



Azienda  
Ospedaliero  
Universitaria  
Careggi



UNIVERSITÀ  
DEGLI STUDI  
FIRENZE



Servizio  
Sanitario  
della  
Toscana



**PiN PiCK**  
PORTALE INTEGRATORI NUTRACEUTICI  
PER UNA SCELTA CONSAPEVOLE

# Cefalea e Fitoterapia

**Fabio Firenzuoli**

Responsabile del CERFIT

Centro di ricerca e innovazione in Fitoterapia

Struttura di riferimento per la Fitoterapia, Regione Toscana

Azienda Ospedaliero Universitaria Careggi, Firenze

Professore a c. Fitoterapia, Università di Firenze

letters to nature

**Xenopus embryo and oocyte microinjection.** hWIP-1 was expressed from the pCS2<sup>+</sup> expression vector. RNA synthesis and microinjection into *Xenopus* embryos have been described<sup>10</sup>.

**Armadillo stabilization assays.** *Drosophila* clone-8 cells, seeded one day earlier and grown to 80% confluence, were incubated with control or Wg-containing conditioned medium from 52 cells. Before incubation with clone-8 cells, the 52 conditioned medium (0.4 ml) was pre-incubated for 25 min at 4°C with 0.4 ml DMEM/F-12 medium from transfected or control 293 cells. After 3 h at 25°C, clone-8 cells were collected, washed in 1 × PBS, 5 mM EDTA, and lysed in 80 µl hypotonic buffer (10 mM Tris, pH 7.5, 0.2 mM MgCl<sub>2</sub>) containing protease inhibitors. After addition of 20 µl 1.25 M sucrose, a membrane-free cytoplasmic fraction was prepared by centrifugation at 100,000g for 30 min at 4°C, resolved by SDS-PAGE, immunoblotted and analysed for Armadillo (mAb N2-7A1; ref. 16), actin (Amersham) and HSP-70 (Sigma).

**Solution binding assay for Wg and XWnt8-Myc.** 200 µl 293-cell conditioned medium containing WIP-1-IgG, WD-IgG, or IgG (each adjusted by ultrafiltration to 60 nM) was incubated with protein A-Sepharose beads at 4°C for 3 h, after which the beads were washed 3 times with PBS and then incubated with 400 µl Wg or XWnt8-Myc conditioned medium at 4°C for 2 h. The beads were separated from unbound material by low-speed centrifugation and washed five times with PBS. Co-precipitates were analysed by immunoblotting with affinity-purified rabbit anti-Wg mAb 9E10 (ref. 17).

**Quantitative binding of XWnt8-AP and hWIP-1.**

(100 µl) containing WIP-1 (10 µg ml<sup>-1</sup>), WIP-1-IgG (4 µg ml<sup>-1</sup>) was used to coat 96-well plate at 4°C. Incubation at 4°C for 4 h with 200 µl 2 mg ml<sup>-1</sup> BSA in balanced salt, 20 mM HEPES, pH 7.0, 150 µl XWnt8-AP in binding buffer was applied to each well and in BSA in binding buffer was applied to each well. After 5 washes with 200 µl each of binding buffer, quantified by measuring alkaline phosphatase activity. A plot of alkaline phosphatase activity, representing bound XWnt8-AP relative to the total concentration of the simple binary binding model (A + B ↔ A·B).

Received 17 December 1998; accepted 20 January 1999.

- Wideman, A. & Nason, R. Mechanisms of Wg signaling in *Drosophila*. *Genes Dev.* **13**, 157-162 (1999).
- Moses, R. T., Brown, J. D. & Treisman, M. Wnt5a modulates cell development. *Development* **124**, 157-162 (1997).
- Chikva, A. et al. Dickkopf 1 is a member of a new family of secreted proteins. *Nature* **391**, 357-362 (1998).
- Hopfl, S., Brown, J. D. & Moses, R. T. Expression of a secreted inhibitor of Wnt signaling in the *Drosophila* embryo. *Genes Dev.* **10**, 2025-2037 (1996).
- Chikva, J. L. & Moses, R. T. Interactions between a secreted inhibitor of Wnt signaling and the Wnt signaling pathway in *Drosophila*. *Development* **124**, 157-162 (1997).
- van Leeuwen, T., Hartmann-Suttor, C. & Nason, R. Biology of the *Drosophila* Wnt5a signaling pathway. *Genes Dev.* **13**, 157-162 (1999).
- Piccolo, S., Sook, C., Gu, B. & DeRobertis, E. M. Drosophila Wnt5a signaling by direct binding of chordin to Wnt5a. *Cell* **97**, 101-111 (1999).
- Zimmerman, L. B., De Juan-Elorza, L. M., & Hartland, R. Wnt5a and its receptors have multiple agonist partners. *J. Biol. Chem.* **274**, 10111-10116 (1999).
- Hsu, D. R., Eisenstein, A. N., Wang, X., Raman, P. M., & Nathans, J. Identification of a novel family of secreted protein factors that antagonize Wnt signaling. *Genes Dev.* **13**, 157-162 (1999).
- Collins, K. M., Fu, M. P., Ballif, E. J. & Nason, R. Expression of the Wnt5a signaling pathway in *Drosophila*. *Genes Dev.* **13**, 157-162 (1999).
- Finch, P. M. et al. Purification and molecular cloning of a secreted protein that antagonizes Wnt signaling. *Proc. Natl Acad. Sci. USA* **94**, 4770-4775 (1997).
- Knäuper, A., Stamenkovic, I., Nishida, M., Ullrich, A., & Nagase, H. Identification of a novel family of metalloproteinases. *J. Biol. Chem.* **273**, 10111-10116 (1998).
- Behagiani, M. K., Treisman, R., Holten, P. & Dams, R. Identification of a novel family of metalloproteinases. *J. Biol. Chem.* **273**, 10111-10116 (1998).
- Hu, X., Saito-Tsujita, J.-P., Woodgett, J. R., Vannier, J., & Cohen, P. S. Identification of a novel family of metalloproteinases. *J. Biol. Chem.* **273**, 10111-10116 (1998).
- Peter, M., Chizhik, S., Swamin, D. & Watanabe, E. A role for Wnt5a in cell adhesion and cytoskeletal integrity during *Drosophila* embryonic development. *Development* **124**, 157-162 (1997).
- Irwin, G. L., Lewis, G. K., Ramesh, G. & Nalway, M. Wnt5a is a novel proto-oncogene product. *Mol. Cell. Biol.* **19**, 1011-1016 (1999).

**Acknowledgements.** We thank R. Moon for XWnt8-Myc plasmid, I. Gordon for the mouse RNA polymerase II cDNA library, and F. Beaudry and S. Maro-Santana for Howard Hughes Medical Institute (1-C34, A, B, C, D).

Correspondence and requests for materials should be addressed to F.F. (firenzuoli@ucl.ac.uk).

**A capsaicin-receptor homologue with a high threshold for noxious heat**

Michael J. Caterina<sup>1</sup>, Tobias A. Rosen<sup>1,†</sup>, Makoto Tominaga<sup>1,†</sup>, Anthony J. Brake<sup>1</sup> & David Julius<sup>1</sup>

<sup>1</sup>Department of Cellular and Molecular Pharmacology, University of California, San Francisco, California 94143-0450, USA

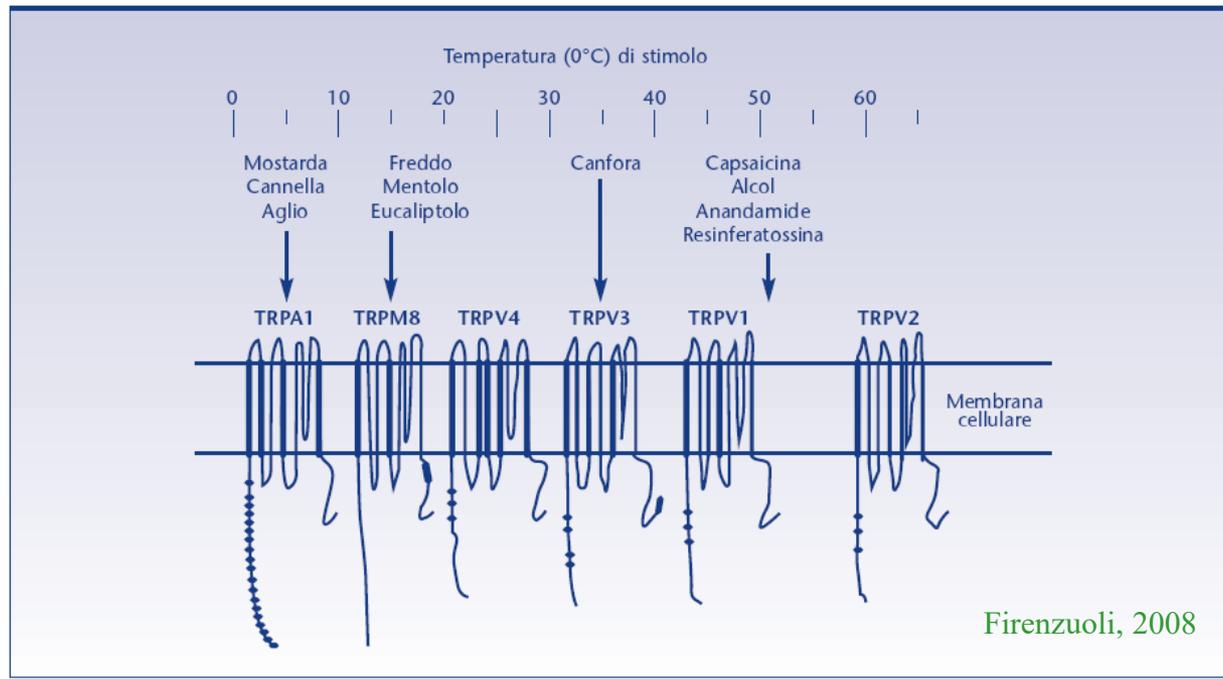
<sup>†</sup>These authors contributed equally to this work

Pain-producing heat is detected by several classes of nociceptive sensory neurons that differ in their thermal response thresholds<sup>1-3</sup>. The cloned capsaicin receptor, also known as the vanilloid receptor subtype 1 (VR1), is a heat-gated ion channel that has been proposed to mediate responses of small-diameter sensory neurons to moderate (43°C) thermal stimuli<sup>4,5</sup>. VR1 is also activated by protons, indicating that it may participate in vivo. Here we describe a novel TRP channel, TRP-ANK, that does not

1999



**Figura 1.** Struttura del TRP (*Transient Receptor Potential*) Implicati nella percezione di stimoli termici, nocicettivi e non, e le sostanze agoniste. La barra della temperatura indica il livello di stimolo per i singoli recettori<sup>2</sup>.



Firenzuoli, 2008

# Umbellularia californica



# Umbellulone

Brief Report

Cephalalgia  
An International Journal of Headache



## Pleasant natural scent with unpleasant effects: Cluster headache-like attacks triggered by *Umbellularia californica*

Cephalalgia

30(6) 744–746

© International Headache Society 2010

Reprints and permissions:

sagepub.co.uk/journalsPermissions.nav

DOI: 10.1111/j.1468-2982.2009.01988.x

cep.sagepub.com



S Benemei<sup>1</sup>, G Appendino<sup>2</sup> and P Geppetti<sup>1</sup>



NIH Public Access

Author Manuscript

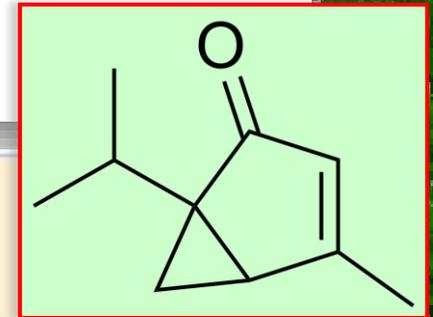
*Pain*. Author manuscript; available in PMC 2013 September 01.

Published in final edited form as:

*Pain*. 2012 September ; 153(9): 1949–1958. doi:10.1016/j.pain.2012.06.012.

## ACTIVATION OF TRPA1 ON DURAL AFFERENTS: A POTENTIAL MECHANISM OF HEADACHE PAIN

Rebecca M. Edelmayer<sup>a</sup>, Larry N. Le<sup>a</sup>, Jin Yan<sup>a</sup>, Xiaomei Wei<sup>a</sup>, Romina Nassini<sup>b</sup>, Serena Materazzi<sup>b</sup>, Delia Preti<sup>c</sup>, Giovanni Appendino<sup>d</sup>, Pierangelo Geppetti<sup>b</sup>, David W. Dodick<sup>e</sup>, Todd W. Vanderah<sup>a</sup>, Frank Porreca<sup>a</sup>, and Gregory Dussor<sup>a</sup>





Azienda  
Ospedaliero  
Universitaria  
Careggi



UNIVERSITÀ  
DEGLI STUDI  
FIRENZE



Servizio  
Sanitario  
della  
Toscana



Cochrane  
Library

Cochrane Database of Systematic Reviews

## Feverfew for preventing migraine (Review)

Wider B, Pittler MH, Ernst E

Wider B, Pittler MH, Ernst E.  
Feverfew for preventing migraine.  
Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD002286.  
DOI: 10.1002/14651858.CD002286.pub3.

# Partenio



RESEARCH

Open Access

## An observational study of fixed-dose *Tanacetum parthenium* nutraceutical preparation for prophylaxis of pediatric headache

Filomena Moscano<sup>1</sup>, Michela Guiducci<sup>2</sup>, Lucia Maltoni<sup>1</sup>, Pasquale Striano<sup>3</sup>, Maria Giuseppina Ledda<sup>4</sup>, Francesco Zoroddu<sup>5</sup>, Umberto Raucci<sup>6</sup>, Maria Pia Villa<sup>2</sup> and Pasquale Parisi<sup>2\*</sup>

### Abstract

**Background:** Migraine is one of the most prevalent chronic pain manifestations of childhood. Despite the multitude of available treatments, parents are often concerned about chronic therapies and pediatricians have insufficient confidence in prescribing prophylactic drugs. Therefore, there is now growing interest for natural supplements used to control recurrent migraine headaches. Such approach may increase acceptance and adherence to long-term prophylaxis therapy in children.

**Methods:** This is an observational multicenter study performed in children ( $n = 91$ ) with migraine, with (MO) or without aura (MA), or tension-type headache (TTH). A fixed-dose *Andrographis paniculata*, CoQ10, riboflavin, and magnesium, was administered for 16 weeks. Patients were evaluated at baseline (T0), at week 8 (T1) and at the end of treatment at week 16 (T2). A follow-up period occurred at week 20 (T3) and week 32 (T4).

**Results:** The herbal supplement significantly reduced the frequency of headaches in TTH patients during treatment period (T0:  $11.97 \pm 1.92$  vs T2:  $5.13 \pm 1.93$ ;  $p < 0.001$ ) and the efficacy was maintained after 16 weeks of treatment withdrawal (T4:  $4.46 \pm 1.75$ ;  $p < 0.001$  vs T0). The frequency of migraine attacks was also reduced in the MO group during treatment (T0:  $9.70 \pm 0.96$  vs T2:  $4.03 \pm 0.75$ ;  $p < 0.01$ ) and after withdrawal (T4:  $2.96 \pm 0.65$ ;  $p < 0.01$  vs T0). Conversely, MA patients showed reduction in migraine's frequency during treatment (T0:  $8.74 \pm 1.91$  vs T2:  $3.78 \pm 2.02$ ;  $p < 0.01$ ) but not at the end of the study (T4:  $5.57 \pm 3.31$ ;  $p > 0.05$  vs T0).

TTH patients did not report significant improvement of pain intensity. A significant effect was observed in the MO group during treatment (T0:  $3.06 \pm 0.11$  vs T2:  $2.14 \pm 0.19$ ;  $p < 0.001$ ) and after treatment withdrawal (T4:  $2.20 \pm 0.21$ ;  $p < 0.001$  vs T0). Likewise, MA group showed a significant treatment effect (T0:  $2.57 \pm 0.20$  vs T2:  $0.86 \pm 0.45$ ;  $p < 0.001$ ) and the efficacy persisted at the end of the study (T4:  $1.00 \pm 0.58$ ;  $p < 0.001$  vs T0).

**Conclusion:** This fixed-dose *Tanacetum parthenium* preparation improved headache frequency and pain intensity in children affected by TTH. Despite the main limits, this study supports the use of nutraceutical in pediatric headache/migraine.

**Keywords:** Nutraceuticals, Pediatric migraine, Observational study, *Tanacetum parthenium*, Prophylaxis



# Partenio



# Petasites

## Original Paper

European  
Neurology

Eur Neurol 2004;51:89–97  
DOI: 10.1159/000076535

Received: September 15, 2003  
Accepted: December 5, 2003  
Published online: January 28, 2004

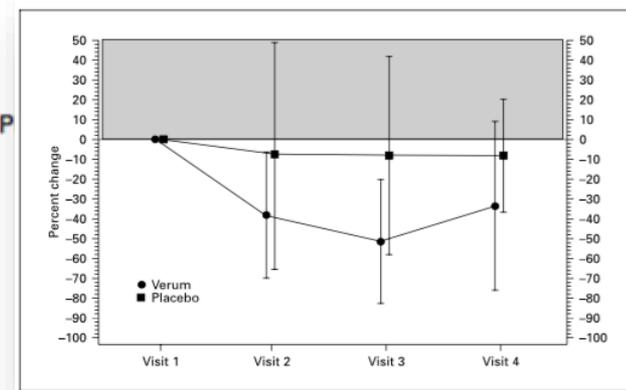
## The First Placebo-Controlled Trial of a Special Butterbur Root Extract for the Prevention of Migraine: Reanalysis of Efficacy Criteria

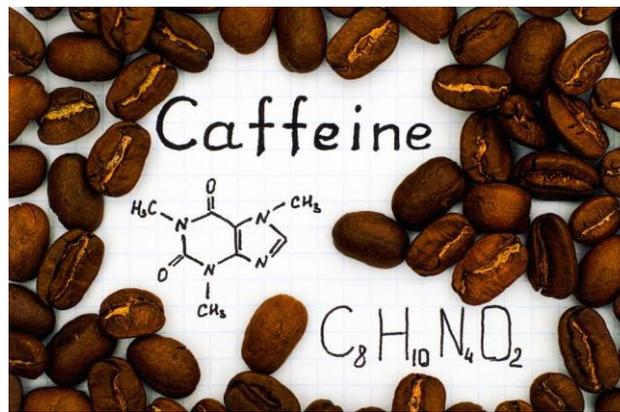


H.C. Diener<sup>a</sup> V.W. Rahlfs<sup>b</sup> U. Danesch<sup>c</sup>

<sup>a</sup>Department of Neurology, University of Essen, Essen, <sup>b</sup>idv Data Analysis and Study P

<sup>c</sup>Weber & Weber GmbH, Inning, Germany



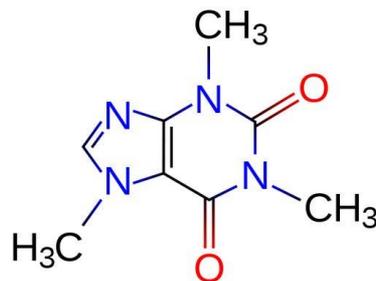


- \* Il più noto costituente del caffè e del tè, ma è presente anche nel cacao e in molte altre piante e semi, è un alcaloide purinico
- \* La dose standard in una normale tazza di caffè varia tra 50 e 100 mg
- \* Dopo l'ingestione orale, la caffeina è rapidamente completamente assorbita (99%), con un picco di concentrazione plasmatica che viene raggiunto in circa un'ora
- \* Diffonde facilmente attraverso tutte le membrane biologiche, inclusa la barriera ematoencefalica e si distribuisce in tutti i fluidi biologici
- \* La caffeina viene metabolizzata dal sistema dei citocromi P450, ed in particolare dall'isoenzima CYP1A2 responsabile per il 90% della clearance della caffeina, e nell'adulto ha una tipica emivita di 5 ore

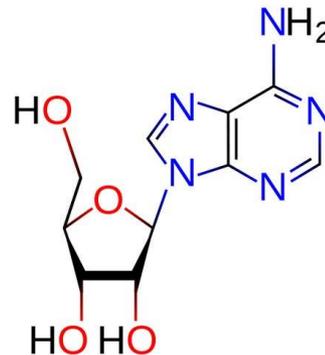
# MECCANISMO D'AZIONE

- \*La caffeina è un antagonista di tutti e quattro i sottotipi recettoriali per adenosina (A1, A2A, A2B, and A3), sebbene con affinità differenti.
- \*La caffeina mostra quindi una discreta selettività per il recettore A2A per l'adenosina, e studi su topi geneticamente privi di questo sottotipo recettoriale lo hanno identificato come responsabile dello stato di veglia della caffeina. Polimorfismi genici sembrano giocare un ruolo primario nelle differenze individuali di risposta alla caffeina
- \*Agisce sul tono vasale inibendo i recettori adenosinici

*caffeina*



*adenosina*



## CEFALEE

- \* I recettori adenosinici sono implicati nella fisiopatologia delle cefalee, ed in particolare dell'emicrania.
- \* Uno studio a doppio-cieco controllato vs placebo e con un disegno crossover disegnato per valutare se la caffeina (60- 130mg) avesse di per se un effetto analgesico nelle cefalee non-emicraniche riportava effetti simili al paracetamolo (Ward et al., 1991).
- \* **La caffeina, e la combinazione di analgesici con la caffeina può essere usata nella cefalea di tipo tensivo, con l'accortezza, per, che un uso troppo frequente potrebbe esporre al rischio di sviluppare la cefalee da uso eccessivo di analgesici.**
- \* L'ipotesi che l'azione analgesica della caffeina potesse essere dovuta ad una azione inibitoria sulla sintesi della prostaglandine, non è stata confermata.



# Farmaci contenenti caffeina

	<b>Caffeina</b>	<b>Paracetamolo</b>	<b>ASA</b>	<b>Propipfenazone</b>	<b>Butalbital</b>
	<b>(mg)</b>	<b>(mg)</b>	<b>(mg)</b>	<b>(mg)</b>	<b>(mg)</b>
<b>Peyona</b>	10/mL	/	/	/	/
<b>Optalidon</b>	25	/	/	125	50
<b>Antireumina</b>	25	175	275	/	/
<b>Neonisdina</b>	25	200	250	/	/
<b>Neonevral</b>	25	200	250	/	/
<b>Neo-Optalidon</b>	25	200	/	125	/
<b>Saridon</b>	25	250	/	150	/
<b>Exedrinil</b>	65	250	250	/	/
<b>Tachicaf</b>	130	1000	/	/	/

**Tabella 1 - Farmaci utilizzabili per il controllo del dolore.**

Classe	Tipologia di farmaco
Analgesici non oppioidi	FANS, paracetamolo
Oppioidi deboli	Codeina, tramadolo, buprenorfina
Oppioidi forti	Morfina, ossicodone, idromorfone, metadone, fentanil ecc.
Aiuvanti	Antidepressivi, anticonvulsivanti, cortisonici, benzodiazepine, fitoterapici
Cannabis	Medicinale galenico

**Tabella 2 - Strategia terapeutica a gradini.**

Dolore lieve	Dolore moderato	Dolore intenso
		Oppioidi forti
	Oppioidi deboli	± Cannabis
FANS/Paracetamolo	± FANS/Paracetamolo	± FANS/Paracetamolo
± aiuvanti ± agopuntura	± aiuvanti ± agopuntura	± aiuvanti ± agopuntura

**LE NOTIZIE DEL MESE SELEZIONATE PER VOI**

**ORA IL MEDICO PRESCRIVE LA MARIJUANA**

La pianta amata dagli hippie entra in farmacia. Come potente antidolorifico

Chi prova forte dolore a causa di una malattia cronica o sta subendo gli effetti collaterali della chemio (come la nausea), da oggi ha un alleato in più. E la Cannabis, più nota per i suoi effetti allucinogeni che per le positive proprietà antidolorifiche e antinfiammatorie.

«Qualunque medico adesso può prescrivere (se si esprime in solo un modo) un farmaco usato dai neurologi e dalla medicina preparata dal farmacista, ed è indicata per lenire sintomi neurologici della «demenza multipla, quelli del Parkinson, del glaucoma, delle malattie infiammatorie croniche (come l'artrite reumatoide), ma è ok anche per l'asma e le coliti croniche dolorose», spiega Fabio Firenzuoli, del Centro di medicina integrativa AOUC Careggi (FI).

«La tisana viene prescritta quando i farmaci per queste malattie, non funzionano più, non sono sufficienti o hanno troppi effetti collaterali... rispetto a un antinfiammatorio o analgesico classico ha la stessa efficacia ma, in diversi casi, anche di più, perché questa pianta riesce ad agire su recettori che la chimica normale non raggiunge», spiega l'esperto. «Se ci si astiene alle dosi prescritte è ben tollerata e non dà dipendenza. Sono esclusi i minori, le donne incinte e chi usa gli psicofarmaci». Alessandro Pellizzari

Selezionato da Starbene: [www.medicinale.it](http://www.medicinale.it)

RESEARCH ARTICLE

Open Access

# Patterns of medicinal cannabis use, strain analysis, and substitution effect among patients with migraine, headache, arthritis, and chronic pain in a medicinal cannabis cohort



Eric P. Baron<sup>1\*</sup>, Philippe Lucas<sup>2,3,4</sup>, Joshua Eades<sup>2</sup> and Olivia Hogue<sup>5</sup>

## Abstract

**Background:** Medicinal cannabis registries typically report pain as the most common reason for use. It would be clinically useful to identify patterns of cannabis treatment in migraine and headache, as compared to arthritis and chronic pain, and to analyze preferred cannabis strains, biochemical profiles, and prescription medication substitutions with cannabis.

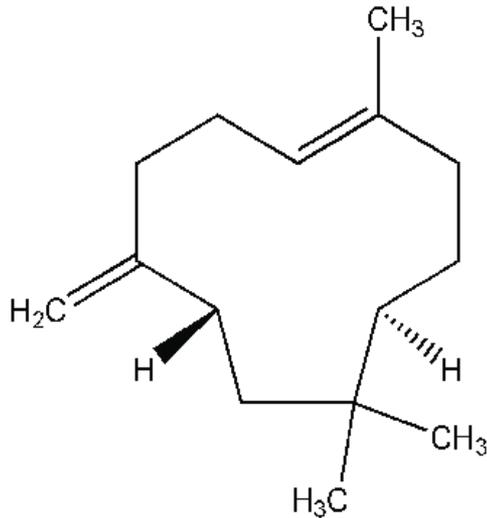
**Methods:** Via electronic survey in medicinal cannabis patients with headache, arthritis, and chronic pain, demographics and patterns of cannabis use including methods, frequency, quantity, preferred strains, cannabinoid and terpene profiles, and prescription substitutions were recorded. Cannabis use for migraine among headache patients was assessed via the ID Migraine™ questionnaire, a validated screen used to predict the probability of migraine.

**Results:** Of 2032 patients, 21 illnesses were treated with cannabis. Pain syndromes accounted for 42.4% ( $n = 861$ ) overall; chronic pain 29.4% ( $n = 598$ ), arthritis 9.3% ( $n = 188$ ), and headache 3.7% ( $n = 75$ ). Across all 21 illnesses, headache was a symptom treated with cannabis in 24.9% ( $n = 505$ ). These patients were given the ID Migraine™ questionnaire, with 68% ( $n = 343$ ) giving 3 "Yes" responses, 20% ( $n = 102$ ) giving 2 "Yes" responses (97% and 93% probability of migraine, respectively). Therefore, 88% ( $n = 445$ ) of headache patients were treating probable migraine with cannabis. Hybrid strains were most preferred across all pain subtypes, with "OG Shark" the most preferred strain in the ID Migraine™ and headache groups. Many pain patients substituted prescription medications with cannabis (41.2–59.5%), most commonly opiates/opioids (40.5–72.8%). Prescription substitution in headache patients included opiates/opioids (43.4%), anti-depressant/anti-anxiety (39%), NSAIDs (21%), triptans (8.1%), anti-convulsants (7.7%), muscle relaxers (7%), ergots (0.4%).

(Continued on next page)



# $\beta$ -cariofillene



- ★ Derivato terpenico, aromatico
- ★ Presente in piccole quantità anche in Melissa, Perilla, Luppolo e Cannabis
- ★ Attivo in particolare come antiinfiammatorio ed analgesico
- ★ Riduce in maniera significativa l'iperalgisia e la produzione di **citochine proinfiammatorie**
- ★ Si lega ai recettori CB2 per i **cannabinoidi**, senza effetti psicoattivi

ORIGINAL ARTICLE

WILEY

# TRPA1 mediates the antinociceptive properties of the constituent of *Crocus sativus* L, safranal

Simone Li Puma<sup>1</sup> | Lorenzo Landini<sup>1</sup> | Sergio J. Macedo Jr<sup>2</sup> | Viola Seravalli<sup>3</sup> |  
Ilaria M. Marone<sup>1</sup> | Elisabetta Coppi<sup>4</sup> | Riccardo Patacchini<sup>5</sup> | Pierangelo Geppetti<sup>1</sup> |  
Serena Materazzi<sup>1</sup> | Romina Nassini<sup>1</sup>  | Francesco De Logu<sup>1</sup>

<sup>1</sup>Department of Health Sciences, Section of Clinical Pharmacology and Oncology, University of Florence, Florence, Italy

<sup>2</sup>Department of Pharmacology, Federal University of Santa Catarina, Florianópolis, Brazil

<sup>3</sup>Department of Health Sciences, Section of Paediatrics, Midwifery, Gynaecology and Nursing, University of Florence, Florence, Italy

<sup>4</sup>Department of Neuroscience, Psychology, Drug Research and Child Health, Section of Pharmacology and Toxicology, University of Florence, Florence, Italy

<sup>5</sup>Department of Pharmacology, Chiesi Farmaceutici SpA, Parma, Italy

#### Correspondence

Romina Nassini, Department of Health Sciences, University of Florence, Florence, Italy.

Email: romina.nassini@unifi.it

#### Funding information

Ministry for University and Scientific Research (MIUR) Rome, Italy, Grant/Award Number: PRIN 201532AHAE\_003; Regione Toscana

#### Abstract

Safranal, contained in *Crocus sativus* L, exerts anti-inflammatory and analgesic effects. However, the underlying mechanisms for such effects are poorly understood. We explored whether safranal targets the transient receptor potential ankyrin 1 (TRPA1) channel, which in nociceptors mediates pain signals. Safranal by binding to specific cysteine/lysine residues, stimulates TRPA1, but not the TRP vanilloid 1 and 4 channels (TRPV1 and TRPV4), evoking calcium responses and currents in human cells and rat and mouse dorsal root ganglion (DRG) neurons. Genetic deletion or pharmacological blockade of TRPA1 attenuated safranal-evoked release of calcitonin gene-related peptide (CGRP) from rat and mouse dorsal spinal cord, and acute nociception in mice. Safranal contracted rat urinary bladder isolated strips in a TRPA1-dependent manner, behaving as a partial agonist. After exposure to safranal the ability of allyl isothiocyanate (TRPA1 agonist), but not that of capsaicin (TRPV1 agonist) or GSK1016790A (TRPV4 agonist), to evoke currents in DRG neurons, contraction of urinary bladder strips and CGRP release from spinal cord slices in rats, and acute nociception in mice underwent desensitization. As previously shown for other herbal extracts, including petasites or parthenolide, safranal might exert analgesic properties by partial agonism and selective desensitization of the TRPA1 channel.

#### KEYWORDS

calcitonin gene-related peptide, neurogenic inflammation, pain, safranal, transient receptor potential ankyrin 1

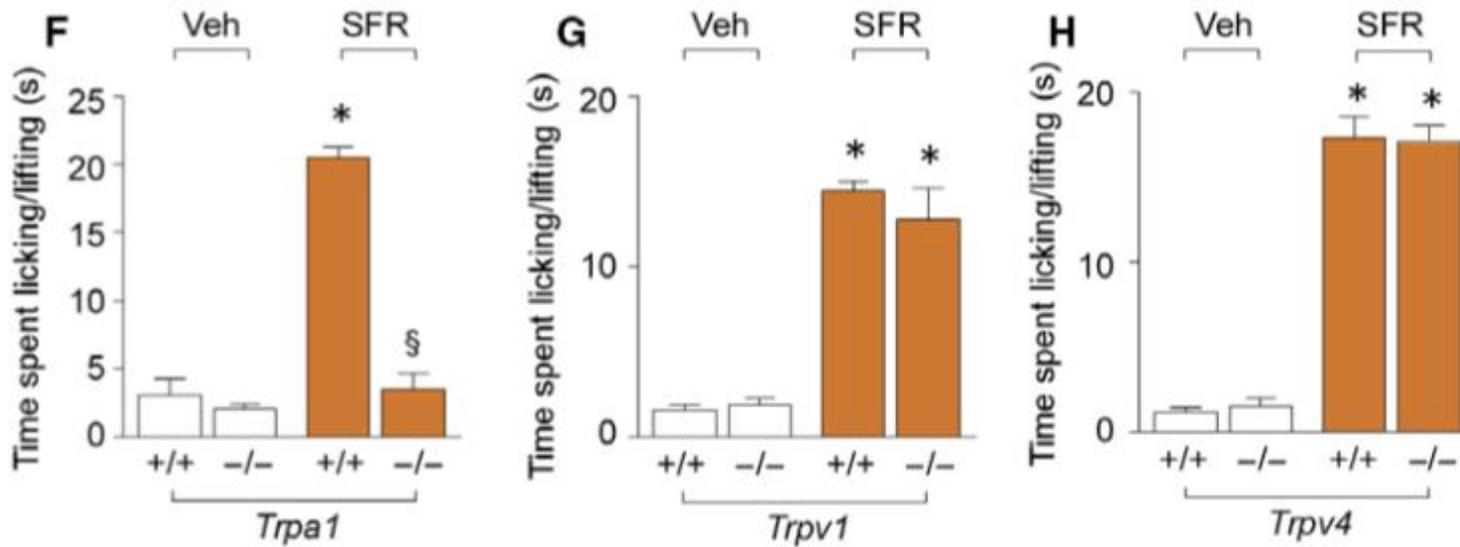


ORIGINAL ARTICLE

WILEY

# TRPA1 mediates the antinociceptive properties of the constituent of *Crocus sativus* L, safranal

Simone Li Puma<sup>1</sup> | Lorenzo Landini<sup>1</sup> | Sergio J. Macedo Jr<sup>2</sup> | Viola Seravalli<sup>3</sup> |  
Ilaria M. Marone<sup>1</sup> | Elisabetta Coppi<sup>4</sup> | Riccardo Patacchini<sup>5</sup> | Pierangelo Geppetti<sup>1</sup> |



Toscana

channel.

KEYWORDS

calcitonin gene-related peptide, neurogenic inflammation, pain, safranal, transient receptor potential ankyrin 1



Contents lists available at ScienceDirect

# Phytomedicine

journal homepage: [www.elsevier.com/locate/phymed](http://www.elsevier.com/locate/phymed)



## Review

### Effects of lavender on anxiety: A systematic review and meta-analysis

Davide Donelli<sup>a,d,e,\*</sup>, Michele Antonelli<sup>a,b,d,e</sup>, Caterina Bellinazzi<sup>b</sup>, Gian Franco Gensini<sup>c</sup>, Fabio Firenzuoli<sup>d</sup>



<sup>a</sup> Terme di Monticelli, Monticelli Terme, 43022 Parma, Italy

<sup>b</sup> Dipartimento di Medicina e Chirurgia, University of Parma, 43125 Parma, Italy

<sup>c</sup> Permanent Commission for Guidelines, Tuscany Region, 50139 Florence, Italy

<sup>d</sup> Research and Innovation Center in Phytotherapy and Integrated Medicine, CERFIT, Referring Center for Phytotherapy of Tuscany Region, Careggi University Hospital, 50139 Florence, Italy

<sup>e</sup> Servizio di Consulenza in Medicina Integrativa e Complementare, 42123 Reggio Emilia, Italy



**ANXIETY**



**LAVENDER  
essential oil**



HAM-A MD = -2.90 [95% CI -4.86 to -0.95],  
p = 0.004, 1173 participants



g = -0.73 [95% CI -1.00 to -0.46],  
p < 0.00001, 1682 participants



# Agnocasto



Electronic Physician (ISSN: 2008-5842)

<http://www.ephysician.ir>

January 2017, Volume: 9, Issue: 1, Pages: 3685-3689, DOI: <http://dx.doi.org/10.19082/3685>

## Systematic Review of Premenstrual, Postmenstrual and Infertility Disorders of Vitex Agnus Castus

Mahmoud Rafieian-Kopaei<sup>1</sup>, Mino Movahedi<sup>2</sup>

<sup>1</sup> Ph.D. in Pharmacology, Full Professor, Medical Plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran

<sup>2</sup> M.D., Gynecologist, Assistant Professor, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

**Type of article:** Systematic review

### Abstract

**Introduction:** Vitex agnus-castus, also called vitex is aboriginal to the Mediterranean region, with long leaves, tender stem, flowers and ripening seeds. The aim of this study was to overview premenstrual, postmenstrual and infertility disorder of Vitex agnus-castus.

**Methods:** This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases. The initial search strategy identified about 87 references. In this study, 43 studies were accepted for further screening, and met all our inclusion criteria (in English, full text, therapeutic effects of Vitex agnus-castus and dated mainly from the year 2009 to 2016).

The search terms were Vitex agnus-castus, premenstrual, postmenstrual, infertility disorder properties and pharmacological effects.

**Result:** Vitex agnus-castus was shown to contribute to the treatment of premenstrual syndrome (PMS). Moreover, the result of the present study showed that this valuable plant is helpful in alleviation of pain resulting from postmenstrual disease. Furthermore, it was found that Vitex agnus-castus is beneficial in infertility disorder.

**Conclusion:** Vitex agnus-castus (AC) is a phytopharmaceutical compound and is shown to be widely used to treat PMS and PMDD. In addition, it was shown to be beneficial in post-menstrual cases and it can also contribute to treatment of infertility cases in both men and women. Dopaminergic compounds available in this plant help to treat premenstrual mastodynia as well as other symptoms of the premenstrual syndrome.

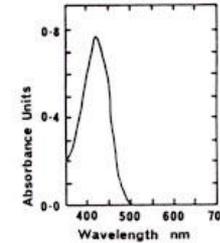
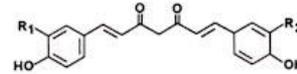
**Keywords:** Vitex agnus-castus, Phytochemicals, Therapeutic effects, Pharmacognosy, Alternative medicine



# Curcuma longa



Chemical Formula:  $C_{21}H_{20}O_6$  Curcumin Molecular Weight: 368.4



Visible spectrum of curcumin as a 0.0005% solution in acetone.

R<sub>1</sub> — R<sub>2</sub> — Compound

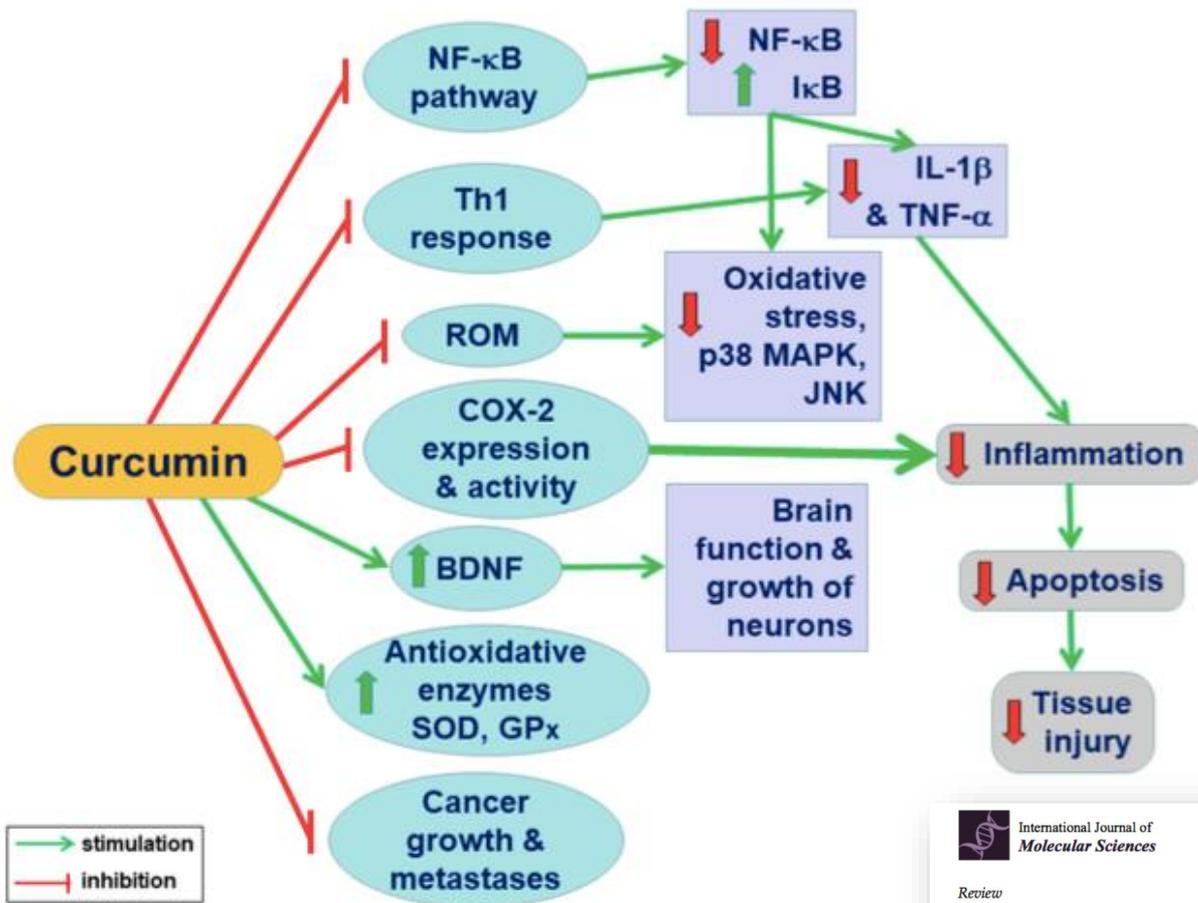
OCH <sub>3</sub>	OCH <sub>3</sub>	Curcumin
OCH <sub>3</sub>	H	Demethoxycurcumin
H	H	Bis-demethoxycurcumin

Colour Shade: Lemon Yellow at pH 3 Orange at pH 10 Solubility: Oil Soluble

Absorptivity of Curcumin:  $E_{1\%}^{1\text{cm}} = 1607$  at 425 nm in ethanol

Figure 4 Curcumin (class phenalone; synonyms turmeric yellow, diferoylmethane, natural yellow 3): structural and physical characteristics of curcumin.

Nella tradizione **depurativo, epatoprotettivo**



F.Firenze, Firenze

Review

## Curcumin: A Potent Protectant against Esophageal and Gastric Disorders

Slawomir Kwiecien , Marcin Magierowski , Jolanta Majka, Agata Ptak-Belowska ,  
Dagmara Wojcik , Zbigniew Sliwowski, Katarzyna Magierowska and Tomasz Brzozowski

Department of Physiology, Faculty of Medicine, Jagiellonian University Medical College, 16 Grzegorzeczka Street, 31-531 Cracow, Poland; skwiecien@cm-uj.krakow.pl (S.K.); m.magierowski@uj.edu.pl (M.M.); jolmaj@poczta.fm (J.M.); agata.ptak-belowska@uj.edu.pl (A.P.-B.); dagmara1.wojcik@uj.edu.pl (D.W.); AgaZS@poczta.fm (Z.S.); katarzyna.magierowska@uj.edu.pl (K.M.)

\* Correspondence: mpbrzozo@cyf-kr.edu.pl; Tel.: +48-12-421-10-06

R. CZEKAJ<sup>1</sup>, J. MAJKA<sup>2</sup>, A. PTAK-BELOWSKA<sup>2</sup>, A. SZLACHCIC<sup>2</sup>, A. TARGOSZ<sup>2</sup>, K. MAGIEROWSKA<sup>2</sup>,  
M. STRZALKA<sup>2</sup>, M. MAGIEROWSKI<sup>1</sup>, T. BRZOZOWSKI<sup>1</sup>

## ROLE OF CURCUMIN IN PROTECTION OF GASTRIC MUCOSA AGAINST STRESS-INDUCED GASTRIC MUCOSAL DAMAGE. INVOLVEMENT OF HYPOACIDITY, VASOACTIVE MEDIATORS AND SENSORY NEUROPEPTIDES

<sup>1</sup>Zeromski Hospital Neurology Ward, Cracow, Poland

<sup>2</sup>Department of Physiology, Jagiellonian University Medical College, Cracow, Poland

J Gastroenterol (2018) 53:618–630  
<https://doi.org/10.1007/s00535-017-1385-3>



ORIGINAL ARTICLE—ALIMENTARY TRACT

## Mechanisms of curcumin-induced gastroprotection against ethanol-induced gastric mucosal lesions

Renata Czekaj<sup>1</sup> · Jolanta Majka<sup>2</sup> · Katarzyna Magierowska<sup>2</sup> · Zbigniew Sliwowski<sup>2</sup> ·  
Marcin Magierowski<sup>2</sup> · Robert Pajdo<sup>2</sup> · Agata Ptak-Belowska<sup>2</sup> · Marcin Surmiak<sup>2</sup> ·  
Slawomir Kwiecien<sup>2</sup> · Tomasz Brzozowski<sup>2</sup>

Received: 25 November 2015 / Accepted: 13 August 2017 / Published online: 30 August 2017  
© The Author(s) 2017. This article is an open access publication



International Journal of  
**Molecular Sciences**

Review

## Curcumin: A Potent Protectant against Esophageal and Gastric Disorders

Slawomir Kwiecien<sup>✉</sup>, Marcin Magierowski<sup>✉</sup>, Jolanta Majka, Agata Ptak-Belowska<sup>✉</sup>,  
Dagmara Wojcik<sup>✉</sup>, Zbigniew Sliwowski, Katarzyna Magierowska and Tomasz Brzozowski<sup>\*✉</sup>

Department of Physiology, Faculty of Medicine, Jagiellonian University Medical College, 16 Grzegorzeczka Street,  
31-531 Cracow, Poland; [skwiecien@cm-uj.krakow.pl](mailto:skwiecien@cm-uj.krakow.pl) (S.K.); [m.magierowski@uj.edu.pl](mailto:m.magierowski@uj.edu.pl) (M.M.);  
[jolmaj@poczta.fm](mailto:jolmaj@poczta.fm) (J.M.); [agata.ptak-belowska@uj.edu.pl](mailto:agata.ptak-belowska@uj.edu.pl) (A.P.-B.); [dagmara1.wojcik@uj.edu.pl](mailto:dagmara1.wojcik@uj.edu.pl) (D.W.);  
[Asa75@poczta.fm](mailto:Asa75@poczta.fm) (T.B.); [katarzyna.magierowska@uj.edu.pl](mailto:katarzyna.magierowska@uj.edu.pl) (K.M.);



Submit a Manuscript: <http://www.wjnet.com/esps/>  
Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>  
DOI: 10.3748/wjg.v22.i9.2736

World J Gastroenterol 2016 March 7; 22(9): 2736-2748  
ISSN 1007-9327 (print) ISSN 2219-2840 (online)  
© 2016 Baishideng Publishing Group Inc. All rights reserved.

REVIEW

## Curcumin as a potential therapeutic candidate for *Helicobacter pylori* associated diseases

Avijit Sarkar, Ronita De, Asish K Mukhopadhyay

Original Paper

Pharmacology

Pharmacology 2013;91:267–274  
DOI: 10.1159/000350190

Received: November 26, 2012  
Accepted after revision: February 20, 2013  
Published online: May 15, 2013

## Mechanisms of the Protective Effects of Curcumin against Indomethacin-Induced Gastric Ulcer in Rats

Mohamed A. Morsy<sup>a,b</sup> Mohamed A. El-Moselhy<sup>c</sup>

<sup>a</sup>Division, College of Clinical Pharmacy, King Faisal University,  
<sup>b</sup>Faculty of Medicine, and <sup>c</sup>Department of Pharmacology and  
<sup>a</sup>, Egypt



# Zenzero

- Inibizione delle ciclo-ossigenasi (dose dipendente)
- Protegge la mucosa gastrica dai danni da etanolo e FANS
- Aumenta la peristalsi intestinale (effetto procinetico, non lassativo)
- Effetto antiemetico per inibizione recettori per la dopamina





# Comparison Between the Efficacy of Ginger and Sumatriptan in the Ablative Treatment of the Common Migraine

Mehdi Maghbooli,\* Farhad Golipour, Alireza Moghimi Esfandabadi and Mehran Yousefi

Zanjan University Of Medical Sciences, VALI-e-ASR Hospital, Neurology Department, Zanjan, Iran

Frequency and torment caused by migraines direct patients toward a variety of remedies. Few studies to date have proposed ginger derivatives for migraine relief. This study aims to evaluate the efficacy of ginger in the ablation of common migraine attack in comparison to sumatriptan therapy. In this double-blinded randomized clinical trial, 100 patients who had acute migraine without aura were randomly allocated to receive either ginger powder or sumatriptan. Time of headache onset, its severity, time interval from headache beginning to taking drug and patient self-estimation about response for five subsequent migraine attacks were recorded by patients. Patients' satisfaction from treatment efficacy and their willingness to continue it was also evaluated after 1 month following intervention. Two hours after using either drug, mean headaches severity decreased significantly. Efficacy of ginger powder and sumatriptan was similar. Clinical adverse effects of ginger powder were less than sumatriptan. Patients' satisfaction and willingness to continue did not differ. The effectiveness of ginger powder in the treatment of common migraine attacks is statistically comparable to sumatriptan. Ginger also poses a better side effect profile than sumatriptan. Copyright © 2013 John Wiley & Sons, Ltd.

*Keywords:* common migraine; ginger; sumatriptan.



# Comparison Between the Efficacy of Ginger and Sumatriptan in the Ablative Treatment of the Common Migraine

414

M. MAGHBOOLI *ET AL.*

**Table 1.** Frequency of mean headache severity before each drug use and 2 h after its intake

Drug		Headache severity				Sum
		Free	Mild <sup>b</sup>	Moderate <sup>c</sup>	Severe <sup>d</sup>	
Sumatriptan	Before	0	22 (11)	56 (28)	22 (11)	100 (50)
	After	44 (22) <sup>a</sup>	48 (24)	8 (4)	0	100 (50)
Ginger powder	Before	0	32 (16)	48 (24)	20 (10)	100 (50)
	After	44 (22)	56 (28)	0	0	100 (50)
Sum	Before	0	27 (27)	52 (52)	21 (21)	100 (100)
	After	44 (44)	52 (52)	4 (4)	0	100 (100)

<sup>a</sup>Digits outside and inside the brackets indicate percent and number of patients.

<sup>b</sup>Headache severity as  $1 \leq \text{VAS} \leq 4$ .

<sup>c</sup>Headache severity as  $5 \leq \text{VAS} \leq 7$ .

<sup>d</sup>Headache severity as  $8 \leq \text{VAS}$ .

P = 0.116.

sumatriptan. Patients' satisfaction and willingness to continue did not differ. The effectiveness of ginger powder in the treatment of common migraine attacks is statistically comparable to sumatriptan. Ginger also poses a better side effect profile than sumatriptan. Copyright © 2013 John Wiley & Sons, Ltd.

**Keywords:** common migraine; ginger; sumatriptan.



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH



7 July 2015  
EMA/HMPC/55843/2011  
Committee on Herbal Medicinal Products (HMPC)

European Union herbal monograph on *Matricaria recutita*  
L., flos  
Final

## CAMOMILLA

### Pianta e/o sostanza vegetale

*Matricaria Chamomilla* L.

(Sin.: *Matricaria recutita* L., *Chamomilla recutita* L.)

Famiglia Asteraceae (Compositae)

### Descrizione

La pianta, chiamata anche *Camomilla comune*, è tradizionalmente usata a livello popolare, non solo in Europa, sia come bevanda ricreativa e salutistica, sia a scopo medicinale, per le sue proprietà rilassanti, antinfiammatorie e antispastiche sulla muscolatura liscia. È indicata in particolare nei disturbi e patologie di tipo infiammatorio della cute e del tubo digerente.

Recenti ricerche cliniche sembrano confermare un debole quanto interessante effetto ansiolitico e antidepressivo.

### Droga vegetale

Capolini (chiamati impropriamente fiori), presenti in Farmacopea Europea.

### Costituenti chimici più importanti

Flavonoidi (apigenina, luteolina), cumarine (umbelliferone), polisaccaridi e un olio essenziale (contenente tra l'altro a-bisabololo, farnesene e matricina che si converte poi in camazulene durante la distillazione).

### Indicazioni e modalità di uso

Tisana ottenuta mediante infusione o decozione al 2-3 % di sommità fiorite può essere assunta alla dose di una-tre tazze al giorno. Indicata in particolare per i disturbi infiammatori del tubo digerente.

La tintura idroalcolica consente una estrazione parziale di flavonoidi e di olio essenziale e presenta una buona attività antinfiammatoria. Posologia media 20-40 gocce tre volte al giorno, dovrebbe tuttavia essere evitata in presenza di esofagite o gastrite per la presenza di alcool (50%). Eventualmente sostituibile con Estratto fluido.

L'Estratto secco, ricco in flavonoidi e polifenoli è privo di solvente, può essere utilizzato in forma di capsule o sciroppi, creme/unguenti, unito o meno a olio essenziale. Posologia media 100-400 mg, due-tre volte al giorno.

La *Camomilla* in varie forme estrattive è presente anche in prodotti alimentari ed erboristici, cosmetici, integratori e medicinali. Utilizzabile anche per sciacqui del cavo orale e impacchi cutanei contro arrossamenti e infiammazioni dermatologiche, così come per fomenti e clisteri.



# Altea

## Pianta e/o sostanza vegetale

*Althaea officinalis* L.

Famiglia: Malvaceae

## Descrizione

L'*Altea*, considerata la cugina maggiore della Malva, in realtà è meno conosciuta perchè più difficile a reperirla come pianta spontanea, e può essere addirittura confusa, impropriamente, con il Malvone. Nella medicina popolare europea viene utilizzata prevalentemente come emolliente, lenitivo, per uso interno ed esterno, sfruttandone le proprietà anti-tussive e antinfiammatorie per lo stomaco.

## Droga vegetale

Radici, fiori e foglie.

## Costituenti chimici più importanti

Tutte le parti della pianta contengono polifenoli e mucillagni, ma la droga più ricca è senz'altro rappresentata dalle radici: mucillagini (fino al 10% nelle radici). Presenti anche steroli, tracce di olio essenziale e antociani (nei fiori). I polisaccaridi che costituiscono le mucillagini dell'*Altea* (arabino-galattani e ramno-galatturonani) esplicano azione antinfiammatoria per uso topico su cute e mucose, rigonfiandosi con acqua e proteggendo come un film le mucose. Interessanti i lavori sperimentali che confermano l'attività sedativa della tosse dei ramno-galatturonani e immunostimolante.

