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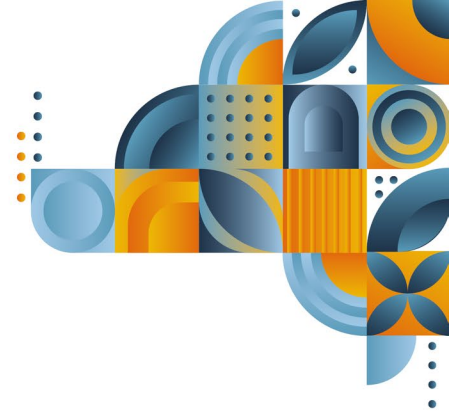
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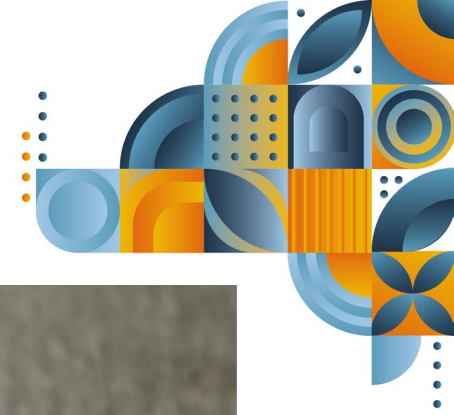
 **MZ**
EVENTS



TITOLO

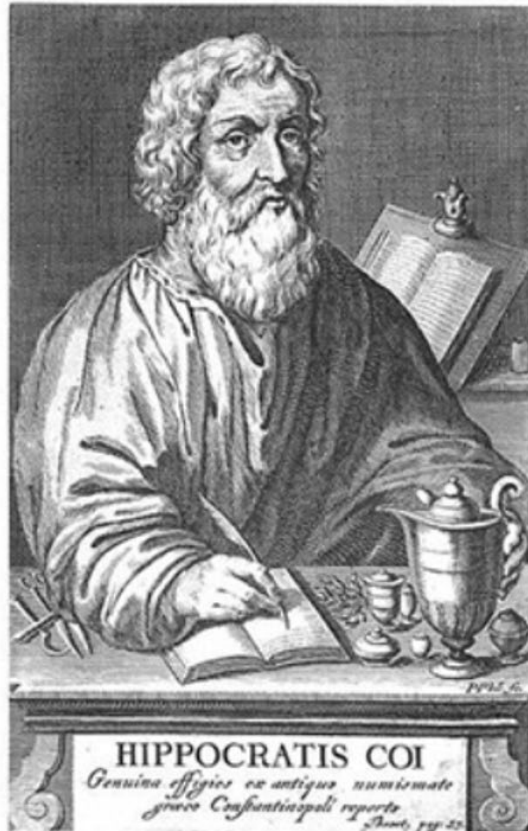
- **Armi non convenzionali: il ruolo dei Nutraceutici.**

Livio Luongo, Department of Experimental Medicine,
University of Campania «L. Vanvitelli»





Storia della nutraceutica



“...le differenze nelle malattie dipendono dall'alimentazione”

Ippocrate (460-377 a.C.)



Journal of Pain Research

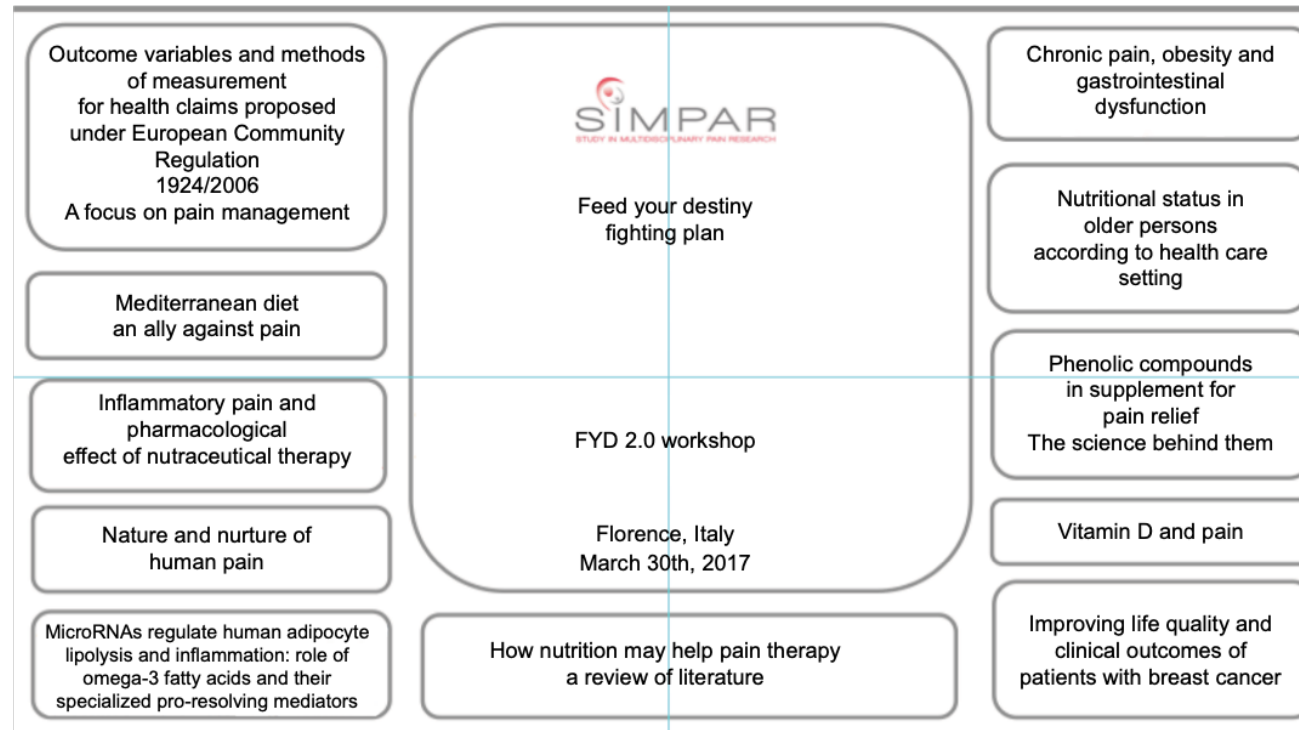
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REVIEW

Second edition of SIMPAR's "Feed Your Destiny" workshop: the role of lifestyle in improving pain management

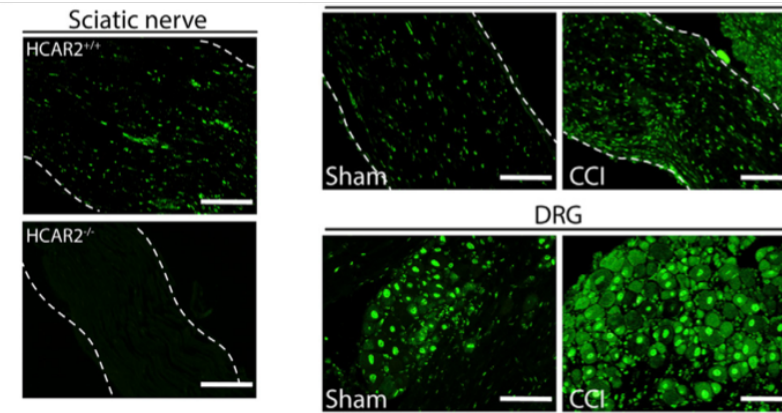
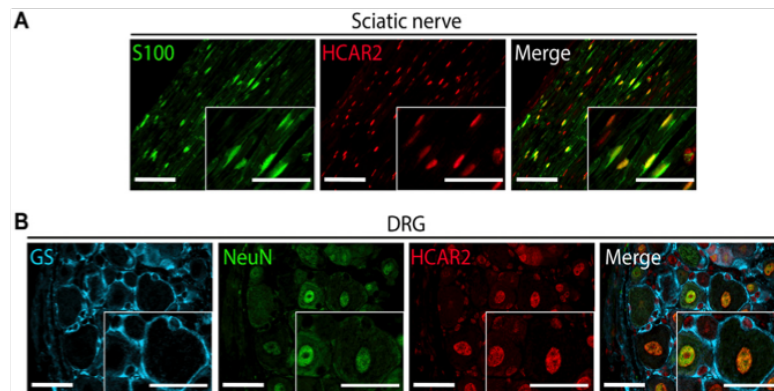
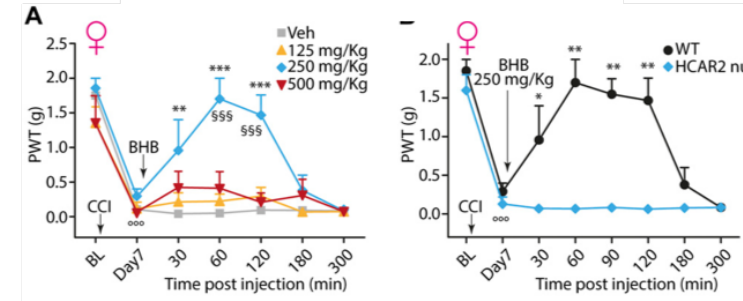
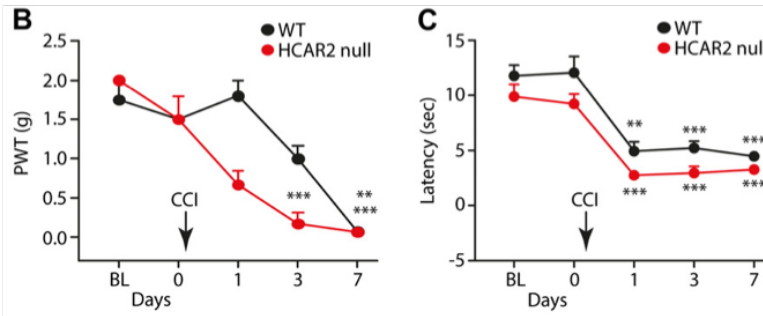
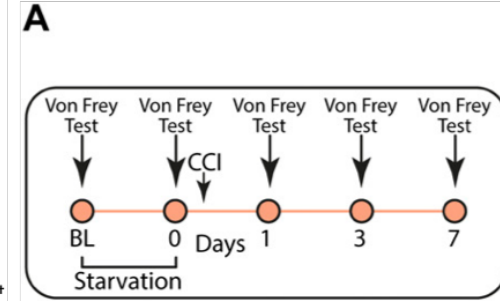


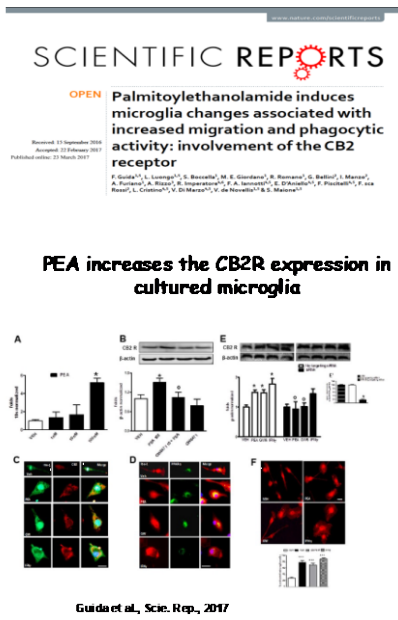
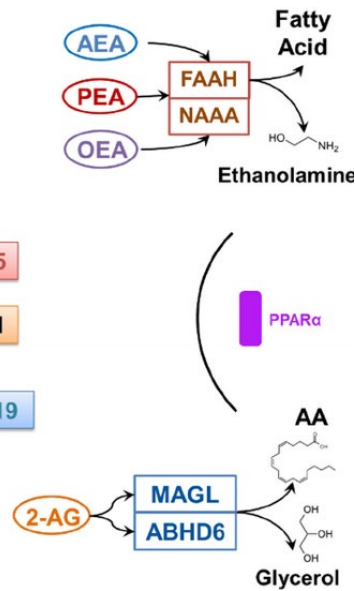
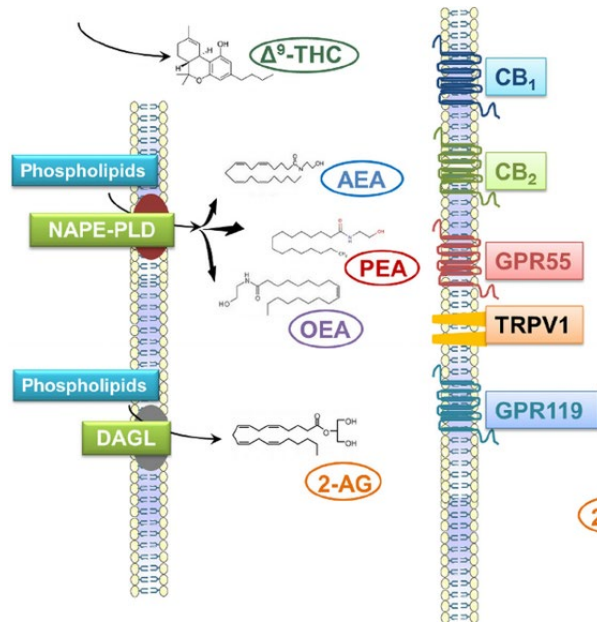


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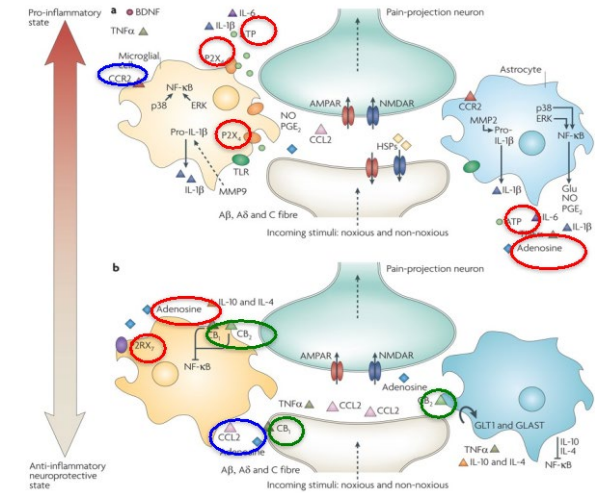
Ketones and pain: unexplored role of hydroxyl carboxylic acid receptor type 2 in the pathophysiology of neuropathic pain

Serena Boccella,* Francesca Guida,* Francesco De Logu,[†] Danilo De Gregorio,* Mariacristina Mazzitelli,[§] Carmela Belardo,* Monica Iannotta,* Nicola Serra,[†] Romina Nassini,[†] Vito de Novellis,* Pierangelo Geppetti,* Sabatino Maione,^{*,1} and Livio Luongo^{*,2}





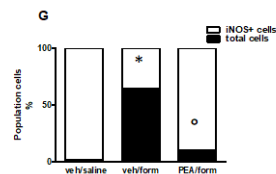
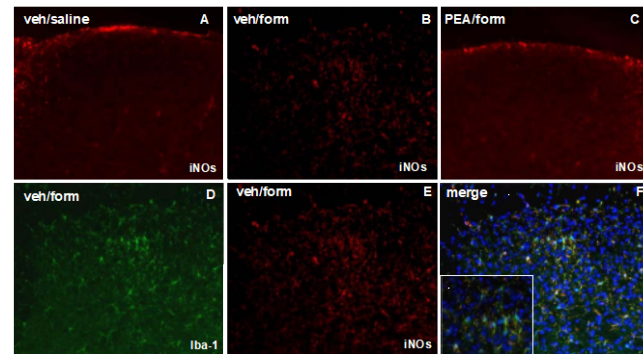
Factors regulating microglial phenotypes



Milligan and Watkins, 2009

Palmitoylethanolamide Reduces Formalin-Induced Neuropathic-Like Behaviour Through Spinal Glial/Microglial Phenotypical Changes in Mice

Livio Luongo^{1,5}, Francesca Guida^{1,5}, Serena Bocella¹, Giulia Bellini¹, Luisa Gatta¹, Francesca Rossa², Vito de Novellis³ and Sabatino Maimone^{1,4}



Ultra-micronized palmitoylethanolamide rescues the cognitive decline-associated loss of neural plasticity in the neuropathic mouse entorhinal cortex-dentate gyrus pathway

Serena Bocella^{1,2}, Claudia Crittiani^{3,4}, Rosaria Romano¹, Monica Iannotta¹, Carmela Belardo¹, Antonio Farina¹, Francesca Guida¹, Fabiana Pisciotta¹, Enza Palazzo¹, Mariacristina Mazziotti¹, Roberta Imperatore¹, Lea Tunisi¹, Vito de Novellis¹, Luigia Cristino¹, Vincenzo Di Marzo¹, Antonio Calignano¹, Sabatino Maimone¹, Livio Luongo¹

¹Department of Experimental Medicine, Pharmacology Division, University of Campania "Luigi Vanvitelli", 80138 Naples, Italy
²Department of Pharmacy, School of Medicine, University of Naples Federico II, Naples, Italy
³Department of Science Group, Institute of Biomedical Sciences, CNR, Naples, Italy
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⁵Department of Science and Technology, University of Naples, Naples, Italy

S. Bocella (✉) | C. Crittiani

Keywords:
 dorsal nerve root
 central afferents
 von Willebrand factor
 cognitive performance
 synaptogenesis

ABSTRACT

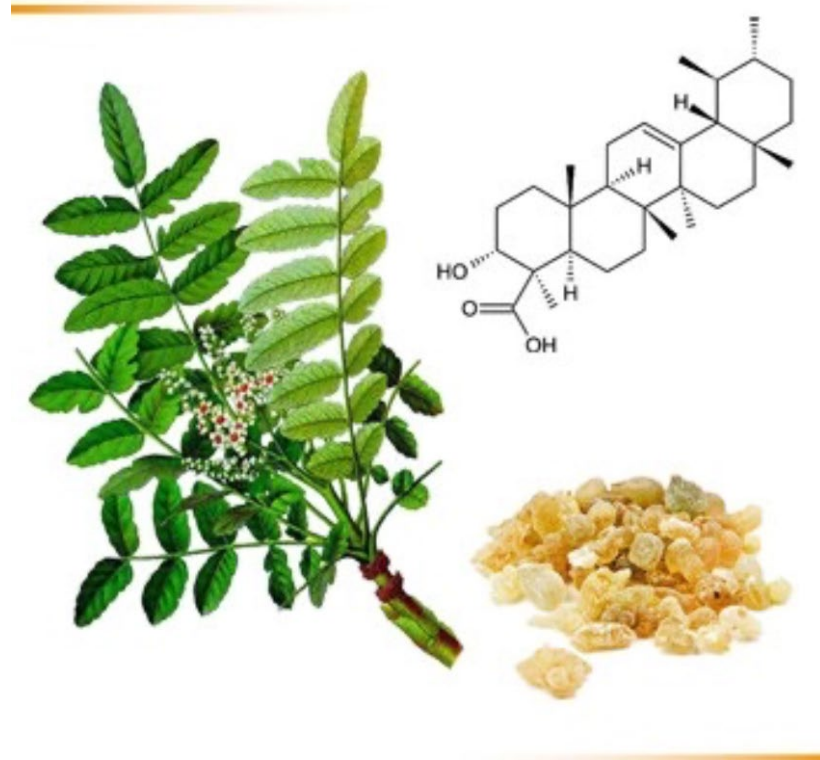
Chronic pain is associated with cognitive deficits. Palmitoylethanolamide (PEA) has been shown to attenuate pain and peripheral cognitive impairment by restoring glutamatergic synapses functioning in the dorsal nerve root (DRG) of the spinal nerve to mice. DRG reduced mechanical and thermal thresholds, spinal sensory and LTP at the lateral entorhinal cortex (LEC)-dentate gyrus (DG) pathway. It decreased also postsynaptic density, volume and dendritic arborization of DG and increased the expression of endocannabinoid receptors 1 and 2 (CB1 and CB2), of the G-protein coupled receptors (GPCRs) metabotropic glutamate receptor 1 and 7 (mGluR1 and mGluR7), of the G-protein coupled receptors (GPCRs) metabotropic glutamate receptor 1 and 7 (mGluR1 and mGluR7), of the G-protein coupled receptors (GPCRs) metabotropic glutamate receptor 1 and 7 (mGluR1 and mGluR7). The levels of endocannabinoid 2-arachidonyl glycerol (2-AG) were instead increased in the LEC. Chronic treatment with PEA, starting from when neuropathic pain was fully developed, was able to reverse mechanical allodynia and thermal hyperalgesia, memory deficit and LTP in DRG cell type, but not in PPARα null mice. PEA also reversed the level of glutamate and the expression of phosphorylated GluR1 subunit, postsynaptic density and synaptogenesis. Altogether, these results suggest that enteroafferent pain negatively affects cognitive behavior and related LTP, glutamatergic synapse and synaptogenesis in the DG. In these conditions PEA treatment alleviates pain and cognitive impairment by restoring LTP and synaptic plasticity changes in the LEC-DG pathway. These outcomes open new perspectives for the use of the bicyclicolethanolamine, such as PEA, for the treatment of neuropathic pain and its central behavioral sequelae.

1. Introduction

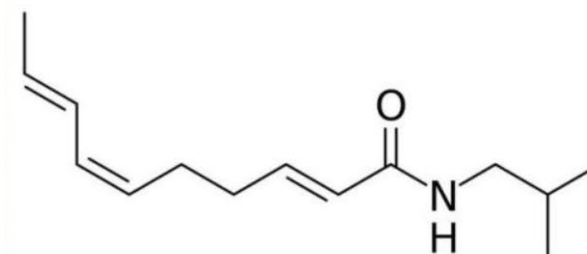
In the last two decades most of studies on chronic pain-related synaptic plasticity changes underlying cognitive/affective consequences (Grueter, 2015; Grueter et al., 2015) have been focused on cortical (Grueter et al., 2012; Grueter et al., 2012) and non-cortical supraspinal structures (Grueter, 2015; Grueter et al., 2015). How chronic pain influences the hippocampus (entorhinal) is still little investigated (Grueter et al., 2015). The hippocampus belongs to the Papez circuit, a neural network that, by connecting the hypothalamus to the limbic

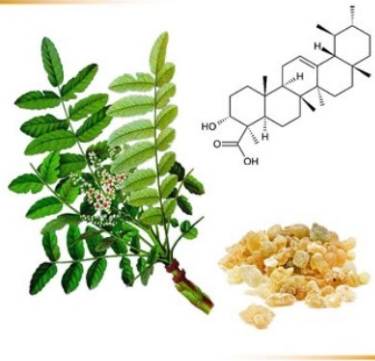
area, represents the anatomical substrate for emotional experiences involved in learning, memory and motivation (Eichenbaum, 2017). Persistent pain altered hippocampal neuron function (Grueter et al., 2015; Grueter et al., 2015) whereas neuropathic pain reduced synaptic plasticity (LTP) at dentate gyrus (DG), CA1, or CA3 synapses (Grueter et al., 2012; Grueter et al., 2012; Mura et al., 2012), as well as DG synaptogenesis (Eichenbaum et al., 2015) and associated pathways (Grueter et al., 2017). Much of the cortical information that arrives at the hippocampus enters through the entorhinal cortex, and much of the neuron projection to the neocortex arises from the

Boswellia Serrata



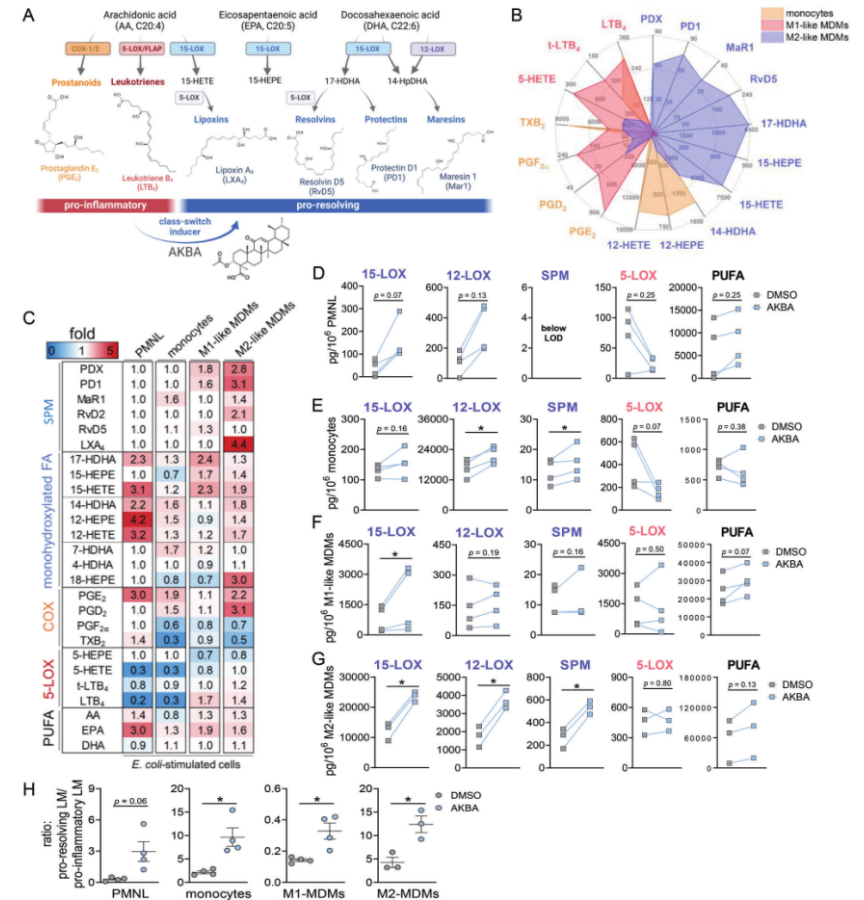
Acmella Olaracea

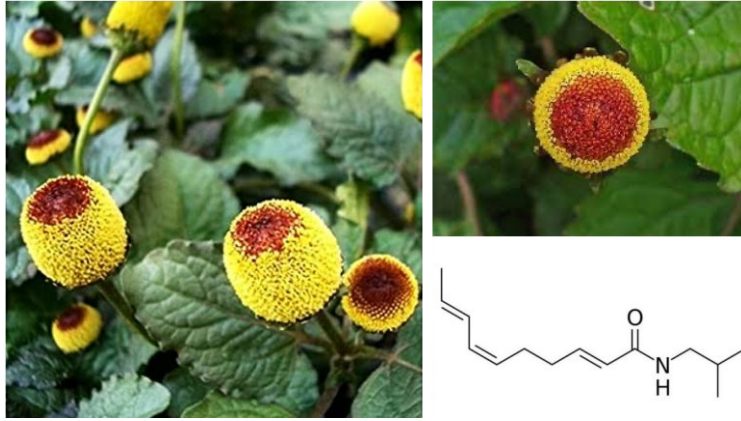




Allosteric Activation of 15-Lipoxygenase-1 by Boswellic Acid Induces the Lipid Mediator Class Switch to Promote Resolution of Inflammation

Friedemann Börner, Simona Pace, Paul M. Jordan, Jana Gerstmeier, Mario Gomez, Antonietta Rossi, Nathaniel C. Gilbert, Marcia E. Newcomer, and Oliver Wéiz*





Targeting Cannabinoid Receptors and Fatty Acid Amide Hydrolase: An Innovative Food-Grade Delivery System of *Zingiber officinale* and *Acmella oleracea* Extracts as Natural Adjuvant in Pain Management

Gioanna Petrangolini¹, Fabio Donzelli¹, Davide Berlanda², Pietro Allegrini¹, Andrea Rossignoli², Michela Stocchi², Antonella Rivero^{2*}

Table 3: Potency (EC₅₀) on human CB2 cell based assay.

Sample	Human CB2 cells		Mock cells	
	EC ₅₀	Dose response curves	EC ₅₀	Dose response curves
<i>Acmella oleracea</i>	12 µg/ml		N.E.	
Sylvestrol	3.66 µM		30.1 µM	
<i>Zingiber officinale</i>	N.E.		N.E.	
6-Gingerol	N.E.		N.E.	
Minalol	44.4 µg/ml		N.E.	
HU210	1.35 nM		N.E.	

Figure 3: Dose response curves on the inhibitory potency on FAAH inhibition assay.



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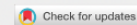
Alkylamides from *Acmella oleracea*: antinociceptive effect and molecular docking with cannabinoid and TRPV1 receptors

Raíssa M. Kao Yien , Anne Caroline C. Gomes , Rodolfo Goetze Fiorot ,

Ana Luísa Palhares Miranda , Gilda A. Neves , Brenda da Silva Andrade , ...show all

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Cite this article <https://doi.org/10.1080/14786419.2022.2142221>



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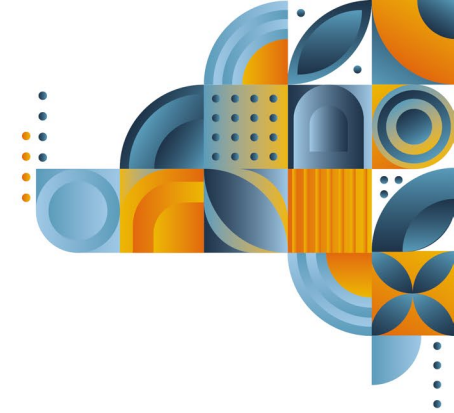


Table 1 Classification and indicative roles of mammalian K2P channels

Family	Channel	Formal name	Gene name	Indicative physiological and/or pathophysiological roles	Reference(s)
TWIK	TWIK-1	K _{2p} 1.1	<i>KCNK1</i>	Renal water and phosphate reabsorption, astrocyte leak current	1, 16, 20
	TWIK-2	K _{2p} 6.1	<i>KCNK6</i>	Hypertension and vascular dysfunction	141
	KCNK7	K _{2p} 7.1	<i>KCNK7</i>	Unknown	NA
TREK	TREK-1	K _{2p} 2.1	<i>KCNK2</i>	Depression, ischemia, nociception, myelinated axons, general anesthesia, ventricular tachycardia, cardiac fibrosis, migraine	See text
	TREK-2	K _{2p} 10.1	<i>KCNK10</i>	Nociception	See text
	TRAAK	K _{2p} 4.1	<i>KCNK4</i>	Myelinated axons, postsurgical neuropathic pain	27, 105, 140
TASK	TASK-1	K _{2p} 3.1	<i>KCNK3</i>	Aldosterone secretion, respiratory stimulation, atrial fibrillation, inflammation, pulmonary hypertension, sleep apnea	See text
	TASK-3	K _{2p} 9.1	<i>KCNK9</i>	Aldosterone secretion, respiratory stimulation, cancer, BBMRs, inflammation, pain, general anesthesia, sleep duration	See text
	TASK-5	K _{2p} 15.1	<i>KCNK15</i>	Unknown	NA
TALK	TASK-2	K _{2p} 5.1	<i>KCNK5</i>	Renal volume control, migraine, Balkan endemic nephropathy	20, 142, 143
	TALK-1	K _{2p} 16.1	<i>KCNK16</i>	Insulin secretion	42
	TALK-2	K _{2p} 17.1	<i>KCNK17</i>	Cardiac conduction disorder	144
THIK	THIK-1	K _{2p} 13.1	<i>KCNK13</i>	Microglial surveillance	32
	THIK-2	K _{2p} 12.1	<i>KCNK12</i>	Unknown	NA
TRESK	TRESK	K _{2p} 18.1	<i>KCNK18</i>	Migraine, nociception	112, 138, 139



Annual Review of Pharmacology and Toxicology
**Two-Pore Domain Potassium
Channels as Drug Targets:
Anesthesia and Beyond**

Alistair Mathie,¹ Emma L. Veale,¹
Kevin P. Cunningham,² Robyn G. Holden,¹
and Paul D. Wright³

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Kent ME4 4TB, United Kingdom; email: a.a.mathie@kent.ac.uk

²Wolfson Centre for Age-Related Diseases, King's College London, London SE1 1UL,
United Kingdom

³LifeArc, Stevenage SG1 2FX, United Kingdom



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RESEARCH PAPER



**TREK1 channel activation as a new analgesic strategy devoid
of opioid adverse effects**

Jérôme Busserolles^{1,2}  | Ismail Ben Soussia³ | Laetitia Pouchol^{1,2} |
Nicolas Marie⁴ | Mathieu Meleine^{1,2} | Maïly Devilliers^{1,2} | Céline Judon^{1,2} |
Julien Schopp^{1,2} | Loïc Clémenceau⁴ | Laura Poupon^{1,2} | Eric Chapuy^{1,2} |
Serge Richard⁵ | Florence Noble⁴ | Florian Lesage³ | Sylvie Ducki⁶ |
Alain Eschalier^{1,2} | Stéphanie Lolonier^{1,2} 



Chemical Senses, 2019, Vol 44, 91—103

doi:10.1093/chemse/bjy069

Original Article

Advance Access publication 26 October 2018



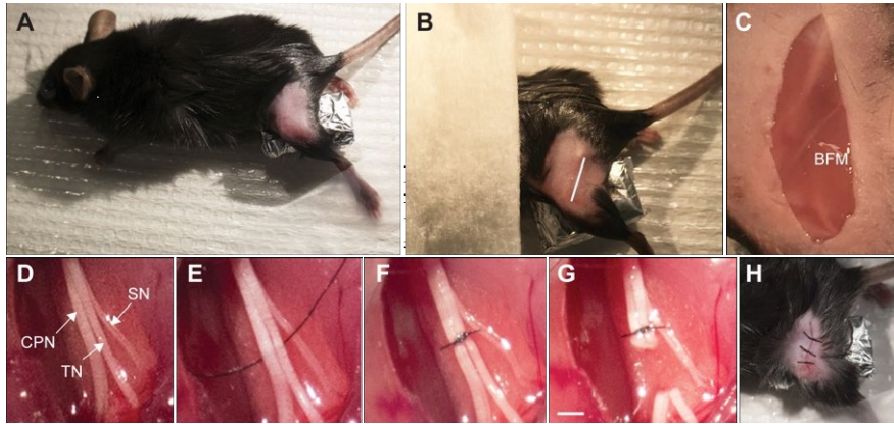
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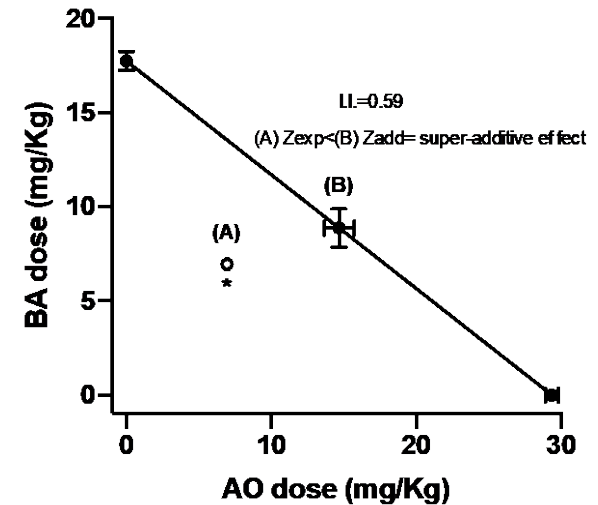
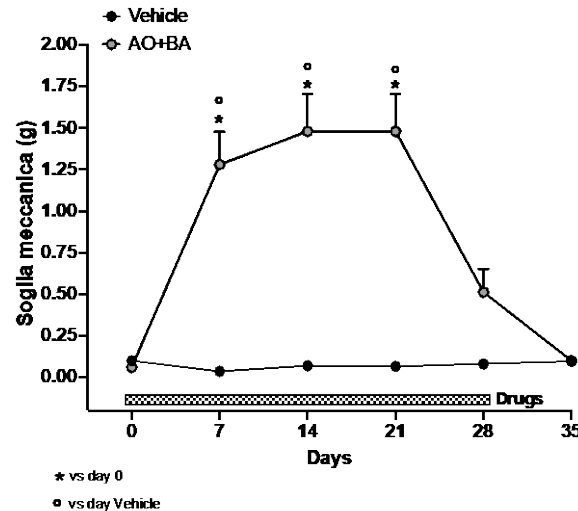
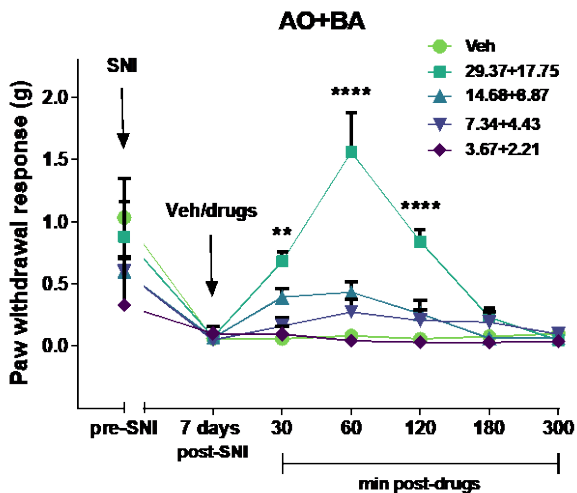
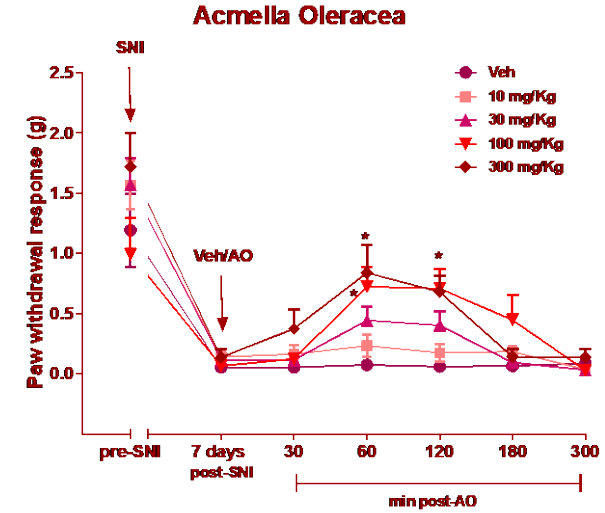
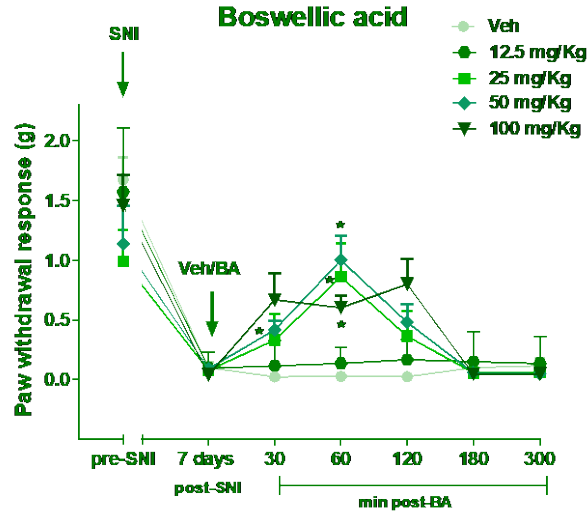
Spilanthol Enhances Sensitivity to Sodium in Mouse Taste Bud Cells

Jiang Xu¹, Brian C. Lewandowski¹, Toshio Miyazawa², Yasutaka Shoji²,
Karen Yee¹ and Bruce P. Bryant¹

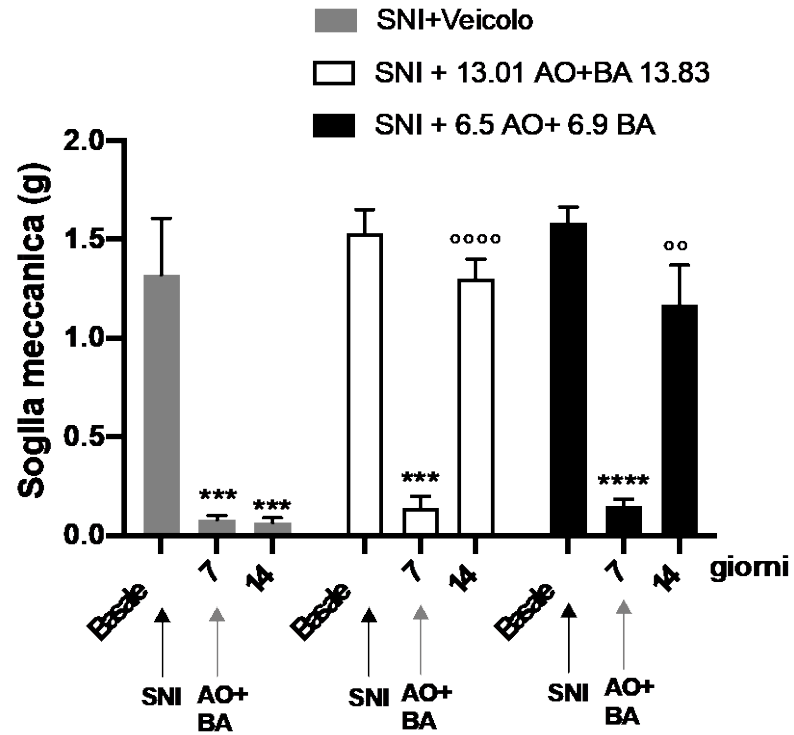
Possible synergistic effect of boswellia serrata and acmella olearacea standardized extracts in the spared nerve injury model of neuropathic pain



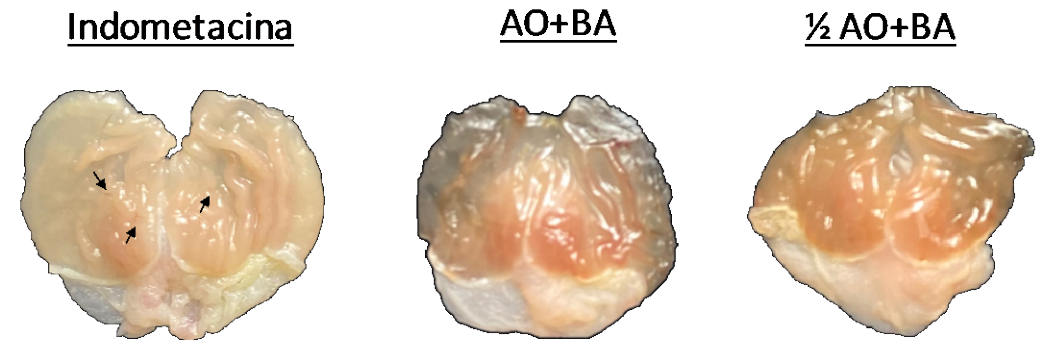
From Cichon et al., 2018



Repeated administration of AO/BS reduced tactile allodynia without affecting the gastric mucosa



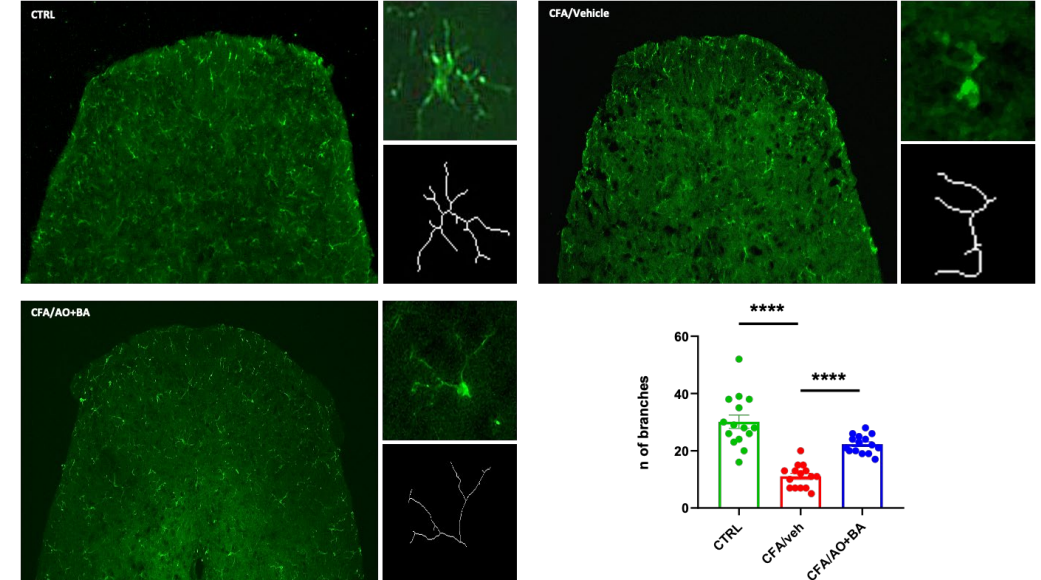
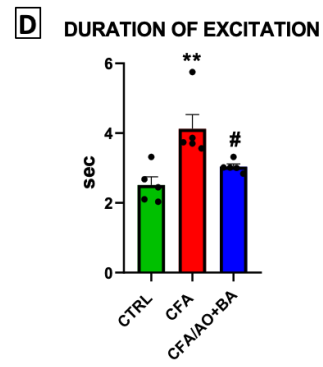
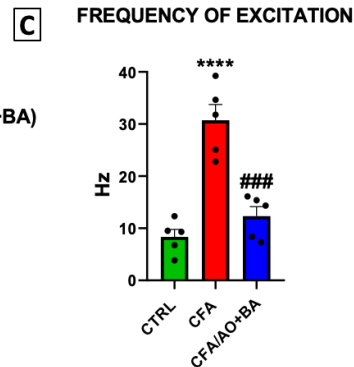
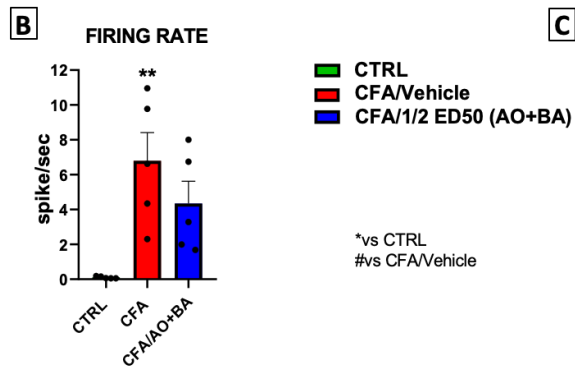
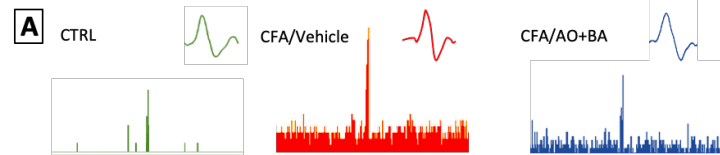
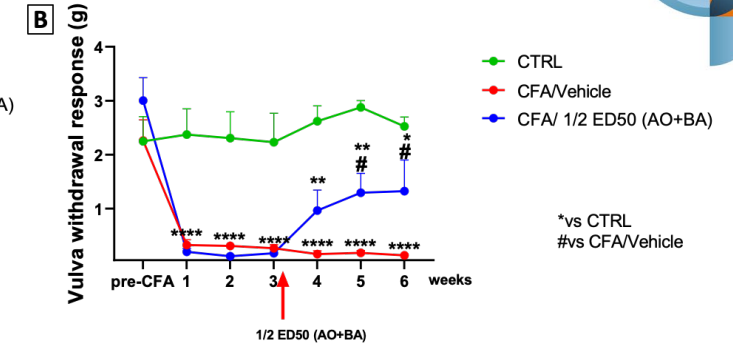
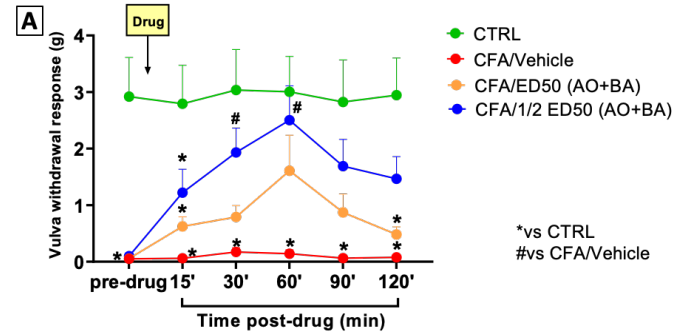
Somministrazioni ripetute di AO+BA non inducono lesioni della mucosa gastrica



Somministrazioni ripetute della combinazione di AO con BA riducono significativamente l'allodinia meccanica nei topi neuropatici, 7 giorni dall'inizio del trattamento



Acmella-boswellia combination in CFA-induced model of vestibulodynia

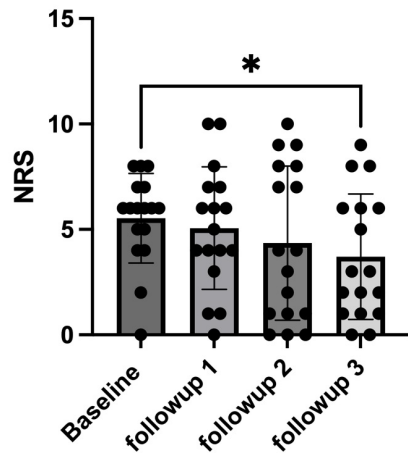




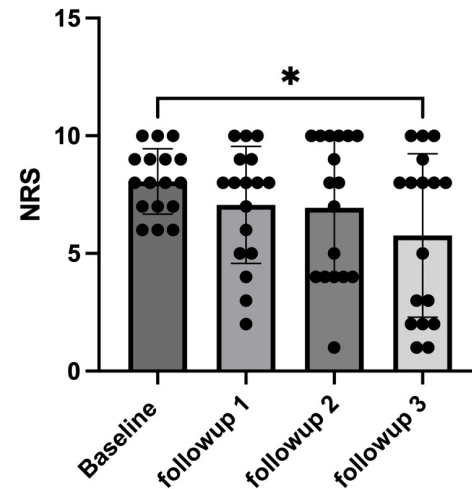
Clinical data:

Combinazione AO/BS come add on therapy in soggetti con dolore cronico con componente neuropatica

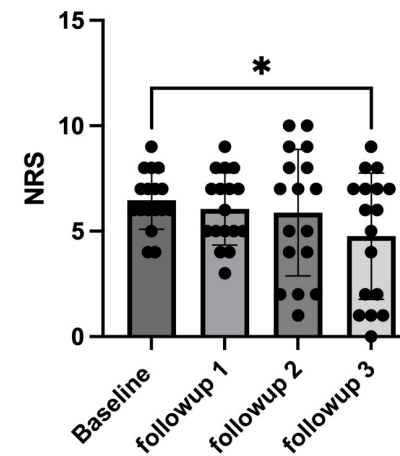
Dolore al momento della visita



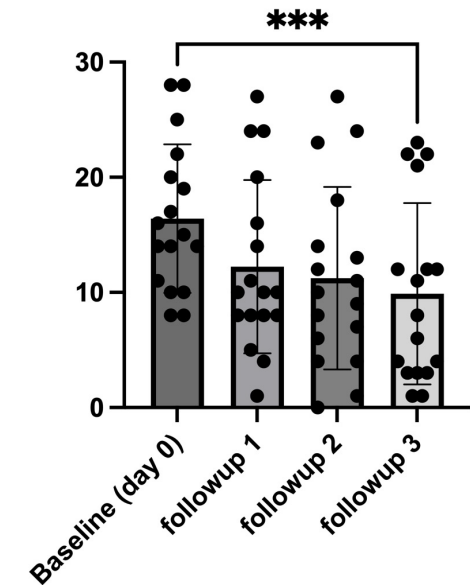
dolore più forte provato
nelle ultime 4 settimane



in media il dolore provato
nelle ultime 4 settimane



PainDETECT





Conclusioni:

La combinazione a dosi fisse sinergiche di estratti di acmella olearcea e boswellia serrata si sta dimostrando un utile adiuvante nella terapia di diverse forme di dolore cronico