Naturopathic Approaches to Pain

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Naturopathic Medicine Overview
Naturopathic medicine

• Naturopathic medicine is a distinct method of primary health care - an art, science, philosophy and practice of diagnosis, treatment, and prevention of illness. Naturopathic physicians seek to restore and maintain optimum health in their patients by emphasizing nature's inherent self-healing process, the *vis medicatrix naturae*. This is accomplished through education and the rational use of natural therapeutics.
Profession

- There are about 5000 licensed naturopathic doctors in North America.
- 16 states and 5 provinces have licensing laws
- Variation in scope of practice
- Many NDs in unlicensed states working on a state law
Licensed jurisdictions www.aanmc.org
Therapies

• Lifestyle counseling
• Clinical nutrition
• Botanical medicine
• Homeopathy
• Acupuncture
• Physical medicine
• Minor surgery, parenteral therapy, other procedures
Naturopathic Principles

• The healing power of nature - *Vis medicatrix naturae*

• First do no harm

• Doctor as teacher

• Treat the cause

• Treat the whole person

• Prevention
The Process of Healing

1. Disturbing factors
2. Disturbance of function
3. Reaction
   - Inflammation, fever
4. Chronic Reaction
5. Degeneration
   - Ulcer, tumor, atrophy, scar, paralysis etc.
6. Discharge

Health
Principles

• The healing power of nature - *Vis medicatrix naturae*

• *Primum non nocere* - First do no harm

• *Docere* - Doctor as teacher

• Treat the cause

• Treat the whole person

• Prevention
Find the Cause: What’s driving the pain?

- Impingement of a nerve
- Metabolic issues
- Nerve damage due to diabetes
- Pain signaling dysfunction
- High systemic levels of inflammation
Doctor as Teacher: The Determinants of Health

- Sleep
- Exercise
- Hydration
- Supportive relationships
- Nutrition
A preliminary study on how hypohydration affects pain perception.

Bear T1,2,3, Philipp M2, Hill S2, Mündel T1.

Author information

Abstract
Chronic pain is a prevalent health issue with one in five people suffering from some form of chronic pain, with loss of productivity and medical costs of chronic pain considerable. However, the treatment of pain can be difficult, as pain perception is complex and can be affected by factors other than tissue damage. This study investigated the effect of hypohydration (mild, voluntary dehydration from ~24 h of limiting fluid intake, mimicking someone drinking less than usual) on a person’s pain perception. Seventeen healthy males (age 27 ± 5 years) visited the laboratory on three occasions, once as a familiarization and then twice again while either euhydrated (urine specific gravity: 1.008 ± 0.005) or hypohydrated (urine specific gravity: 1.024 ± 0.003, and ~1.4 ± 0.9% body mass). Each visit, they performed a cold pressor test, where their feet were placed in cold water (0-3 °C) for a maximum of 4 min. Measures of hydration status, pain sensitivity, pain threshold, and catastrophization were taken. We found that hypohydration predicted increased pain sensitivity (β = 0.43), trait pain catastrophizing, and baseline pain sensitivity (β = 0.37 and 0.47, respectively). These results are consistent with previous research, and suggest that a person’s hydration status may be an important factor in their perception of acute pain.

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Keywords: Analysis/statistical methods; Cold pressor; Hydration; Pain; Sensation/perception; Young adults
Excess vitamin D
> 100 ng/mL (250 nmol/L) with hypercalcemia

Optimal range
40 - 100 ng/mL (100–250 nmol/L)

Insufficiency range
< 20 - 40 ng/mL (50–100 nmol/L)

Deficiency
< 20 ng/mL (50 nmol/L)

Figure 2.1—Interpretation of Serum 25(OH)D Levels
Consider the whole person: Inflammation

• Higher inflammatory states in the body can exacerbate pain
• Dietary imbalances, such as excess Omega 6 fats in proportion to Omega 3 fats, and high insulin states can contribute
• But excess saturated fats might contribute to inflammation too
NF-kappaB enters the nucleus and binds with DNA to activate genes which encode for the increased production of inflammatory mediators.

- IL-6 → CRP
- Cyclooxygenase-2 → Prostaglandins, Thromboxanes
- IL-1 → Collagenase/MMP
- Lipooxygenase → Leukotrienes
- Inducible nitric oxide synthase → Nitric oxide
- TNFα → Adhesion molecules

Increased production of inflammatory mediators - such as cytokines, prostaglandins, leukotrienes - promotes cellular dysfunction and tissue destruction.

Health problems:
- Pain
- Inflammation
- Cardiovascular disease, thrombosis
- Insulin resistance
- Autoimmune and rheumatic disease
- Cancer
- Neurodegeneration

Nutritional Perspectives: Journal of the Council on Nutrition of the American Chiropractic Association
Vol. 28, No. 3
## Supplement Facts

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<thead>
<tr>
<th></th>
<th>Amount per Serving</th>
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<tr>
<td>Calories from Fat</td>
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<td>Total Fat</td>
<td>1 g</td>
<td>2%*</td>
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<tr>
<td>Neptune Krill Oil (NKO®)</td>
<td>1 g (1,000 mg)</td>
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<tr>
<td>Omega-3 Fatty Acids</td>
<td>230 mg</td>
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<tr>
<td>Eicosapentaenoic Acid (EPA)</td>
<td>120 mg</td>
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<td>Docosahexaenoic Acid (DHA)</td>
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<td>Phospholipids</td>
<td>390 mg</td>
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<td>Esterified Astaxanthin</td>
<td>750 mcg</td>
<td>†</td>
</tr>
</tbody>
</table>

* Percent Daily Values are based on 2,000 calorie diet.
† Daily Value not established.

### Other Ingredients:

- Softgel Capsule (gelatin, glycerin, water) and Glycerin. Contains shellfish (krill).
- Not manufactured with yeast, wheat, gluten, soy, milk, egg or fish ingredients. Produced in a GMP facility that processes other ingredients containing these allergens.

**Caution:** For adults only. Consult physician if pregnant/nursing, taking medication (especially anticoagulant or anti-platelet medications), or have a medical condition. Do not use this product if you have a seafood allergy. Keep out of reach of children.

Natural color variation may occur in this product.

Do Not Eat Freshness Packet. Keep in Bottle.

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Store in a cool, dry place after opening. Please Recycle.

Family owned since 1988.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.
Topical capsaicin for pain management: therapeutic potential and mechanisms of action of the new high-concentration capsaicin 8% patch

P. Anand1* and K. Bley2

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2 NeurogesX, Inc., 2215 Bridgepointe Parkway, Suite 200, San Mateo, CA 94404, USA
* Corresponding author. E-mail: p.anand@imperial.ac.uk

Summary. Topical capsaicin formulations are used for pain management. Safety and modest efficacy of low-concentration capsaicin formulations, which require repeated daily self-administration, are supported by meta-analyses of numerous studies. A high-concentration capsaicin 8% patch (QutenzaTM) was recently approved in the EU and USA. A single 60-min application in patients with neuropathic pain produced effective pain relief for up to 12 weeks. Advantages of the high-concentration capsaicin patch include longer duration of effect, patient compliance, and low risk for systemic effects or drug-drug interactions. The mechanism of action of topical capsaicin has been ascribed to depletion of substance P. However, experimental and clinical studies show that depletion of substance P from nociceptors is only a correlate of capsaicin treatment and has little, if any, causative role in pain relief. Rather, topical capsaicin acts in the skin to attenuate cutaneous hypersensitivity and reduce pain by a process best described as ‘defunctionalization’ of nociceptor fibres. Defunctionalization is due to a number of effects that include temporary loss of membrane potential, inability to transport neurotransmitter factors leading to altered phenotype, and reversible retraction of epidermal and dermal nerve fibre terminals. Peripheral neuropathic hyperalgesia is mediated by diverse mechanisms, including altered expression of the capsaicin receptor TRPV1 or other key ion channels in affected or intact adjacent peripheral nociceptive nerve fibres, aberrant re-innervation, and collateral sprouting, all of which are defunctionalized by topical capsaicin. Evidence suggests that the utility of topical capsaicin may extend beyond painful peripheral neuropathies.

Keywords: capsaicin; nerve growth factor; neuropathic pain; nociceptor; TRPV1

Editor's key points

- Topical capsaicin is used in pain management.
- The mechanism of action (MoA) was thought to be by depletion of substance P.
- A more likely MoA is described as ‘defunctionalization’, and involves alteration of several mechanisms involved in pain.
- A new higher concentration (8%) patch shows promise in pain management.

Topical capsaicin formulations are widely used to manage chronic pain, although their mechanism of action remains uncertain. Furthermore, we seek to elucidate
BCQ® combines Boswellia and Curcumin extracts with Quercetin, a potent flavonoid, and Bromelain, a proteolytic enzyme derived from the pineapple plant. This powerful formula provides antioxidants and may help reduce substance P levels in the body. In addition, BCQ supports a healthy inflammatory response, which may aid in reducing minor pain.* The nutrients in this distinctive formula are also known to support gastrointestinal function and help maintain healthy connective tissue.*

Recommended Dosage: 1-3 capsules 2 to 4 times daily, ideally between meals, or as directed by a healthcare practitioner.

**Supplement Facts**

<table>
<thead>
<tr>
<th>Serving Size: 3 capsules</th>
<th>Amount per Serving</th>
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</thead>
<tbody>
<tr>
<td><strong>Boswellia serrata Gum Extract</strong></td>
<td>600mg* (alpha &amp; beta Boswellic acids min. 30% by HPLC)</td>
</tr>
<tr>
<td><strong>Bromelain (high potency)</strong></td>
<td>300mg*</td>
</tr>
<tr>
<td><strong>Curcumin longa Rhizome Extract</strong></td>
<td>600mg* (total Curcuminoids min. 85-90% by HPLC)</td>
</tr>
<tr>
<td><strong>Quercetin dihydrate</strong></td>
<td>300mg* (min. 90% by HPLC)</td>
</tr>
</tbody>
</table>
| * Daily Value not established

Other Ingredients: Gelatin Capsule, Magnesium Silicate, Silicated Cellulose, Silica and Leucine.

If pregnant, consult your physician before taking.
Examples of herbal nervines/anodynes

• Passiflora incarnata – Passionflower
• Hypericum perforatum – St. Johns Wort
• Piscidia erythrina – Jamaican dogwood
• Salix nigra – black willow bark
Passiflora incarnata attenuation of neuropathic allodynia and vulvodynia apropos GABA-ergic and opioidergic antinociceptive and behavioural mechanisms.

Aman U¹, Subhan F², Shahid M³, Akbar S⁴, Ahmad N⁵, Ali G⁶, Fawad K⁷, Sewell RD⁸.

Abstract

BACKGROUND: Passiflora incarnata is widely used as an anxiolytic and sedative due to its putative GABAergic properties. Passiflora incarnata L. methanolic extract (PI-ME) was evaluated in an animal model of streptozotocin-induced diabetic neuropathic allodynia and vulvodynia in rats along with antinociceptive, anxiolytic and sedative activities in mice in order to examine possible underlying mechanisms.

METHODS: PI-ME was tested preliminary for qualitative phytochemical analysis and then quantitatively by proximate and GC-MS analysis. The antinociceptive property was evaluated using the abdominal constriction assay and hot plate test. The anxiolytic activity was performed in a stair case model and sedative activity in an open field test. The antagonistic activities were evaluated using naloxone and/or pentylenetetrazole (PTZ). PI-ME was evaluated for prospective anti-allodynic and anti-vulvodynic properties in a rat model of streptozotocin induced neuropathic pain using the static and dynamic testing paradigms of mechanical allodynia and vulvodynia.

RESULTS: GC-MS analysis revealed that PI-ME contained predominant quantities of oleamide (9-octadecenamide), palmitic acid (hexadecanoic acid) and 3-hydroxy-dodecanoic acid, among other active constituents. In the abdominal constriction assay and hot plate test, PI-ME produced dose dependent, naloxone and pentylenetetrazole reversible antinociception suggesting an involvement of opioidergic and GABAergic mechanisms. In the stair case test, PI-ME at 200 mg/kg increased the number of steps climbed while at 600 mg/kg a significant decrease was observed. The rearing incidence was diminished by PI-ME at all tested doses and in the open field test, PI-ME decreased locomotor activity to an extent that was analogous to diazepam. The effects of PI-ME were antagonized by PTZ in both the staircase and open field tests implicating GABAergic mechanisms in its anxiolytic and sedative activities. In the streptozotocin-induced neuropathic nociceptive model, PI-ME (200 and 300 mg/kg) exhibited static and dynamic anti-allodynic effects exemplified by an increase in paw withdrawal threshold and paw withdrawal latency. PI-ME relieved only the dynamic component of vulvodynia by increasing flinching response latency.

CONCLUSIONS: These findings suggest that Passiflora incarnata might be useful for treating neuropathic pain. The antinociceptive and behavioural findings inferring that its activity may stem from underlying opioidergic and GABAergic mechanisms though a potential oleamide-sourced cannabinimimetic involvement is also discussed.


[PubMed - indexed for MEDLINE]   Free PMC Article
Herbal anodynes

• Can be useful but can interact with drugs:
• Increase or decrease drug level in the body
• Add to the effect of the drug in a way that is too much for the patient (too much sedation)
• Not automatically out of the question – but doctor must look at metabolic pathway of drug and herb and what the literature says about reports of interactions
Natural pharmacology

- Natural substances can have powerful effects on pain
- In the naturopathic model we would address causes and determinants of health first
- Sometimes these substances work synergistically
- They are not always a replacement for prescription medicines – but interactions must be anticipated and avoided
Peripheral neuropathy in obstetrics: efficacy and safety of α-lipoic acid supplementation.

Costantino M¹, Guaraldi C, Costantino D, De Grazia S, Unfer V.

Abstract

OBJECTIVE: Neuropathic pain during pregnancy is a common condition due to the physical changes and compression around pregnancy and childbirth that make pregnant women more prone to develop several medical conditions such as carpal tunnel syndrome, sciatica, meralgia paraesthetica and other nerve entrapment syndromes. Most of the treatments usually performed to counteract neuropathic pain are contraindicated in pregnancy so that, the management of these highly invalidating conditions remains an issue in the clinical practice. We aimed to review the efficacy and safety of alpha lipoic acid supplementation in the treatment of neuropathic pain.

DISCUSSION: Lipoic acid is a co-factor essential in the regulation of mitochondrial energy. It has been demonstrated that lipoic acid supplementation is involved in several biochemical processes and actions, exerting important antioxidant and anti-inflammatory activity and significantly improving pain and paraesthesia in patients with sciatica, carpal tunnel syndrome and diabetic neuropathy.

CONCLUSIONS: Efficacy of lipoic acid is combined with a high safety profile, making this molecule a novel candidate for the management of several diseases. Data reported so far are promising and dietary supplementation with lipoic acid seems a useful tool to contrast neuropathic pain during pregnancy.

PMID: 25317815
Herb-drug interactions with St John's wort (Hypericum perforatum): an update on clinical observations.

Borrelli F¹, Izzo AA

Abstract
St John's wort (SJW) extracts, prepared from the aerial parts of Hypericum perforatum, contain numerous pharmacologically active ingredients, including naphthodianthrones (e.g., hypericin and its derivatives), phloroglucinols derivatives (e.g., hyperforin, which inhibits the reuptake of a number of neurotransmitters, including serotonin), and flavonoids. Such extracts are widely used for the treatment of mild-to-moderate depression. As a monotherapy, SJW has an encouraging safety profile. However, relevant and, in some cases, life-threatening interactions have been reported, particularly with drugs which are substrate of cytochrome P450 and/or P-glycoprotein. Well-documented SJW interactions include (1) reduced blood cyclosporin concentration, as suggested by multiple case reports as well as by clinical trials, (2) serotonin syndrome or lethargy when SJW was given with serotonin reuptake inhibitors, (3) unwanted pregnancies in women while using oral contraceptives and SJW, and (4) reduced plasma drug concentration of antiretroviral (e.g., indinavir, nevirapine) and anticancer (i.e., irinotecan, imatinib) drugs. Hyperforin, which is believed to contribute to the antidepressant action of St John's wort, is also strongly suspected to be responsible of most of the described interactions.


Author information

Abstract

BACKGROUND: Vitamin C is an immune-relevant micronutrient, which is depleted in viral infections and this deficiency seems to play a critical role in the pathogenesis of herpes infections and in the development of postherpetic neuralgia. The objective of this observational multicenter study was to evaluate the utilization, safety and efficacy of intravenously administrated vitamin C in patients with shingles.

MATERIAL/METHODS: Between April 2009 and December 2010 16 general practitioners recorded data of 67 participants with symptomatic herpes zoster who received vitamin C intravenously (Pascorbin® 7.5 g/50 ml) for approximately 2 weeks in addition to standard treatment. The assessment of pain (VAS) and the dermatologic symptoms of shingles such as hemorrhagic lesions and the number of efflorescences were investigated in a follow-up observation phase of up to 12 weeks.

RESULTS: Mean declines of pain scores (VAS), number of affected dermatomes and efflorescences, and the presence of hemorrhagic vesicles between the baseline and follow-up assessments at 2 and 12 weeks were statistically significant. Overall, 6.4% of the participants experienced post-herpetic neuralgia. Common complaints such as general fatigue and impaired concentration also improved during the study. The effects and the tolerability of the treatment were evaluated positively by the physicians. The risk of developing PHN was reduced.

CONCLUSIONS: The data presented here provide evidence that concomitant use of intravenously administered ascorbic acid may have beneficial effects on herpes zoster-associated pain, dermatologic findings and accompanying common complaints. To confirm our findings, randomized, placebo-controlled clinical studies are necessary.
Endocannabinoid system and pain: an introduction.
Burston JJ1, Woodhams SG2.

Abstract
The endocannabinoid (EC) system consists of two main receptors: cannabinoid type 1 receptor cannabinoid receptors are found in both the central nervous system (CNS) and periphery, whereas the cannabinoid type 2 receptor cannabinoid receptor is found principally in the immune system and to a lesser extent in the CNS. The EC family consists of two classes of well characterised ligands; the N-acyl ethanolamines, such as N-arachidonoyl ethanolamide or anandamide (AEA), and the monoacylglycerols, such as 2-arachidonoyl glycerol. The various synthetic and catabolic pathways for these enzymes have been (with the exception of AEA synthesis) elucidated. To date, much work has examined the role of EC in nociceptive processing and the potential of targeting the EC system to produce analgesia. Cannabinoid receptors and ligands are found at almost every level of the pain pathway from peripheral sites, such as peripheral nerves and immune cells, to central integration sites such as the spinal cord, and higher brain regions such as the periaqueductal grey and the rostral ventrolateral medulla associated with descending control of pain. EC have been shown to induce analgesia in preclinical models of acute nociception and chronic pain states. The purpose of this review is to critically evaluate the evidence for the role of EC in the pain pathway and the therapeutic potential of EC to produce analgesia. We also review the present clinical work conducted with EC, and examine whether targeting the EC system might offer a novel target for analgesics, and also potentially disease-modifying interventions for pathophysiological pain states.
Polyphenols

New Pharmacological Approaches Using Polyphenols on the Physiopathology of Neuropathic Pain

Pere Boadas-Vaello¹,*, José Miguel Vela² and Enrique Verdú¹

¹Group of Clinical Anatomy, Embryology, and Neuroscience (NEOMA); Department of Medical Sciences, University of Girona, E-17071 Girona, Spain; ²ESTEVE, Drug Discovery and Preclinical Development. Parc Científic de Barcelona, E-08028 Barcelona, Spain

Abstract: Polyphenols constitute a group of a paramount importance within the natural products in the plant kingdom, with an approximate amount of 8000 phenolic structures currently known. Fruits, vegetables, whole grains and several other foods and beverages (as tea, chocolate and wine, for instance) are rich and important sources of polyphenols. The scientific literature provides pre-clinical experimental evidence on the antinociceptive effects of polyphenolic compounds, found in plant extracts, in animal models of neuropathic pain. But not only neuropathic pain is attenuated: in fact, nociceptive pain, caused by stimulation of nerve fibers (either somatic or visceral) responding only to stimuli approaching or exceeding harmful intensity thresholds (nociceptors), and also inflammatory pain, which is associated with tissue damage and infiltration of immune cells, are both reduced and alleviated by polyphenols. In the present work, the antinociceptive effects of polyphenols are reviewed.
Table 1. Anti-nociceptive effects of polyphenols (for details see text).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Chemical Structure</th>
<th>Polyphenol Group</th>
<th>Proposed Mechanism of Action</th>
<th>Dose and Route of Administration</th>
<th>Pharmacological Effects Shown in Animal Models</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quercetin</td>
<td><img src="image" alt="Quercetin Structure" /></td>
<td>Flavonol</td>
<td>Involving interaction with L-arginine-NO, serotonin, and GABAergic systems. Scavenges reactive oxygen and nitrogen species. Inhibits phosphodiesterases. Exerts inhibitory effects on prominent pro-inflammatory signaling pathways (STAT1, NF-kappaB, MAPK).</td>
<td>STZ: 100 mg/kg (p.o.) [61]; chemotherapy: 25-100 mg/kg (i.p.) [64]; formalin/carrageenan: 10-100 mg/kg (i.p.) [65].</td>
<td>↓ Hyperalgesia and/or allodynia after: (i) STZ-induced diabetic neuropathic pain, (ii) chemotherapy-induced neuropathic pain, (iii) formalin/carrageenan-induced pain.</td>
</tr>
<tr>
<td>Baicalin</td>
<td><img src="image" alt="Baicalin Structure" /></td>
<td>Flavone</td>
<td>Inhibition of TNF-α, NO, PGE2 and ROS overexpression. Down-regulation of TRPV1 mRNA and protein expression.</td>
<td>SNL: 2 µg/µL (i.t.) [74]; formalin/carrageenan: 150 mg/kg (p.o) [75], 10-100 mg/kg (i.p.) [77].</td>
<td>↓ Hyperalgesia and/or allodynia after: (i) spinal nerve ligation, (ii) formalin/carrageenan-induced pain.</td>
</tr>
<tr>
<td>Puerarin</td>
<td>Isoflavonoid</td>
<td>Reduced expression of pro-inflammatory cytokines (IL-6, IL-1β, TNF-α). Reduced expression of purinergic receptors (P2X3, P2X2a, P2X3, P2X5).</td>
<td>CCI and STZ: 4-10 mM (i.t. [80]; CCI: 100 mg/kg (i.p.) [81].</td>
<td>↓ Hyperalgesia and/or allodynia after: (i) chronic constriction injury (CCI), (ii) STZ-induced diabetic neuropathic pain.</td>
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<tr>
<td>Myricitrin</td>
<td>Flavonoid</td>
<td>Inhibition of the activation of nociceptors via inhibition of PKC pathways. Inhibition of pro-inflammatory mediators (TNF-α, NO). Modulation of ion channels and p38MAPK.</td>
<td>PSNL and CFA: 30 mg/kg (i.p.) [87]; acetic acid-induced visceral pain: 0.01-10 mg/kg (i.p.) [88]; intraplantar injection of algogens: 10-100 mg/kg (i.p.) [89].</td>
<td>↓ Mechanical allodynia after: (i) partial ligation of the sciatic nerve (PSNL), (ii) inflammatory pain induced by CFA, (iii) acetic acid-induced visceral pain, (iv) intraplantar injection of a variety of chemical algogens, (v) formalin/carrageenan-induced pain.</td>
<td></td>
</tr>
<tr>
<td>Epigallocatechin-3-gallate</td>
<td>Flavanol</td>
<td>Reduction of myeloperoxidase, iNOS and COX-2 activities. Reduction of pro-inflammatory cytokines (TNF-α, IL-1β). Modulation of p38MAPK, JNK, NF-kappaB pathways.</td>
<td>SCI: 50 mg/kg (i.p.) [93], 10-20 mg/kg (i.v.) [95], 20 mg/kg (i.v.) [96]; CCI: 1 mg/kg (i.t.) [42]; STZ: 2g/L in water drink [97]; CFA: 60 and 120 mg/kg (p.o) [104]; post-traumatic: 25 mg/kg (i.p.) [105].</td>
<td>↓ Hyperalgesia and/or allodynia after: (i) spinal cord injury (SCI), (ii) chronic constriction injury (CCI), (iii) STZ-induced diabetic neuropathic pain, (iv) alcoholic neuropathy, (v) inflammatory pain induced by CFA, (vi) mouse model of post-traumatic osteoarthritis.</td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Chemical Structure</td>
<td>Polyphenol Group</td>
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<tr>
<td>Curcumin</td>
<td><img src="image1.png" alt="Curcumin Structure" /></td>
<td>Phenolic acid</td>
<td>Modulation of ERK, STAT3, JNK, NF-kappaB pathways. Reduced expression of BDNF, COX2, 11-β-HSD1, CX3CR1, and pro-inflammatory cytokines (TNF-α, IL-1β, IL-6).</td>
<td>CCI: 50 mg/kg (p.o.) [50], 12.5-50 mg/kg (i.p.) [53]; SNL: 200 μg (i.t.) [115]; STZ: 60 mg/kg (p.o.) [114], 50 mg/kg (i.p.) [117]; formalin/carrageenan: 3-400 mg/kg (p.o.) [119]; CFA: 100 mg/kg (i.p.) [122], 10-30 mg/kg (i.p.) [123]; postoperative pain: 50 mg/kg (i.p.) [124].</td>
<td>↓ Hyperalgesia and/or allodynia after: (i) chronic constriction injury (CCI), (ii) spinal nerve ligation (SNL), (iii) STZ-induced diabetic neuropathic pain, (iv) formalin/carrageenan-induced pain, (v) inflammatory pain induced by CFA, (vi) mice models of postoperative pain.</td>
</tr>
<tr>
<td>Resveratrol</td>
<td><img src="image2.png" alt="Resveratrol Structure" /></td>
<td>Stilbene</td>
<td>Reduction of NOS and COX2 activity and NO production. Inhibition of AMPK and production of IL-6. Down-regulation of NMDA (NR1, NR2B) expression.</td>
<td>CCI: 30 mg/kg (p.o.) [133]; SNL: 30 μg/μL (i.t.) [131]; STZ: 10-20 mg/kg (i.p.) [129], 5-20 mg/kg (p.o.) [130]; formalin/carrageenan: 0.4-50 mg/kg (i.p.) [138].</td>
<td>↓ Hyperalgesia and/or allodynia after: (i) chronic constriction injury (CCI), (ii) spinal nerve ligation (SNL), (iii) STZ-induced diabetic neuropathic pain, (iv) formalin/carrageenan-induced pain.</td>
</tr>
</tbody>
</table>
Individualization

- Everyone is different, and while statistically probabilities about what is likely to work are very, very valuable, there can be very different needs among people with the same condition.
Molecular targets of dietary agents for prevention and therapy of cancer.

Communication is important

- Practitioners should share information not just work in parallel
- This helps avoid interactions
- It can also be good for the patient – and remove tension from all of their health care
Over a third of patients in this survey who used CAM and had a primary care physician did not disclose their use of CAM therapy.
Thank you and good luck

• Fraser Smith, MATD, ND
• fsmith@nuhs.edu