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FACOLTÀ DI AGRARIA

TASTE CHEMISTRY MAKES SENSE:

from food plants new bioactive compounds for agrifood and pharmaceutical industry

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DISMA- Dipartimento di Scienze Molecolari Agroalimentari

TRIP as a journey :

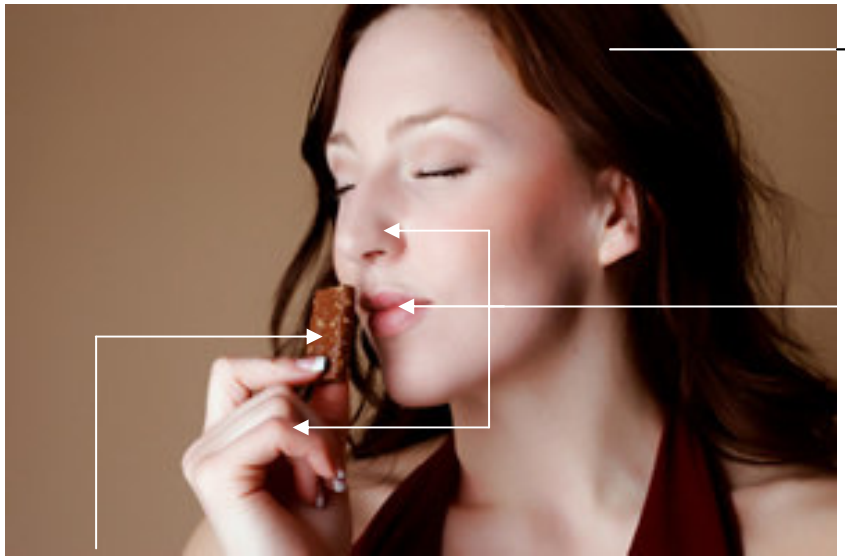
- inside human body and its functions
- through “unusual” tastes and gustative sensations
- from infancy to adult age

A trip inside the body: what is a receptor?

A receptor is a “molecular detector”, usually a protein, activated by a stimulus that can be **chemical** or **physical.**

We have millions of these detectors, spread inside and on the surface of our body.

Receptors are the perifery, brain is the “headquarter”:



OUTPUT (brain) → **OK!**

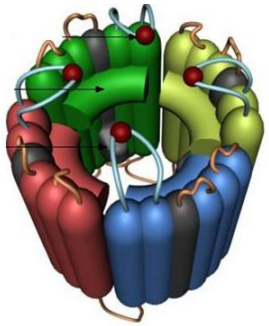
RECEPTORS (olfactory mucosa, tongue papillae, oral cavity, skin)

INPUT (stimulus)

Let’s have a trip **inside** the gustatory receptors…

The two families of receptors for the so called "fundamental" tastes:

SALTY
SOUR



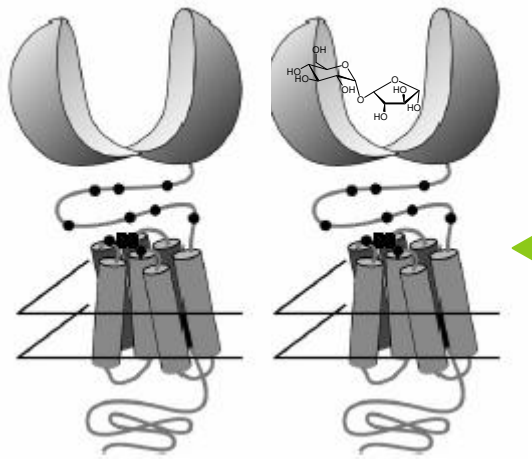
ion channels

(direct activation)

Na^+

H^+

SWEET
BITTER
UMAMI



GPCRs

several organic compounds

A new family of receptors: the chemesthetic gustative sensations

HOT
COOLING
PUNGENT
LACRIMATING
TINGLING
NUMBING…

TR(I)P

ion channels, indirect activation

organic molecules or physical stimuli as touch, temperature change...

TR(I)P : Transient Receptor (Ionic) Potential

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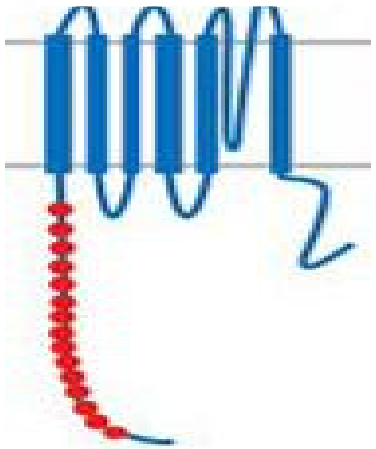
How does a TR(I)P receptor work?

stimulus →  → Ca $^{2+}$ release → signal

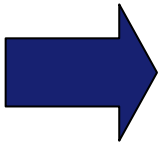
Activation
(conformational change?)

What do the TR(I)Ps do?

•Perception of **“unusual” and “strong”** gustative **sensations (*chemesthesis*)**

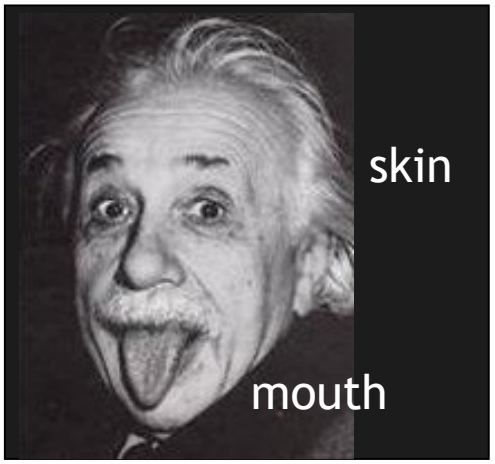
•Perception of **external signals** from environment and from other organisms (*sensing*) : temperature, light, sound, touch, pheromones…

•**Perception of pain stimuli**



TR(I)Ps are crucial sensors for **self defense** mechanisms!

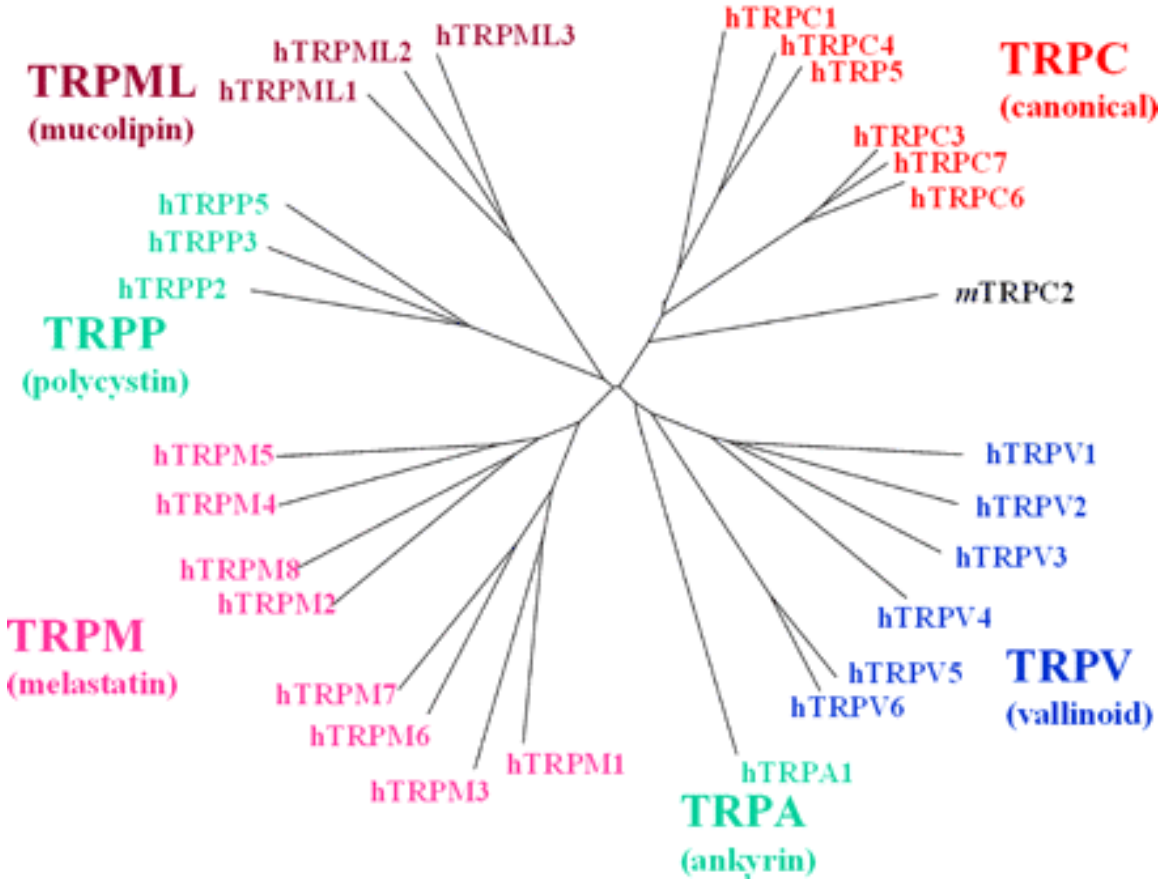
Where are the TR(I)P receptors?



TR(I)Ps are ubiquitarious

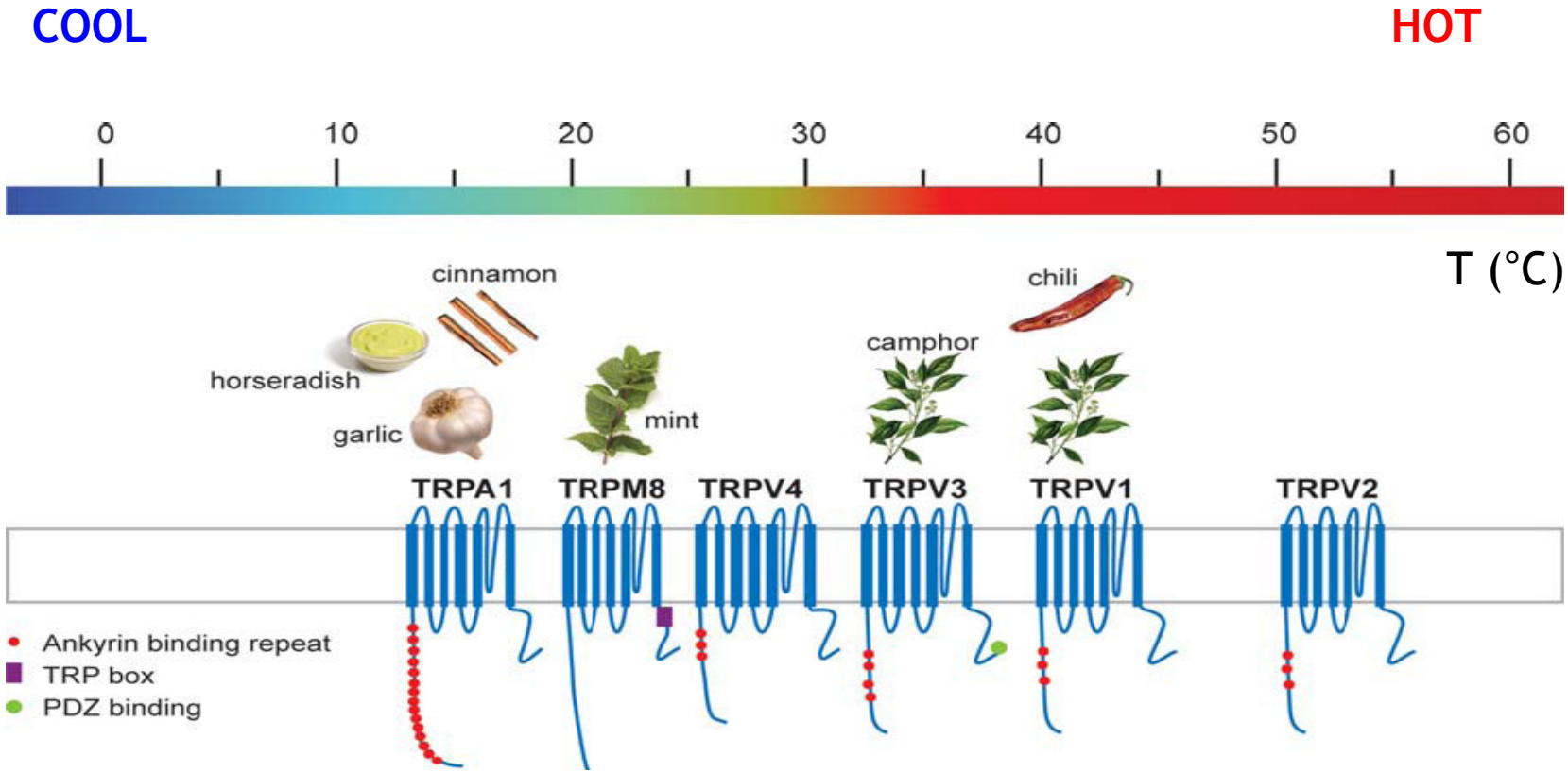
TR(I)Ps are highly conserved

How many TR(I)P receptors do we have?



D.E. Clapham, *Nature*, 426, 517-524, **2003**

Taste and temperature: TRPVs, TRPM8, TRPA1



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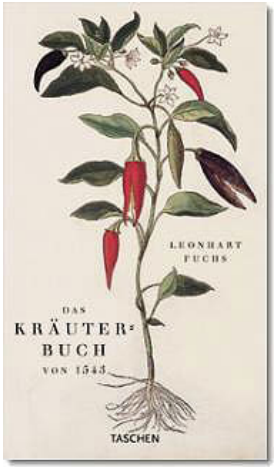
A famous TR(I)P: the capsaicin receptor TRPV1

The Atzech were treating nasal congestion with hot pepper

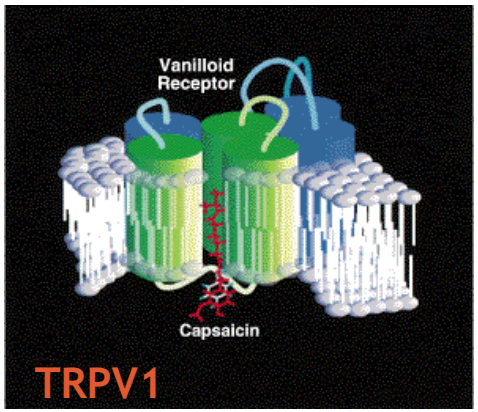
Capsicum described in "New Kreuterbuch" by Leonhart Fuchs (1543)



Hot pepper "helpeth greatly the digestion of meates", John Gerard (Herbal, 1597)

1957: Nicholas Jancsò hypothesised the existence of a specific receptor;

TRPV1 was cloned in 1997 by David Julius and coll.



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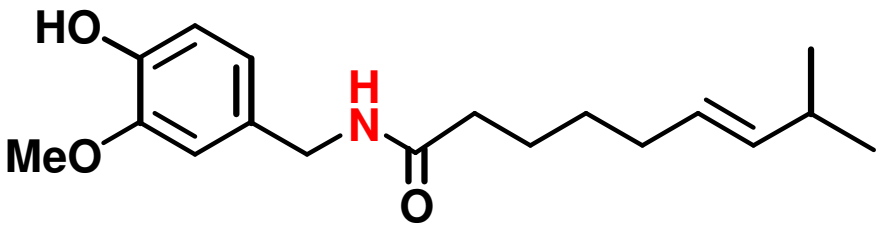
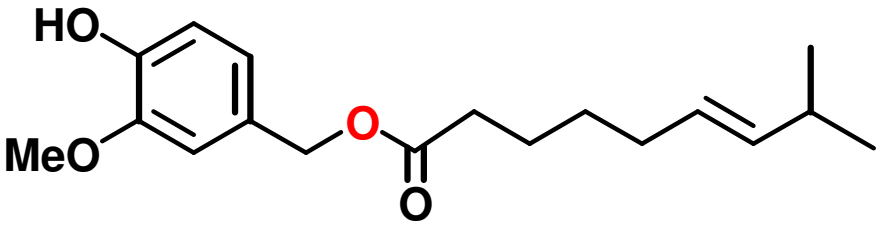
2000: generation of knock-out mice for TRPV1 receptor. TRPV1 -/- animals can not taste the difference between chili and bell peppers.



capsaicin, *hot*



capsiate, *inactive*

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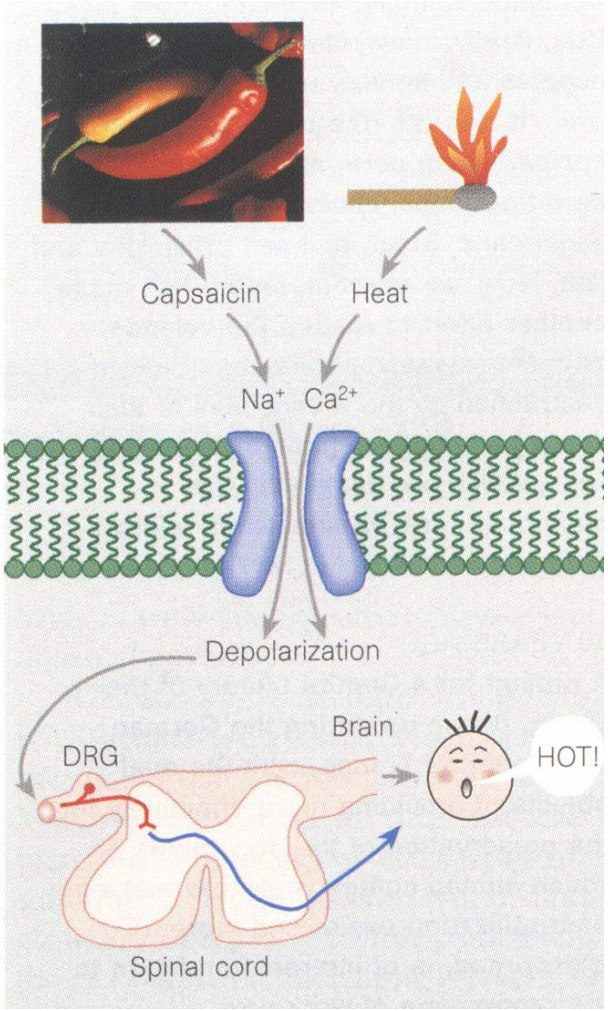
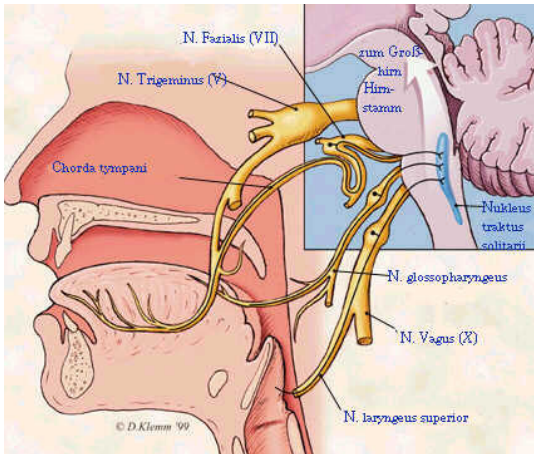
TR(I)Ps and pain perception /1





TR(I)P active compounds in food are perceived by the body as “harmless painful sensations ”. The ability to “resist” to this pain increase with age and repeated exposition, by a **desensitisation** mechanism.

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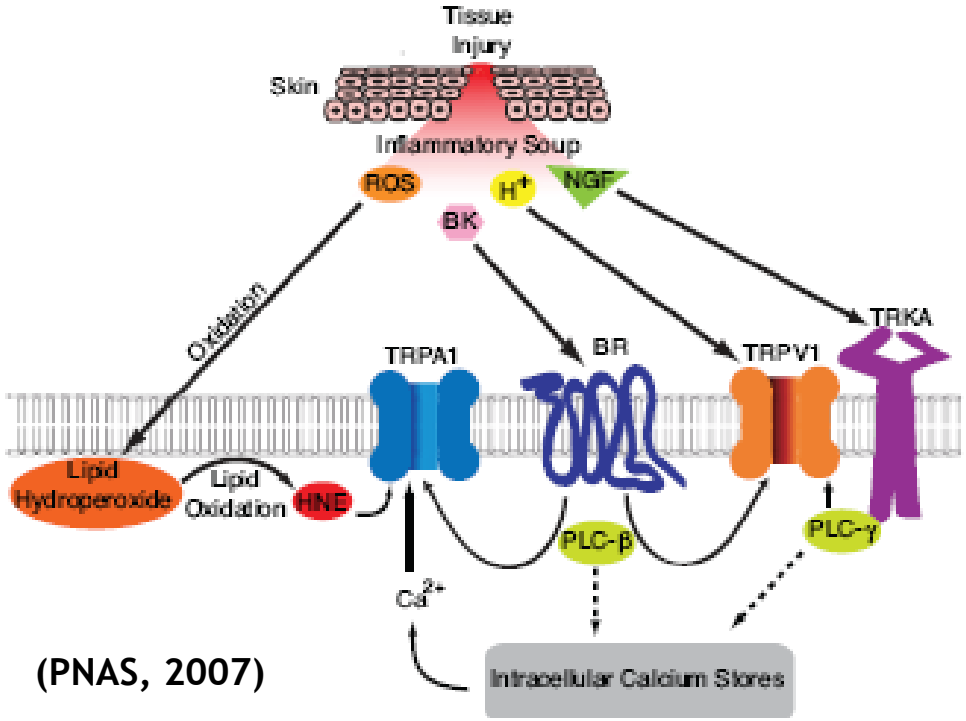
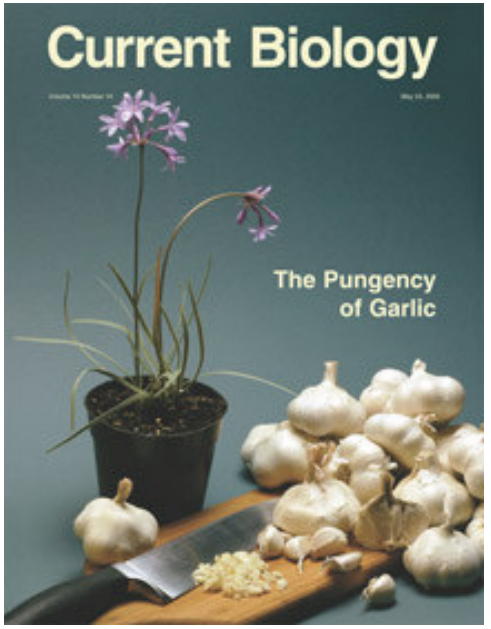
TR(I)Ps and pain perception /2:



(PNAS, 2007)



Marcello Trevisani*, Jan Siemens†, Serena Materazzi*, Diana M. Bautista†, Romina Nassini*, Barbara Campi‡, Noritaka Imamachi§, Eunice Andrè‡, Riccardo Patacchini¶, Graeme S. Cottrell‖, Raffaele Gatti‡, Allan I. Basbaum§, Nigel W. Bunnett‖, David Julius†**, and Pierangelo Geppetti*‡**

Agonists of TRPA1 and TRPV1 can block the pain generated during inflammatory processes → analgesic effect!

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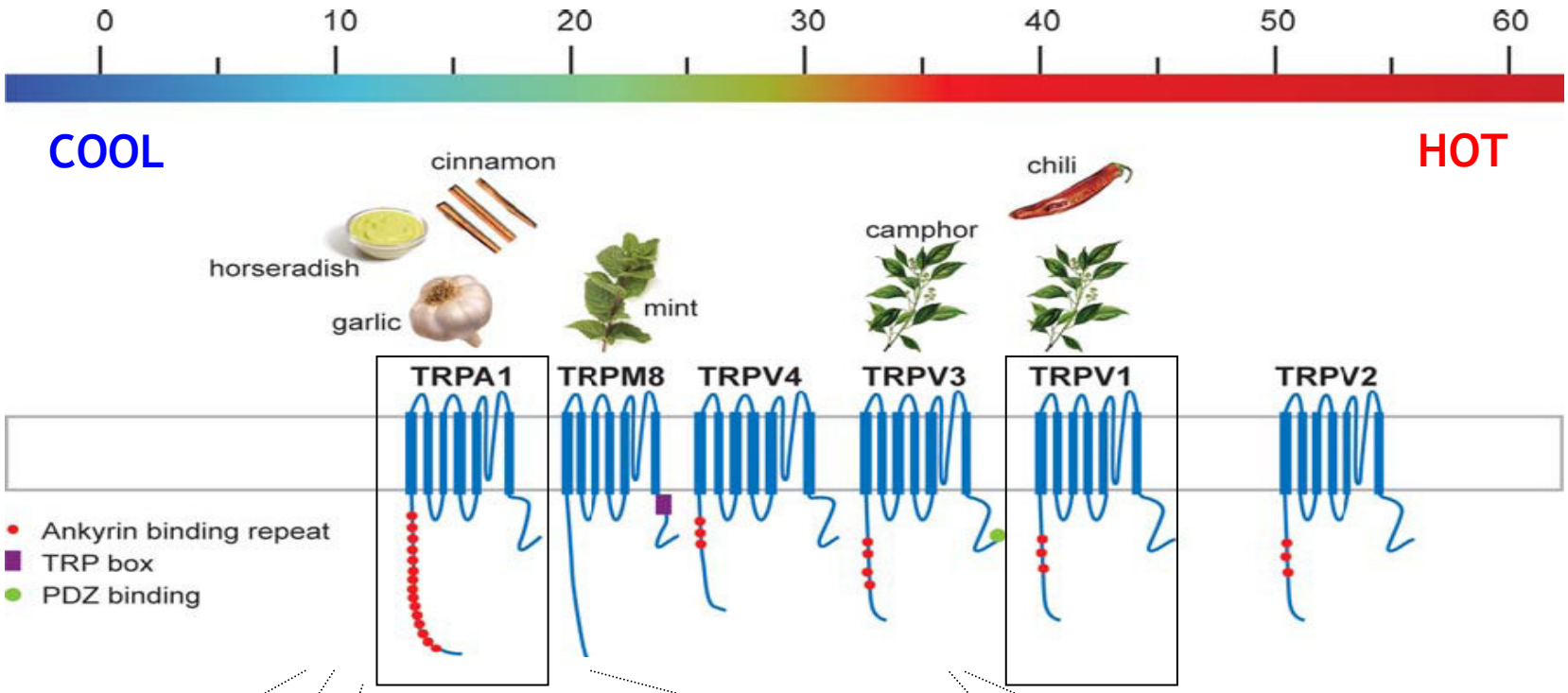
TR(I)Ps active compounds in food:



ginger

onions

mustard

Cruciferae (broccoli, cabbage, brussel sprouts, rocket..)

Perilla frutescens (kaennip, shiso)

clove

oregano

…and many more!

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A TR(I)P in Korea: kaennip

Perilla frutescens, **kaennip** (깻잎).

Taste: very “unusual” and penetrating aroma and taste to western consumers (“cinnamon”, “licorice”, “anice”, “cooling”, “astringent”…).

Folk medicine: many curative properties.

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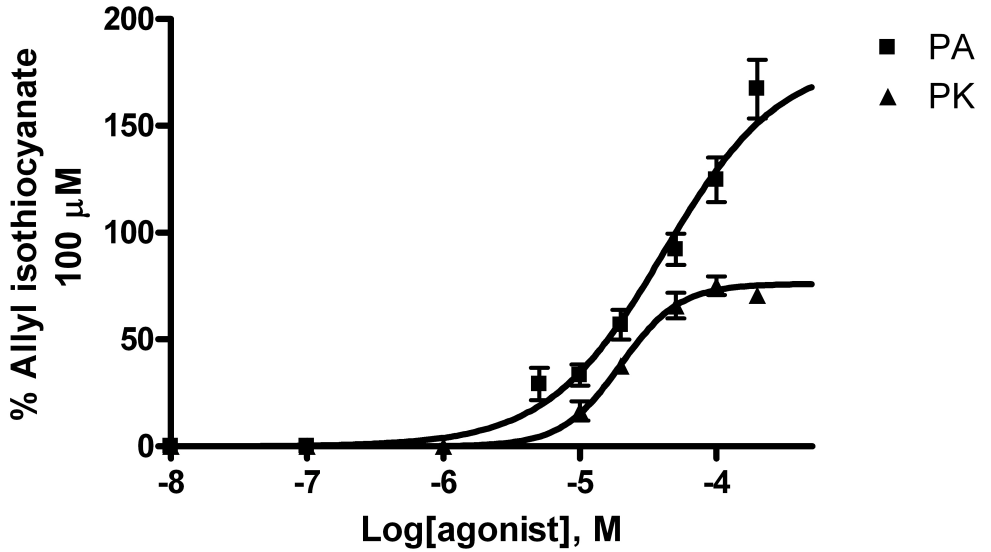
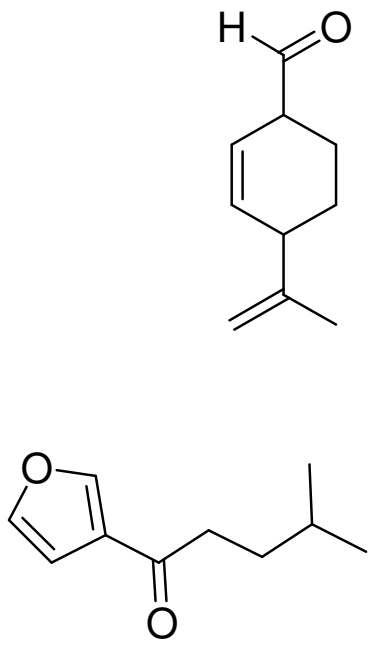
The main components of the essential oils from P. frutescens are perillaldeyde PA and perillaketone PK.





PA and PK strongly activate *in vitro* the cloned TRPA1 receptor.

A. Bassoli, G. Borgonovo, G. Morini, V. Di Marzo, L. De Petrocellis, A. Schiano Morello., J.Biorg.& Med. Chem, 2009

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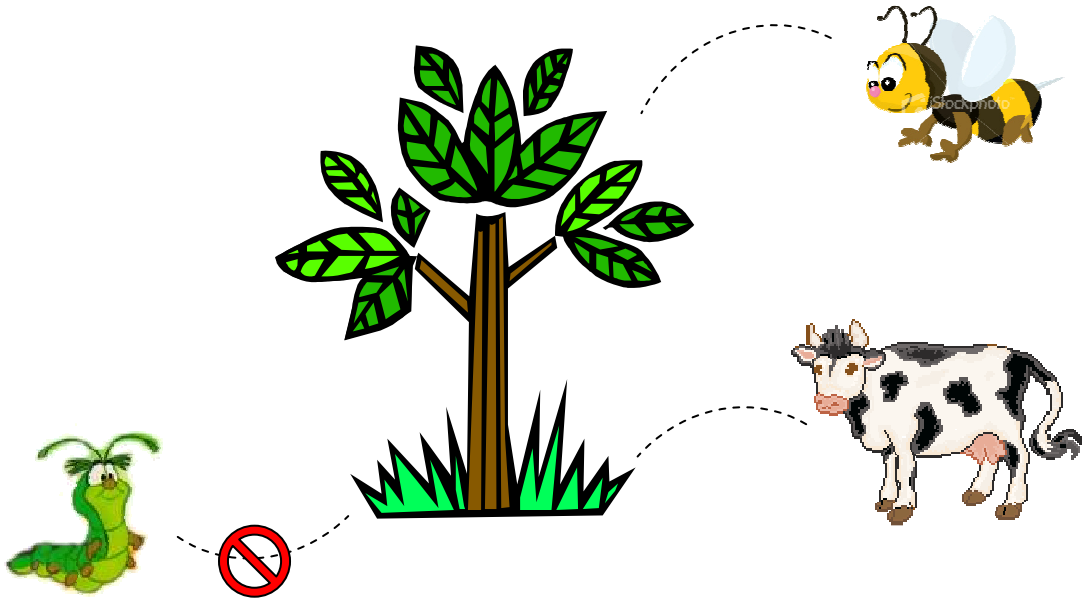
Applications of taste active compounds:

Traditional gastronomy-flavour

Pharmaceutical industry

Chemical sensing (recognition - attraction – defense)

…



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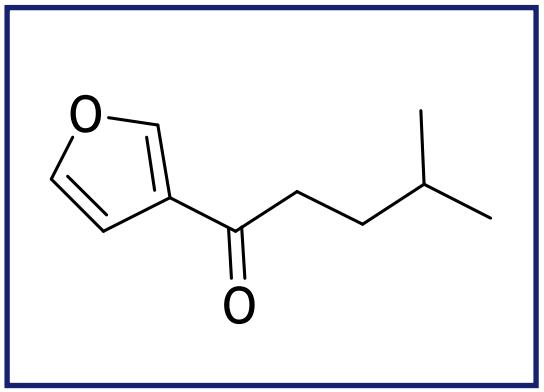
Applications: PK as a natural lead for drug design:



SYNTHESIS OF ANALOGUES:

Modifications in lenght chain, functional groups, arylated position, substituents etc.

Efficacy: maximal response of the agonist expressed as percentage of the analogous effect observed with mustard oil 100 μM.
Potency (EC50): concentration of test substance required to produce half-maximal increases in $[Ca^{2+}]$.

A. Bassoli et al., 2011 (unpublished)

In vitro assays with TRPA1 receptor

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Applications:PK derivatives, *in vitro* assays on TRPA1

Cpd	Log P (calculated)	Efficacy (%Allylisothiocyanate 100μM)	Potency (pEC50%)
(-)-PA	**1.82**	**181.2 ± 11.3**	**4.39 ± 0.09**
PK	**1.72**	**80.8 ± 0.3**	**4.67 ± 0.03**
1	**1.78**	**97.13**	**5.1**
2	**1.99**	**54.9 ± 2.6**	**4.59 ± 0.05**
3	**1.03**	**Inactive up to 200μM**	**-**
4	**0.98**	**163.1 ± 13.6**	**4.63 ± 0.10**
5	**0.43**	**88.4 ± 2.0**	**4.48 ± 0.02**
6	**0.96**	**58.1±4.9**	**4.08±0.07**
7	**-0.12**	**Inactive up to 200μM**	**-**
8	**2.26**	**85.8 ± 1.1**	**4.56 ± 0.01**
9	**0.36**	**32.7 (Inactive up to 100μM)**	**>3**
11	**2.20**	**124.0 ± 6.8**	**5.59 ± 0.09**
12	**2.76**	**142.3 ± 3.0**	**6.39 ± 0.04**

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A taste of Italy: lampascioni
(Leopoldia comosa, Muscari comosum)

Taste: bitter, sometimes pungent, refreshing.
Folk medicine: diuretic, antiinflammatory.

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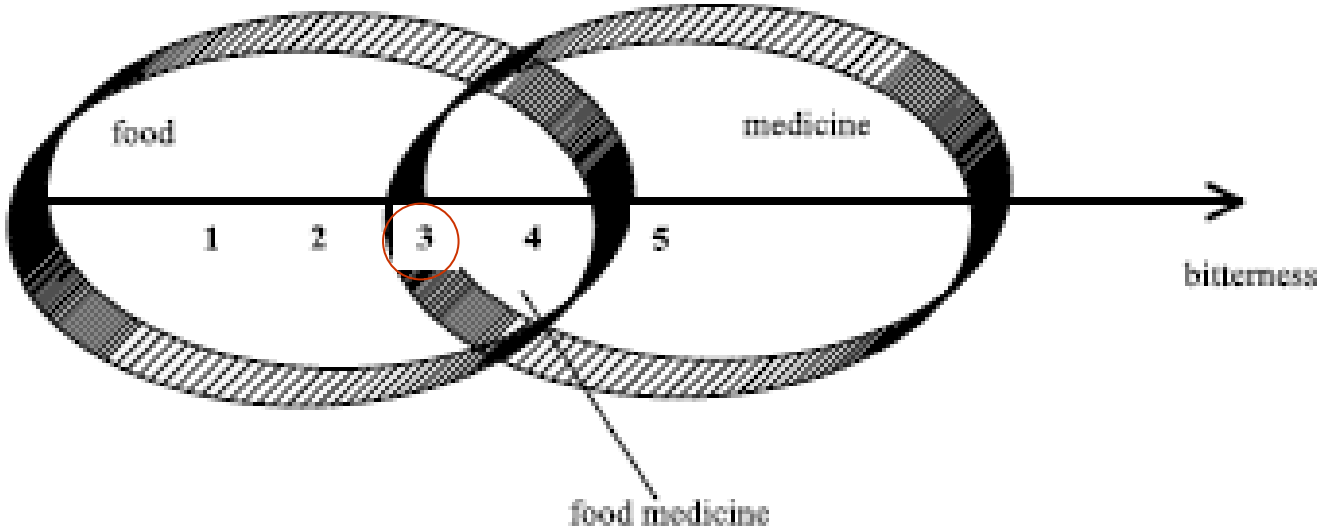
Lampascioni as food-medicine

Taste perception in modern ethnobiology has been poorly investigated.

In several communities there is a tradition paradigm for herbs:

"bitter you shall eat it (*food*)…… too bitter you would not (*medicine*)"



1: hilfkuq (whorls of *Papaver rhoeas*)
2: ngjumës (whorls and shoots of *Chondrilla juncea*)
3: çëpuljin ta kuqë (bulbs of *Leopoldia comosa*)
4: çikour (whorls of wild *Cichorium intybus*)
5: marrubi (leaves of *Marrubium incanum* and *Marrubium vulgare*)

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Bioactivity

Strong antioxidant activity of *lampascione* extracts (Pieroni A. et al., *2002)*

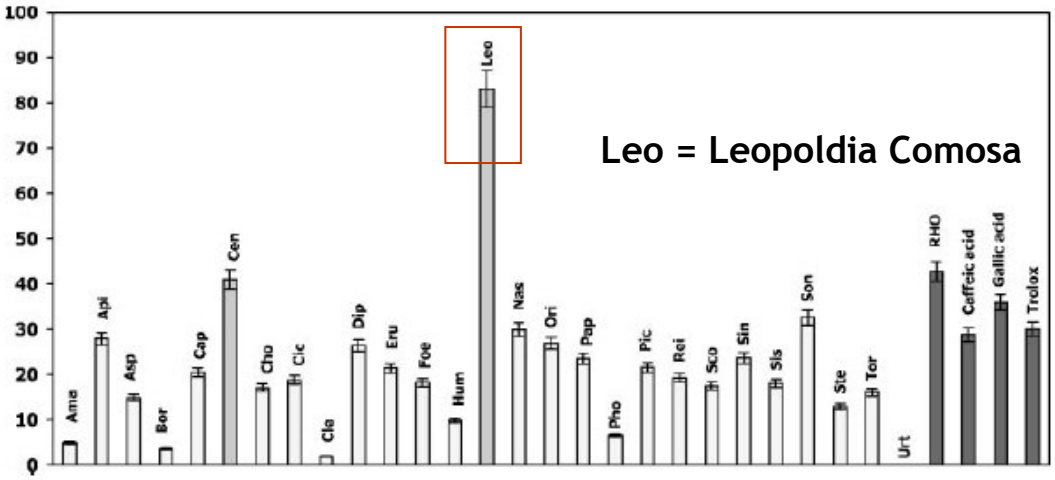

Figure 1. FRSA of the Arbëreshë plant extracts in the DPPH assay ($n = 3$ experiments); plant extracts: 2.5 mg/mL final conc.; pure compounds: 100μM final conc

Contents lists available at ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jethpharm

Effects of extracts from Italian medicinal plants on planktonic growth, biofilm formation and adherence of methicillin-resistant *Staphylococcus aureus*

Cassandra L. Quave[a,*], Lisa R.W. Plano[b,1], Traci Pantuso[a], Bradley C. Bennett[a]

[a] Florida International University, Department of Biological Sciences and Center for Ethnobiology and Natural Products, 1200 SW 8th Street, HLSI 320, Miami, FL 33199, USA
[b] University of Miami Miller School of Medicine, Department of Microbiology and Immunology, RMSB Room 3066, 1600 NW 10th Avenue, Miami, FL 33136, USA

Antifouling activity on *Staphylococcus aureus (Quave et al., 2008)*

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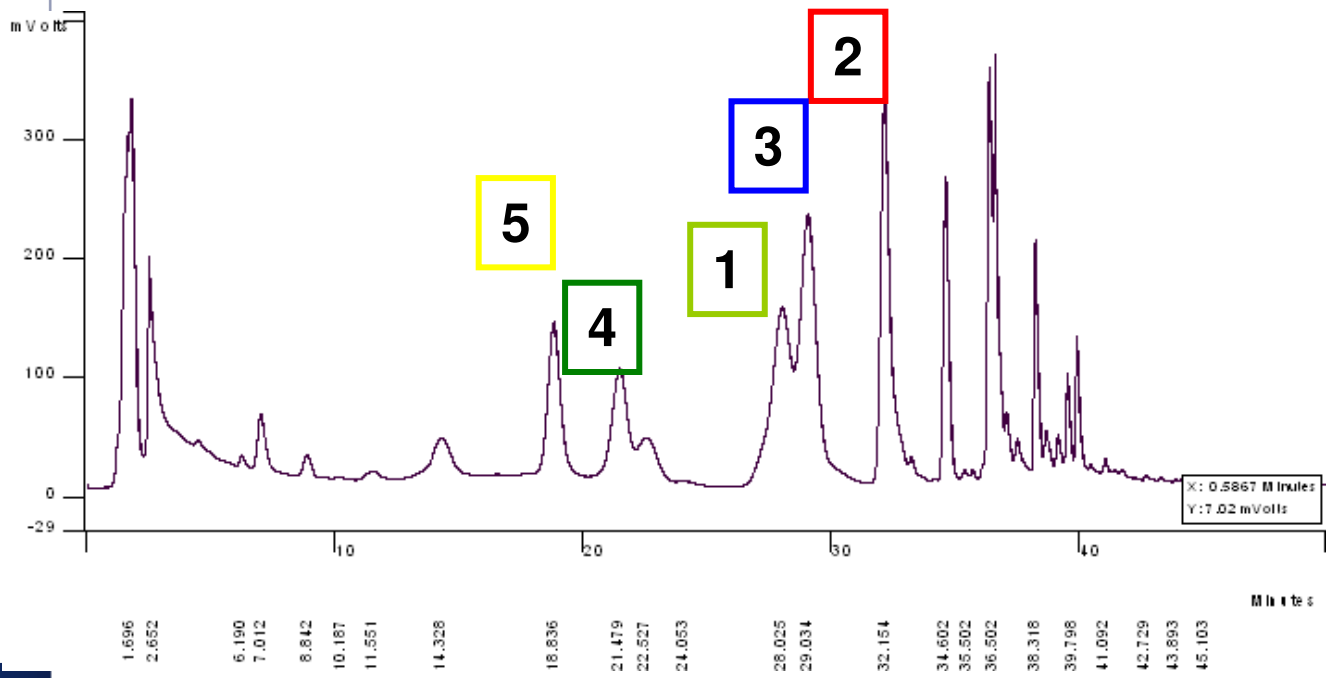
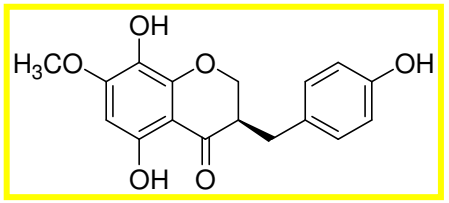
Lampascioni, taste guided analysis

Dry bulbs (50 g)		
solvent	**extract (mg)**	**taste** (1000 ppm in water)
hexane	334	sl. bitter astringent
diethylether	250	bitter, pleasant, astringent, grassy, sl. cooling
dichloromethane	43	sl. bitter, unpleasant astringent
ethanol	320	very bitter, grassy
water	13753	sl. bitter, tingling

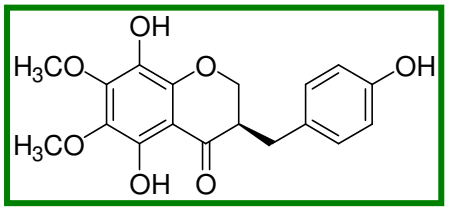
Lampascioni, taste guided analysis

RPHPLC, ethereal exctract

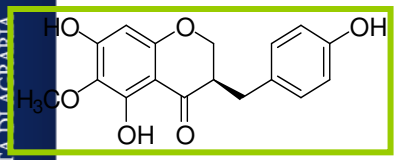




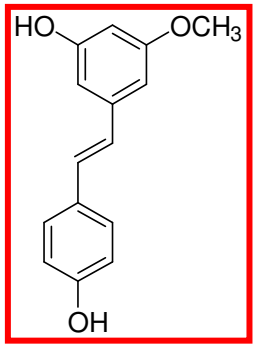
8-O-demethyl-7-O-methyl-3,9-dihydropunctatina (5)



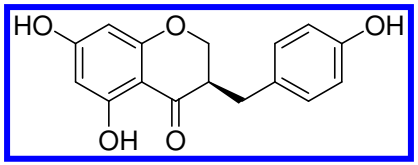
muscomin (4)



3,9-dihydroeucomnalin (1)



3-[(E)-2-(4-hydroxyphenyl)vinyl]-5-methoxyphenol (2)



4'-demethyl-3,9-dihydroeucomin (3)

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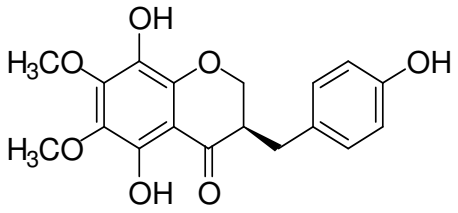
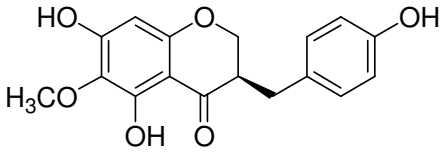
Biological assays on isolated compounds:

	TASTE (sensory evaluation)	*IN VITRO* ACTIVITY (cloned receptors)
 **muscomin** **1**	**Bitter**, pleasant, grassy	**Active on bitter receptor T2R14**
 **3,9-dihydroeucomnalin** **2**	Sl. bitter, **tingling**	**Active on TRPA1** pEC50% = 4.15+/-0.44 100μM

A. Bassoli et al.,*Chemistry & Biodiversity*, 2008

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Some taste properties indicate the presence of specific bioactive compounds in food and food plants.

These compounds and their derivatives can find many applications both in food industry and in pharmaceutical industry.

…WHAT ELSE?

LET'S GO FURTHER WITH OUR TRIP!

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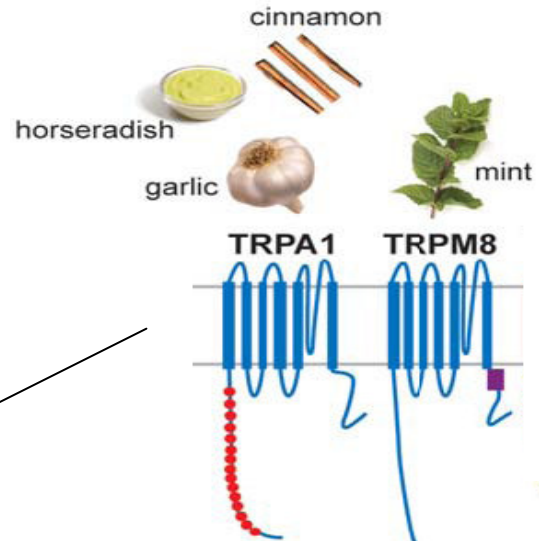
TR(I)Ps and cancer



TRPA1 active glucosinolates from cruciferae have a protective action against cancer

TRPM8 is overexpressed in some tissues, as prostate cells: search for anticancer agents

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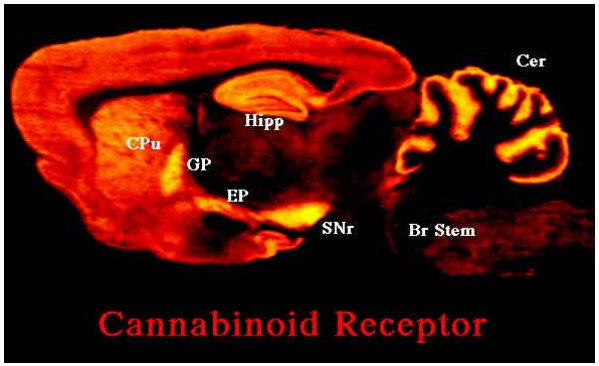
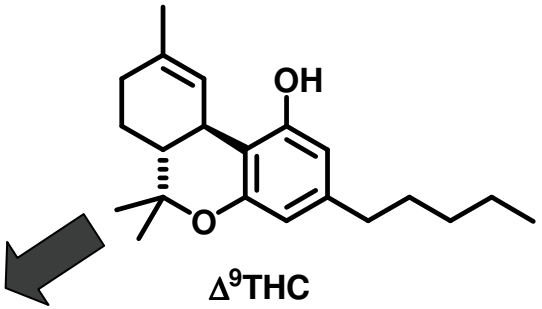
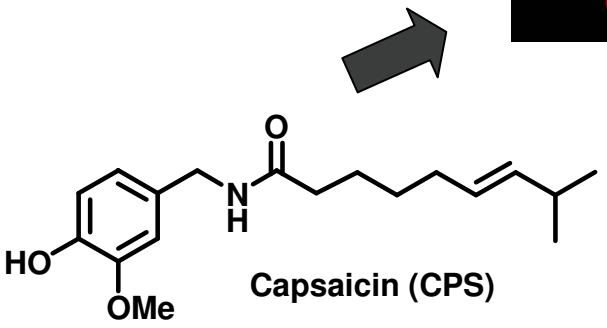
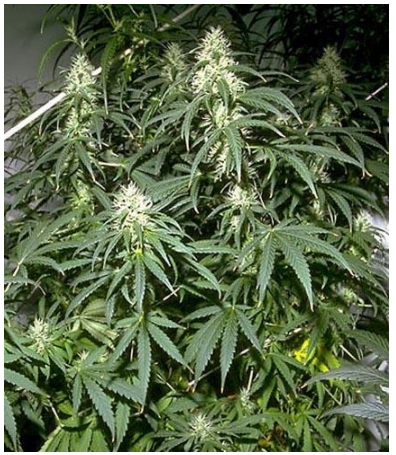
TR(I)Ps and drugs: the "cannabis connection"







TR(I)Ps and the endocannabinoids receptor



Angela Bassoli- DISMA
June 2011

UNIVERSITÀ DEGLI STUDI DI MILANO
FACOLTÀ DI AGRARIA

A "pain endurance" menu'?

In regions with hard "environmental" conditions such as:

- Extreme climate conditions
- Poor economic developement and hard physical work
- Resistance to pain as a cultural tradition

food is generally rich in TR(I)P active compounds

Can a "TR(I)P enriched" diet help to raise the threshold of pain endurance?

Angela Bassoli- DISMA
June 2011

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An extra mechanism to prevent/bear pain?

PAIN RESISTENCE THRESHOLD ↑

PHYSICAL AND MENTAL FATIGUE ↓

?

Applications: functional food, energy drink, sport…

Angela Bassoli- DISMA
June 2011

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CONCLUSIONS:

Some taste properties (particularly chemesthesis) indicate the presence of specific bioactive compounds.

Traditional food and food plants are an incredible source of such compounds.

These compounds and their derivatives can find many applications in **gastronomy**, **food industry** , in **agropharma** and **pharmaceutical industry** and in **medicine**.

New frontiers for these “unusual tastes” are still to be discovered.