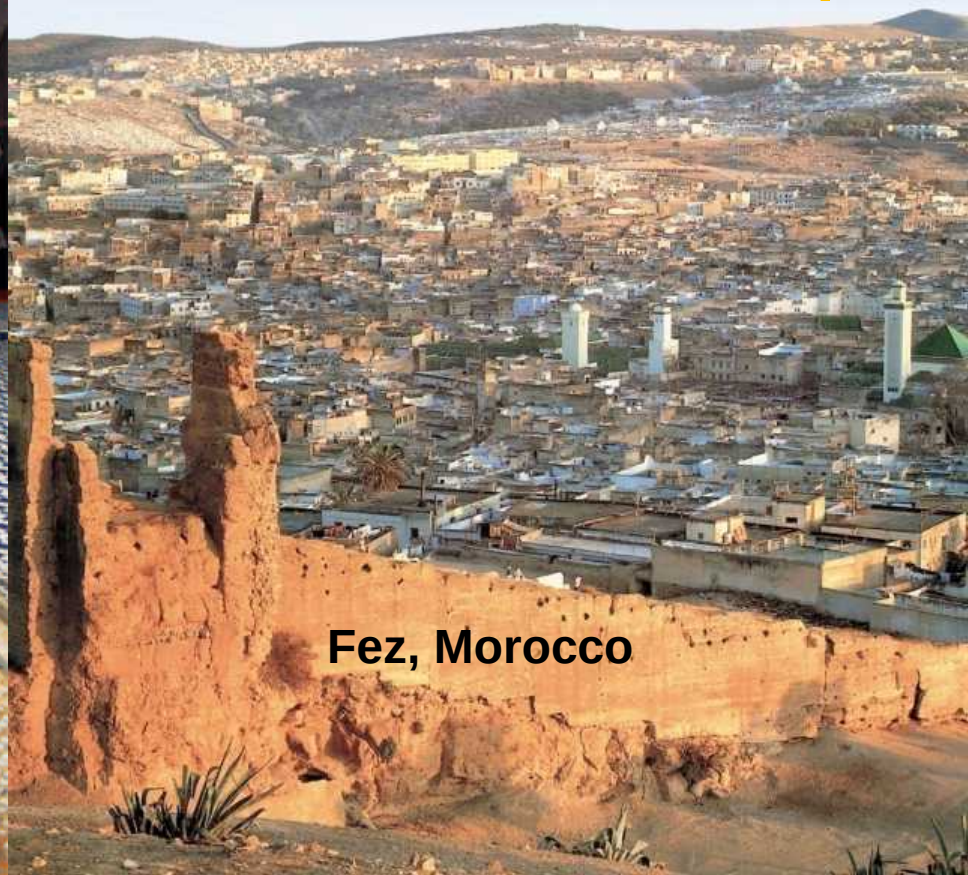
Aissaoui Abderrahime
Zizi Soumaya
Farah Gaamoussi

Many thanks
for your attention!
Dankeschön
Muchas gracias
Merci beaucoup



Fez, Morocco