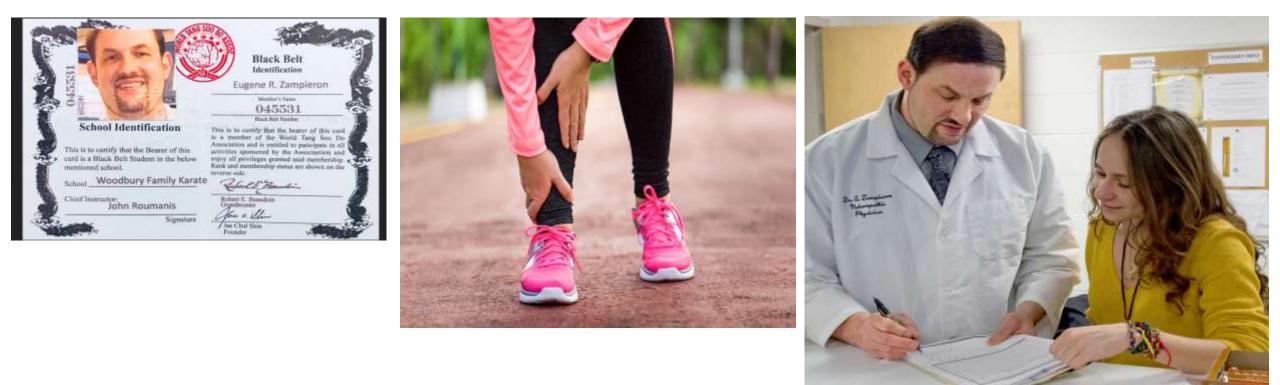
Pain Management Secrets of an Aging Martial Artist: Botanical Medicine and Protocols for Injury, Pain and Inflammation



Dr. Eugene R Zampieron, ND, MH, RH(AHG)

Naturopathic physician \* Herbalist \* Author \* 'Founding father' and Senior faculty member, University of Bridgeport College of Naturopathic medicine

## Table of contents of lecture

- Part one
  - PAIN statistics pain physiology
  - Nociception
- Part two
  - Pillars of TCM sports medicine
    - Don't use ice
    - Internal botanicals
    - External botanicals
    - Manual medicine

#### • Part three

- Chinese concepts of pain and
- Materia medica of 11 top TCM herbs
- Liniments, plasters, and poultices(Gaos) to move blocked Qi, stagnant lymphatic fluid, stagnant blood. These formulas are covered in your handouts due to time constraints
- Cools injured area without ice
- Part four
  - Western, Eclectic and Rainforest herbs in the fight against pain

#### NOTE:

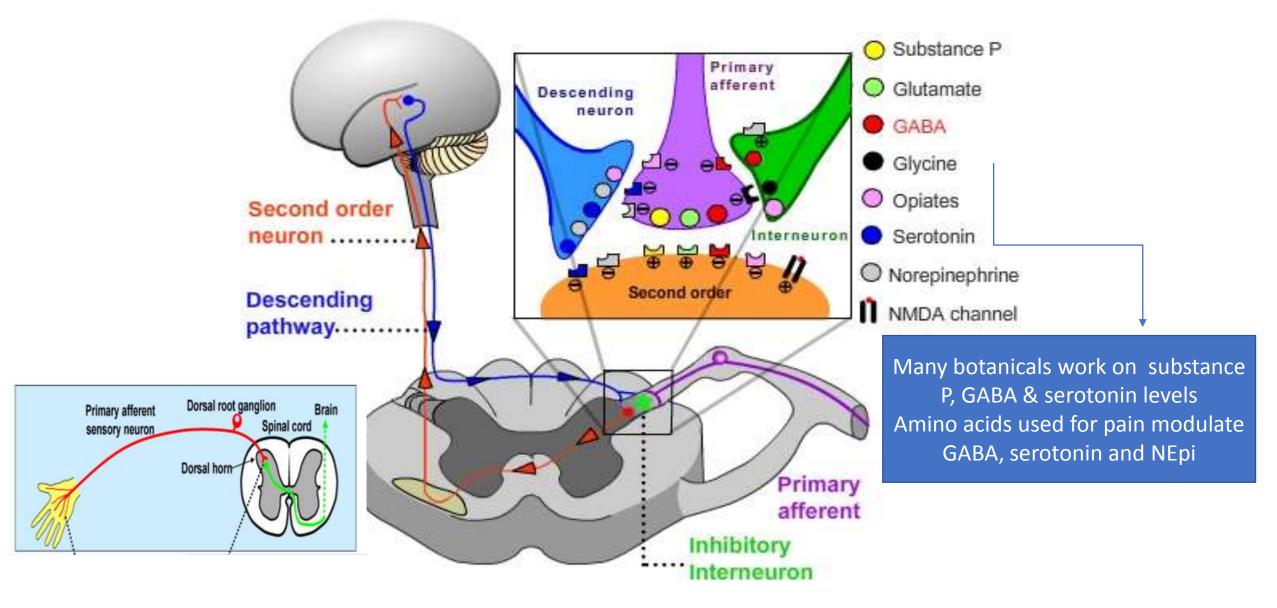
Handouts (non CME) contain how to make formulas and CASES on how to treat common musculoskeletal injury and pain syndromes (many of my own!)

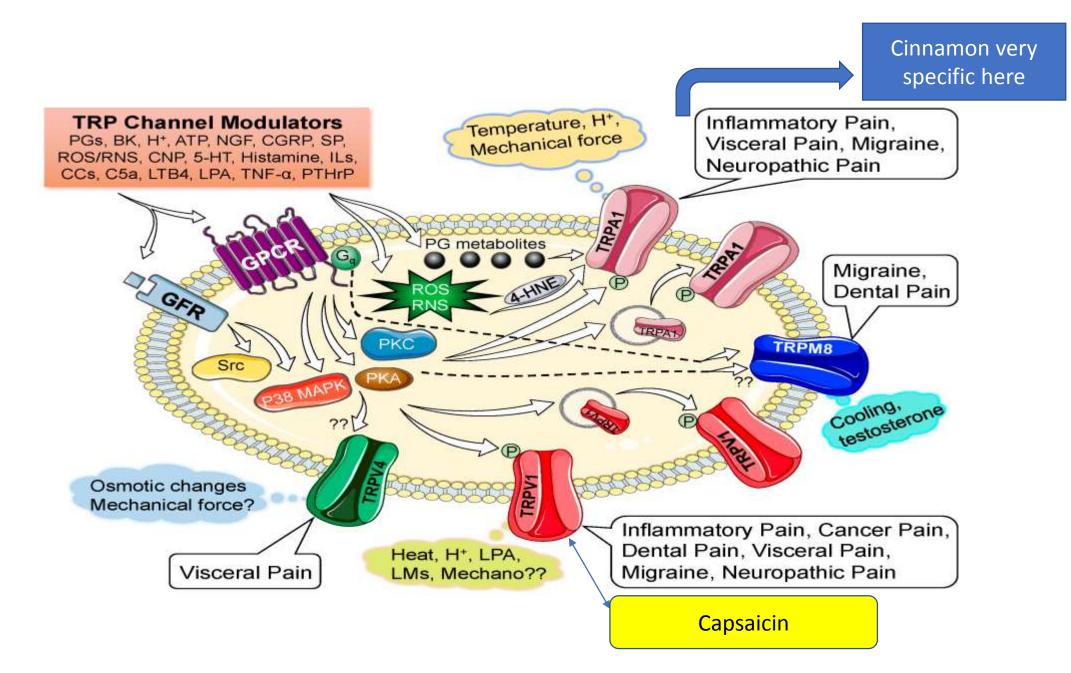
### National Health Interview Survey (NHIS) in 2012

- Musculoskeletal medical conditions were reported by 126.6 million adults in US - more than one in two persons age 18 and over, and nearly three out of four age 65 and over
- Rate of chronic musculoskeletal conditions found in adult population is 76% greater than that of chronic circulatory conditions (coronary and heart conditions)
- Twice that of all chronic respiratory conditions
- Age-adjusted basis, musculoskeletal conditions are reported by 54 persons per every 100 in population

REF; United States Bone and Joint Initiative (USBJI)- part of the Global Alliance for Musculoskeletal Health <u>www.usbji.org</u>

### **Nociceptive Modulation**





REF for image: https://res.mdpi.com/pharmaceuticals/pharmaceuticals-09-00072/article\_deploy/html/images/pharmaceuticals-09-00072-g001.png

Nociceptive pain pathway and *Pain interruption* occurs in 5 phases: Like drugs, *herbs can work on all levels* 

### Nociceptive pain occurs in 5 phases:

- 1) Transduction
- 2) Conduction
- 3) Transmission
- 4) Modulation
- 5) Perception

1) **Tranduction**  $\rightarrow$  TRP channel modulators receive info from external sources  $\rightarrow$  peripheral terminals of nociceptive C fibers and A-delta (A $\delta$ ) fibers are depolarized by noxious mechanical, thermal, or chemical energy.

Neurotransmitters, substance P, ATP, prostaglandins, bradykinin, serotonin, histamine, and hydrogen ions (acid pH), etc. play a role in this stage of transduction, as do the transient **receptor** potential cation channel subfamily V member 1 (**TrpV1**) and others

## Nociceptive pain and pain interruption 5 phases:

#### 2) Conduction $\rightarrow$

- action potential travels thru
  - *a delta fibers* → Fast (100 microseconds) which will elicit sharp prickling electric acute pain,
  - These use aspartate, glutamate, Substance P and calcitonin gene related product..
  - Slow C fibers→ slow seconds to minutes elicit burning aching throbbing nauseated pain
  - This uses substance P

The dorsal horn accepts the signal is divided into distinct gray matter laminae.

#### 3) Transmission $\rightarrow$

- The dorsal horn accepts the signal is divided into distinct gray matter laminae
- presynaptic terminals of A delta and C fibers to release a variety of pronociceptive substances into the synaptic cleft
- Activation of postsynaptic receptors like NMDA/glutamate results in an influx of ions that depolarize second order neurons and interneurons. Magnesium usually block these, as does GABA
- Signal info is carried to various areas of the brain

## Nociceptive pain and pain interruption 5 phases

- 4) Modulation → Peripheral & Central acting
- processes that inhibit(anesthetic) or suppress transduction, conduction or transmission
- Modulation is divided into peripheral and central modulation
- Drugs, herbs, amino acids, acupuncture, physical medicine, hydrotherapy and other interventions work at these levels

- Peripheral  $\rightarrow$ 
  - Dampen the sensitization of nociceptor terminals
  - inhibiting depolarization and repolarization of the axonal membrane
  - eugenol (see ref next slide)rich herbs work hereby inhibiting voltage gate sodium channels
  - stimulate the fast Aβ fibers in the area of injury with TENS, electro acupuncture or intense alternating hydrotherapy which dampen pain

#### Molecular mechanism for local anesthetic action of eugenol in the rat trigeminal system.

Park CK<sup>1</sup>, Kim K, Jung SJ, Kim MJ, Ahn DK, Hong SD, Kim JS, Oh SB.

Author information

#### Abstract

Eugenol in allspice and cloves may work in humans like this

anares several

Eugenol is widely used in dentistry as a local analgesic agent, because of its ability to allay to pharmacological actions with local anesthetics which include inhibition of voltage-gated sort nannel (VGSC) and activation of transient receptor potential vanilloid subtype 1 (TRPV1). In the present study, we investigated the mects of eugenol on pain behaviors in orofacial area, and as an attempt to elucidate its mechanism we characterized inhibitory effects of eugenol on VGSCs in trigeminal ganglion (TG) neurons. TG neurons were classified into four types on the basis of their neurochemical and electrophysiological properties such as cell size, shapes of action potential (AP), isolectin-B(4) (IB(4)) binding, and were analyzed for the association of their distinctive electrophysiological properties and mRNA expression of Na(v)1.8 and TRPV1 by using single-cell RT-PCR following whole-cell recordings. Subcutaneous injection of eugenol reduced the thermal nociception and capsaicin-induced thermal hyperalgesia in a dose-dependent manner. Eugenol also diminished digastric electromyogram evoked by noxious electrical stimulation to anterior tooth pulp, which was attributable to the blockade of AP conduction on inferior alveolar nerve. At cellular level, eugenol reversibly inhibited APs and VGSCs in IB(4)+/TRPV1+/Na(v)1.8+ nociceptive TG neurons (Type I-Type III) and IB(4)-/TRPV1-/Na(v)1.8- nociceptive TG neurons (Type IV). Both TTX-resistant I(Na) in Type I-Type III neurons and TTX-sensitive I(Na) in Type IV neurons were sensitive to eugenol. Taken together, these results suggest that eugenol may serve as local anesthetics for other pathological pain conditions in addition to its wide use in dental clinic.

## Modulation: central acting

- Central modulation
  - Opioids → able to activate the endorphin receptors: Mu, Kappa and Delta. Mu receptors are responsible for most of the analgesic effect of opioids and are present on neurons in the spinal cord, brainstem and midbrain.
  - Blocks the calcium channels and inhibits Glutamate in the dorsal horn
  - Augments the release of catecholamines and serotonergic from the descending terminal into the dorsal horn space
  - This is why in my patients, taking certain amino acids like 5HTP and D-Phenylalanine and DL Phenylalanine has been shown to help modulate chronic pain and restore the bodies natural opioids depleted in chronic pain
  - {<u>Acupunct Electrother Res.</u> 1982;7(2-3):157-72.}

- Central modulation
  - We can also modulate our own endogenous opioids such as enkephalins, endorphins dymorphins
  - Enkephalins are also strong Mu agonists, which augments catecholamine release
  - Anandamide, the agent of bliss, is involved in stress response and central pain modulation and is *part of the endogenous cannabinoid system*
  - Cannabinoids release endogenous opioids and can help with pain
  - Many psychotropic drugs, which work on neurotransmitters have been used in pain management
    - <u>https://onlinelibrary.wiley.com/doi/epdf/1</u> 0.1111/j.1365-2044.1978.tb08391.x

## Dopamine precursor depletion influences pain affect rather than pain sensation

#### Author information

#### Abstract

Pain is a multidimensional experience, which includes sensory, cognitive, dopaminergic neurotransmission plays an important role in human pain per aspects of pain perception remain to be elucidated. To address this questi This may be how Phenylalanine and Tyrosine work, as "pain distancers", like the herb ghost pipe we will see later

ion

in 22 healthy human subjects using Acute Phenylalanine and Tyrosine Depletion (APTD). During APTD and a control condition we applied brief painful laser stimuli to the hand, assessed different aspects of pain perception, and recorded electroencephalographic responses. APTD-induced decreases of cerebral dopaminergic activity did not influence sensory aspects of pain perception. In contrast, APTD yielded increases of pain unpleasantness. The increases of unpleasantness ratings positively correlated with effectiveness of APTD. Our finding of an influence of dopaminergic neurotransmission on affective but not sensory aspects of phasic pain suggests that analgesic effects of dopamine might be mediated by indirect effects on pain affect rather than by direct effects on ascending nociceptive signals. These findings contribute to our understanding of the complex relationship between dopamine and pain perception, which may play a role in various clinical pain states.

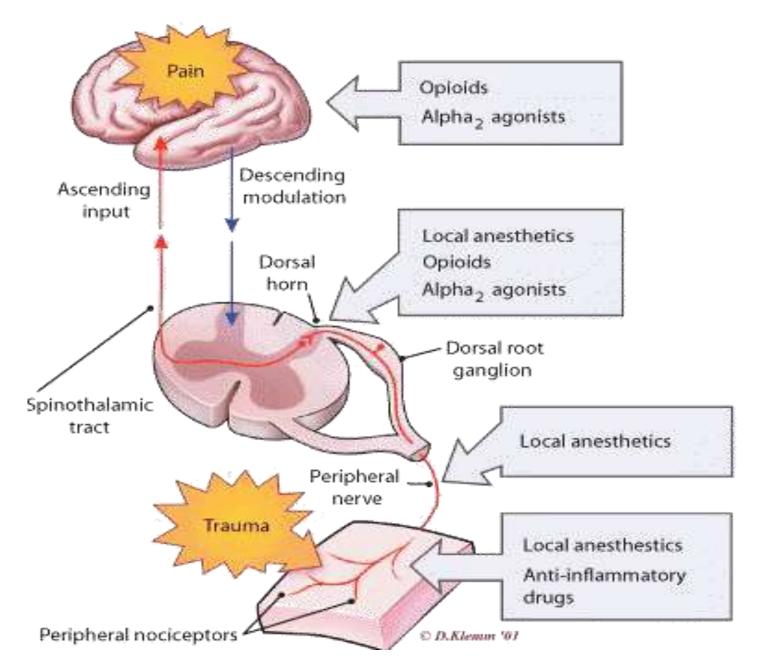
PMID: 24760082 PMCID: PMC3997524 DOI: 10.1371/journal.pone.0096167

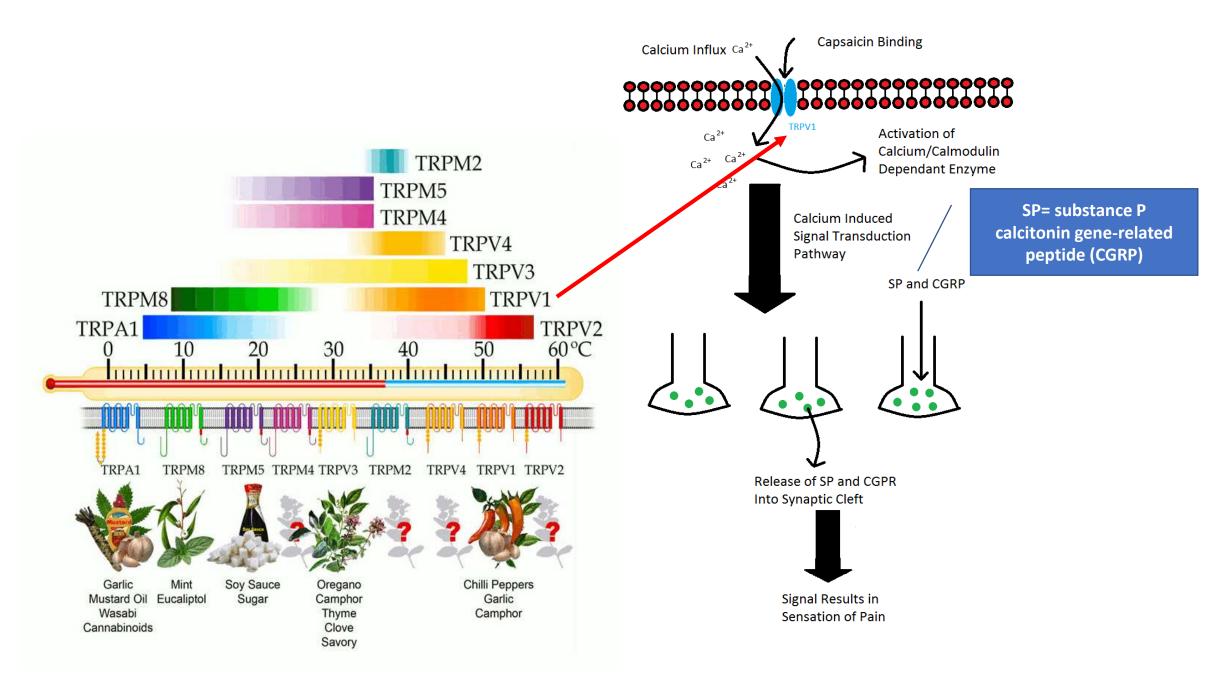
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#### **Providing Postoperative Pain Relief**

## Where pain drugs act in the pathway





### How TCM doc's see PAIN

	Syndrome	Characteristics	Sample Herbs
	Draft (Wind) pain	External: muscles, joints, or ligaments are painful Internal: migrating pain, often affecting the limbs	External: chiang-huo, tu-huo, cinnamon twig, siler, clematis, chin- chiu, angelica Internal: gastrodia, uncaria, haliotis, silkworm, scorpion, centipede, earthworm
	Cold pain	External: Cold evil congested and stagnated in the meridian vessels Internal: yang deficiency with internal generation of cold. Fixed location and spasmodic pain.	External: aconite, ma-huang, asarum Internal: aconite, cinnamon bark, dry ginger, evodia, long pepper, galangal, fennel
	Wet pain	Rain evil and dew wetness obstruct the functioning of qi. Wetness is characteristically sticky, greasy, and stagnant, and the pain that arises is heavy, binding, and confining (as if wrapped tightly by a bandage), and aggravated by a rainy, wet environment.	atractylodes, stephania, acanthopanax, chaenomeles, coix, akebia, lysimachia (desmodium)
	Heat pain	Heat toxin that exhausts and scorches ying and causes entanglement and stagnation of ying manifests as heat pain. Typically manifests with redness and swelling.	lonicera, forsythia, taraxacum, viola, subprostrata, paris, prunella, isatis root, sophora.
	Qi pain	Caused by emotional factors, which lead to dysfunction of the qi of the viscera. Its feature is pain with distention, usually in the chest and abdomen and aggravated by emotional disturbance.	saussurea, cyperus, lindera, bupleurum, blue citrus, citrus, aquilaria, acronychia, litchi seed, citrus seed, melia
	Blood stasis pain	Long-term stagnation with disturbance of blood vessels (e.g., chronic inflammation) or traumatic injury caused blood stasis pain. Its distinguishing feature is pin-prick (or stabbing) pain with a fixed location.	tang-kuei, cnidium, red peony, corydalis, salvia, leonurus, san-chi, myrrh, frankincense, trogopterus, persica, carthamus, sparganium, zedoaria.
	Worm pain	Intermittent pain, generally around the umbilicus, caused by intestinal parasites	quisqualis, areca seed, torreya, omphalia
	Food pain	Overindulgence in food and erratic eating and drinking habits cause food pain. It is intensified by applying pressure over the abdomen.	crataegus, malt, raphanus, gallus
	Phlegm-fluid pain	Phlegm-fluid stagnation and retention produce fluid pain, which affects the upward and downward movement of qi with symptoms of chest and subcostal pain, usually related to difficulty in breathing and shortness of breath.	typhonium, sinapis, lepidium
	Deficiency pain	Associated with the functional degeneration of the viscera and depletion and damage of the qi and blood. Typically manifests as persistent pain. Pain may be associated with qi deficiency (fatigue), blood deficiency (palpitations), yin deficiency (restless heat of the palms and feet), or yang deficiency (cold extremities).	Qi: astragalus, codonopsis or ginseng, atractylodes, licorice Blood: millettia, achyranthes, peony Yang: epimedium, morinda, eucommia, cibotium, dipsacus, drynaria Yin: turtle shell, loranthus, ligustrum

## **Pillars of Chinese sports medicine**

- Knowledge passed down through millennia from karate, martial arts and kung fu schools:
- Don't use ice!!!
  - Old saying...lce is for dead people
  - {Use herbal ice}
- Topical herbal therapy
- Internal herbal therapy
- Manual and manipulative therapy
- Cupping
- Prevention

## TCM - ICE

Problems with ICE therapy according to TCM:

- drives damp and cold into the site
- congeals and solidifies the traumatic wastes
- creates a 'superglue'
- fascia and muscle fibers stick to injured area
- ligament and tendons develop scar tissue
- impedes the flow of blood and qi to the area

## **Pillars of TCM sports medicine**

- Moxibustion
- Cupping
- Chinese massage
- \* Bone setting (like manipulation)
- Bleeding
- Acupressure
- Acupuncture

- External therapy
  - **Cooling Liniments** → High ETOH, apply with friction; used for acute injuries apply with rule of 3-9
  - Warming Liniments→ used for end stage acute and chronic injuries; strong qi and blood movers
  - GAOS→ Plasters; herbs made into paste and adhered on a thick sticky cloth membrane; purchase in a roll
  - Poultices→ Ground herbs mixed in viscous medium (eggs whites) and adhered with ace bandages, towels etc

## **TCM FOR Pain, Trauma Inflammation**

#### (BLUE we have time to discuss) Materia Medica Contents

- Angelica spp. (Du Huo, Dong gui, Qiang huo, Bai zhi)
- Drynaria (Gu shi Bu)
- Dipsacus (Xu duan)
- Codonopsis (Dang shen)
- Epimedium (Yin yang huo)
- Eucommia (Du Zhong)
- Panax notoginseng (San qi)
- Myrrh (Mo yao)
- Gummi Olibanum/Boswellia
- Achyranthus (Nui xi)
- Paeoniae lactiflora & rubra (Bai shao & Chi Shao)

- Salvia miltiorrhiza (Dan shen)
- Ligusticum (Chuan xiang)
- Dragon's blood (Xuè jié)
- Safflower (Hong hwa)
- Rhizoma rhei (Rheum palmatum)
- Cortex phellodendron (Huang bi)
- Corydalis (Yan hu suo)
- Radix Scute (Huang qin)
- Liquid amber (LuLu Tong)
- Hu zhang (Japanese knotweed)

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## Boswellia can be used topically over inflamed joints, but beware of adulterants

Phytomedicine. 2008 Jun;15(6-7):400-7. doi: 10.1016/j.phymed.2007.11.019. Epub 2008 Jan 28.

Boswellic acids: A leukotriene inhibitor also effective through topical application in inflammatory disorders.

Singh S<sup>1</sup>, Khajuria A, Taneja SC, Johri RK, Singh J,

Author information

#### Boswellia can be used with other herbal agents topically for joint pain

#### Abstract

Boswellic acids (BA), a natural mixture isolated from oneo gum resmon boswenia semata comprised or nour major pehtacyclic triterpene acids: beta-boswellic acid (the most abundant), 3-acteyl-beta-boswellic acid, 11-keto-beta-boswellic acid, and 3-acetyl-11-keto-beta-boswellic acid, is reported to be effective as anti-inflammatory, immunomodulatory, anti-tumor, anti-asthmatic and in Chron's disease. It inhibits pro-inflammatory mediators in the body, specifically leukotrienes via inhibition of 5-lipoxygenase, the key enzyme of leukotriene synthesis, is the scientifically proved mechanism for its anti-inflammatory/anti-arthritic activity. All previous work on BA for its biological activity has been done through the systemic application but no pre-clinical data reported for its anti-inflammatory activity by topical application. We here by report anti-inflammatory activity of BA through this route by applying different acute and chronic models of inflammation i.e., arachidonic acid and croton oil-induced mouse ear edema, carrageenan-induced rats paw edema and adjuvant-induced developing arthritis in rats. The results of the study revealed that the effect observed through this route is in accordance to the study conducted with the systemic route, thus establishing that BA when used through topical application is as effective as through the systemic route.



P.O. Box 144345, Austin, TX 78714-4345 Phone: 512-926-4900 x129; Fax: 512-926-2345 Contact: <u>Public Relations</u> Website: <u>www.herbalgram.org</u>

#### ABC ADVISORY

ABC-AHP-NCNPR Botanical Adulterants Prevention Program Published Bulletin on Boswellia Resin Adulteration

### Radix Achyranthes spp. a key ingredient in many pain formulas

Jamaican name: Devils ass whip, TCM name: Ox knee



- Contains steroidal saponins & Phytoecdysteroids
- Used for the same thing in China and Jamaica
- Aching back & knees, build muscle and strength of sinews
- Weakness of lower limbs caused by deficient Kidney and Liver
- Descends flow of blood and liver fire
- Nourishes bones and sinews, aids arthritis
- Dose 6-15 g/day

Photo by DrZ Amaranthaceae family

#### Achyranthes can be in both topical and internal pain formulas

## Antinociceptive activity of methanolic extract of leaves of Achyranthes aspera Linn. (Amaranthaceae) in animal models of nociception.

#### Author information

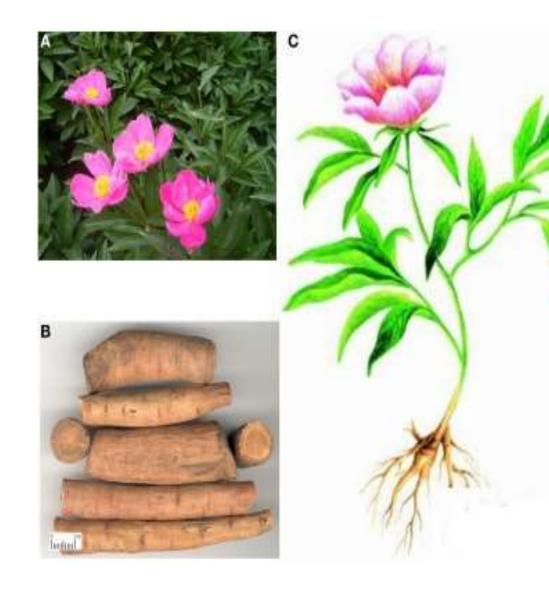
#### Abstract

Antinociceptive activity of methanolic extract of leaves of A. aspera was studied by

## Good results compared to morphine control group

nociception like acetic acid induced writhing syndrome test and central/narcotic models like hot plate and tail flick tests. The methanolic extract of the plant, administered orally (@ 300, 600 and 900 mg/kg, body weight) and the standard drug (piroxicam; 10 mg/kg body weight, po) produced significant analgesic activity in acetic acid induced writhing syndrome as compared to the vehicle treated control group. In the hot plate analgesic test, in A. aspera at the above doses and the standard drug treated group (morphine sulphate @ 1.5 mg/kg, ip), the duration of reaction time (sec) increased dose dependently and significantly compared to the control group. In the test and standard group compared to the control group. The plant possesses significant antinociceptive property as evidenced in all the animal models of nociception. It might possibly exert its effect through diverse mechanism that may involve both central and peripheral pathways. The preliminary phytochemical investigation revealed the presence of steroids, alkaloids and triterpene in the methanolic extract of leaves of A. aspera which may be responsible for its antinociceptive activity.

## Peony: Red or White Paeonia lactiflora & rubra



- Powerful antispasmodic
- White builds blood
- Red cools blood and breaks up blood stasis after trauma
- Specific for DOMS
- Active ingredient Paeoniflorin and other glycosides called TGP... total glycosides of Peony

## Assessment of the Therapeutic Effect of Total Glucosides of Peony for Juvenile Idiopathic Arthritis: A Systematic Review and Meta-Analysis.

In conclusion, TGP is safe and efficacious for the treatment of JIA with few AEs. TGP, which has similar effects on nonbiologic DMARDs, is a special type of nonbiologic DMARD for the treatment of JIA.

#### Abstract

Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children; some clinical trials have reported the effects of total glucosides of peony (TGP) in the treatment of JIA. However, no systematic review has yet been conducted. In this study, we assessed the efficacy and safety in patients with JIA enrolled in randomized controlled trials (RCTs) of TGP. We extracted data for studies searched from 8 electronic databases that were searched and also evaluated the methodological quality of the included studies. We assessed the following outcome measures: overall response rate, pain, tender joint count (TJC), swollen joint count (SJC), duration of morning stiffness (DMS), grip strength (GS), rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and adverse effects (AEs) in short term (4-8 weeks), intermediate term (9-26 weeks), and long term (>26 weeks). The final analysis showed that TGP acted as a unique nonbiologic disease-modifying antirheumatic drug (nonbiologic DMARD), and its therapeutic effects were safe and efficacious for the treatment of JIA with few AEs. However, more high-quality RCTs are needed to confirm these therapeutic effects.

Free pdf of article - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4976154/ TGP = Total Glycosides of Peony

# Radix *Ligustici wallichii known as* Chuan Xiong Sichuan lovage root



- Often combined with peony and other herbs in The Apiaceae or Umbelliferae plant family, {Dang quai, Cnidium, Angelica spp.}.
- Blocks pain in extremities caused by a blockage in meridians.
- Seasonal change pains
- Allows Qi and blood to flow freely to feed sinews, tendons, muscles, ligaments, and other connective tissue.

### Radix Ligustici wallichii

Controlled clinical trials of therapeutic effects of Chinese herbs promoting blood circulation and removing blood stasis on the treatment of reflex sympathetic dystrophy with type of stagnation of vital energy and blood stasis.

#### Abstract

**OBJECTIVE:** To observe clinical results of Chinese herbs promoting blood circu treatment of reflex sympathetic dystrophy (RSD) with type of stagnation of *x*ital ended.

METHODS: RSD with type of stagnation of vital energy and blood stasis was dis

temperature, perspiration, damp and acro-edema, with middle level pain. From 2006 to 2008, 58 patients with RSD of stagnation of vital energy and blood stasis were randomly divided into the treatment group (30 cases) and the control group (28 cases). The former were treated with Chinese medicine to activate blood circulation and improve bone and muscle nourishment. Chinese medicine includes: Caesalpinia Sappan 10 g, Ligusticum Chuanxiong 6 g, Frankincense 6 g, Angelica 10 g, Safflower 6 g, Myrrh 6 g, Ground Beetle 10 g, Araliaceae 3 g, Radix Paeoniae Rubra 10 g, Pericarpium Citri Reticulatae 5 g, Lawn Pennywort Herb 15 g, Manis Pentadactyla 10 g, Corydalis Yanhusuo 10 g, Rhizoma Drynariae 15 g, which were boiled into decoction and the patients were take orally everyday with a course of treatment for 10 days, together with the boiled Chinese traditional medicine of stretching muscle and activating blood circulation to fume and wash the limbs twice everyday. The compatibility of medicines in prescription includes: Lycopodium Japanicum Grass 10 g, Gentiana Macrophylla Pall 10 g, Radix Angelicae Pubescentis 10 g, Angelica 10 g, Uncaria 10 g, Frankincense 6 g, Myrrh 6 g, Safflower 6 g. Control group were treated with a placebo of the same color for oral use and external application. The delivery times, method and the time of therapy were all the same as the treatment group. After 30 days' treatment, the effective indexes of VAS pain score and swelling condition were observed in both groups.

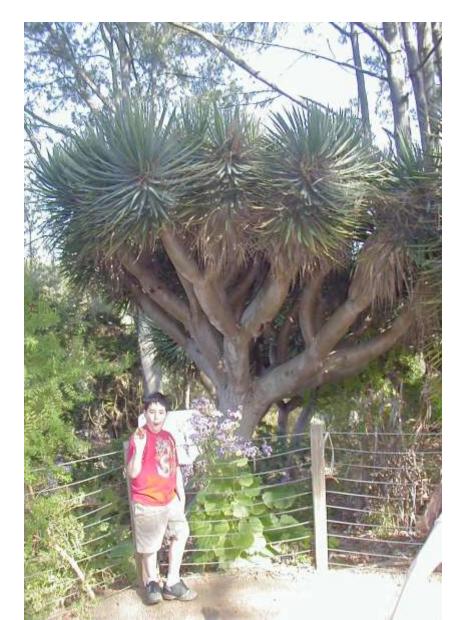
RSD is common after trauma

**RESULTS:** VAS pain score: the treatment group decreased (3.8 + - 0.8) points and the control group decreased (1.0 + - 0.3) points, the difference between the two groups was significantly (P < 0.01). There was significantly difference in volume decrease of the swelling limb between treatment group (21.8 +/- 2.5) ml and the control group (10.3 +/- 2.1) ml (P < 0.01). The efficiency difference between treatment group and control group was significantly (P<0.01).

**CONCLUSION:** With the different treatment based on different syndrome and emphasis on the nourishment of bone and soft tissue, treated by Chinese medicine to promote blood circulation and remove blood stasis in stagnation of vital energy and blood stasis, RSD get a favorable result.

### Dragon's blood (xuè jié)

Photo of Draceana, Dr E Zampieron; Son Kevin in San Diego CA,2003



Dragon's blood, a deep red resin, is a wellknown traditional medicine, obtained from four different sources:

- 1. Croton spp. (syn. Sangre de draco, Euphorbiaceae)
- 2. Dracaena spp. (syn. Zanzibar drop, Dracaenaceae)
- 3. Daemonorops spp. (syn. Jerang or Djerang, Palmaceae)
- *4. Pterocarpus* spp. (syn. East India Kino or Malabar Kino, Fabaceae).

### Note the Dragon's Blood Resin from the Wood of Croton lechleri



- Can dissolve blood stasis, dredge meridians and vessels, resolve swelling and alleviate pain
- Used for symptoms of injuries from falls fractures, contusions and sprains; served as a miraculous herb in treating swelling and pain due to stasis
- Usually combined with other stasisresolving analgesics. For instance it is combined with Boswellia and myrrh

#### Dragon's blood inhibits chronic inflammatory and neuropathic pain responses by blocking the synthesis and release of substance P in rats.

#### Abstract

As a traditional Chinese medicine, dragon's blood (DB) is widely u thousands of years due to its potent anti-inflammatory and analger observed that intragastric administration of DB at dosages of 0.14

## Historical & Ethnobotanical use supports this in vitro effects

inhibited paw edema, hyperalgesia, cyclooxygenase-2 (COX-2) protein expression, or preprotachykinin-A mRNA expression in carrageenan-inflamed or sciatic nerve-injured (chronic constriction injury) rats, respectively. A short-term (15 s or 10 min) pre-exposure of cultured rat dorsal root ganglion (DRG) neurons to DB (0.3, 3, and 30  $\mu$ g/ml) or its component cochinchinenin B (CB; 0.1, 1, and 10  $\mu$ M) blocked capsaicin-evoked increases in both the intracellular calcium ion concentration and the substance P release. Moreover, a long-term (180 min) exposure of cultured rat DRG neurons to DB or CB significantly attenuated bradykinin-induced substance P release. These findings indicate that DB exerts anti-inflammatory and analgesic effects by blocking the synthesis and release of substance P through inhibition of COX-2 protein induction and intracellular calcium ion concentration. Therefore, DB may serve as a promising potent therapeutic agent for treatment of chronic pain, and its effective component CB might partly contribute to anti-inflammatory and analgesic effects.

#### PMID: 22198006

[PubMed - indexed for MEDLINE] Free full text

### Safflower (Hong hwa) Key ingredient in Herbal Ice



- Flos *Carthamus tinctoria {*Safflower} TCM name: Hong hwa
- Dispels congealed blood and alleviates pain Make HERBAL ICE with EQUAL PARTS
- Rhizoma rhei (Chinese rhubarb)
- Radix Scute baicalensis (Scute)
- Cortex Phellodendron spp
- Herba Taraxacum
- Fructus gardenia
- Flos Carthamni
  - (Safflower) Macerate and tincture x 3 weeks
- San Huang San is FIRST STEP IN ANY INJURY!!
- Dr. Z recommends patient sleep with a San Huang San poultice, changing periodically with fresh herbs

## Efficacy of hooking therapy and safflower injection on lumbar disc herniation and the impact on IL-6 and NO in the patients.

#### Abstract

**OBJECTIVE:** To explore the clinical efficacy and the effect mechanism of hooking therap herniation (LDH).

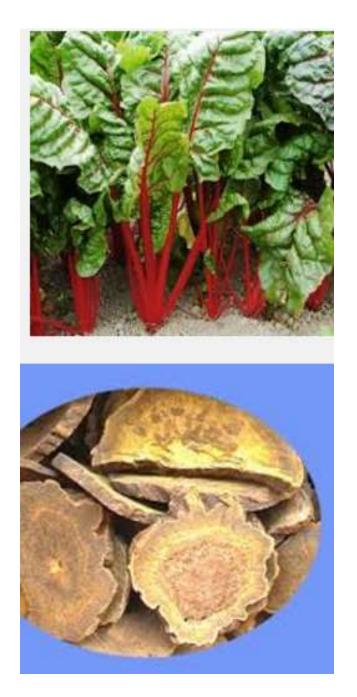
#### Dr Z has seen topical safflower work just a well as injections

**METHODS:** Sixty patients of LDH were randomized into an observation group and a control group at ratio of 1 to 1, 30 cases in each one. In the control group, safflower injection was applied to three points of lumbar region, once a day. Seven treatments made one session, and totally 2 sessions were required. In the observation group, under local anesthesia, the big hook needle was used to stimulate the three points of lumbar region first, followed by the safflower injection, once every 6 to 7 days. If the efficacy was not satisfactory enough, the second treatment was given. The visual analogue scale (VAS) and the modified Japanese Orthopaedic Association (M-JOA) scores were observed before and after treatment in the patients of the two groups and the clinical efficacy was evaluated. The levels of peripheral interleukin-6 (IL-6) and nitric oxide (NO) were determined.

**RESULTS:** VAS and M-JOA scores were all improved apparently after treatment as compared with those before treatment in the patients of the two groups (both P < 0.01). The improvements in the observation group were much more obvious than those in the control group (both P < 0.01). In the observation group, the curative and remarkably effective rate was 76/7% (23/30) and the total effective rate was 96.7% (29/ 30), better than 43.3% (13/30) and 70.0% (21/30) in the control group separately (both P < 0.05). After treatment, the levels of IL-6 and NO were all reduced as compared with those before treatment in the two groups; (both P < 0.01). The above indices were changed more obviously in the observation group as compared with those in the control group (both P < 0.01).

**CONCLUSION:** The combined therapy of hooking therapy and safflower injection apparently relieves pain and clinical symptoms of LDH. The effect mechanism is relevant with reducing the levels of IL-6 and NO in the peripheral blood.

DMID: 26064162



## Rhizoma Rhei (Da Huang) and other Emodin containing Botanicals for Inflammation (found in Herbal Ice)

- Actions:
  - Activating blood and resolving stasis
  - Drives stasis downwards
  - Clears stasis-heat
- Often combined with blood-activating and stasisresolving herbs such as Tao Ren (dry ripe seed of the peach tree *Prunus persica*), Hong Hwa (safflower petals) and *Salvia miltiorrhiza* Dan shen

## In vitro & vivo assessment of a herbal formula used topically for bone fracture treatment.

#### Abstract

AIM OF THE STUDY: A novel topical paste used for fracture healing (FH), consisting of the extracts of six herbs, Radix Dipsaci, Ramulus Sambucus Williamsii, Rhizoma Notoginseng, Flos Carthami, Rhizoma Rhei and Fructus Gardeniae, was developed according to the classical theory of traditional Chinese medicine. This study aimed to determine the effectiveness of this formula, and some of its important chemical components in the promotion of fracture healing. The transdermal

transport of FH was also examined.

MATERIALS AND METHODS: The osteogenic chemical marker components were assessed to cells (HUVEC) and murine macrophage RAW2 transdermal absorption were determined using levels and biomechanical properties of the hea Western medicine doesn't use pastes or poultices for fractures. Maybe they should? I use this formula regularly and add Western herbs like comfrey

**RESULTS:** FH significantly increased the cell proliferation in UMR-106 and HUVEC cells and inhibited the nitric oxide production in murine macrophage in dose-dependent manner. Its important chemical components asperosaponin VI, ginsenoside Rg1 and emodin were shown to be acting positively in the respective in vitro studies. FH paste significantly improved the bone healing in the rabbit fracture model, as was indicated by the increases in callus size at weeks 2-5, and the elevations in bone specific alkaline phosphatase activities at weeks 5-6. The analysis using LC/MS/MS also showed the presence of important chemical marker components of the FH formula in the plasma after 8 weeks of topical treatment.

**CONCLUSION:** This study presents the first scientific evidence of the efficacy of a herbal paste in the promotion of fracture healing. There were evidences of transdermal transport of the chemical components, control the inflammation through nitric oxide inhibition, promotion of angiogenesis, and bone healing in the in vitro tests, as well as in the experimental animal.

# Scute: works topically too Human Trials in OA

Active ingredients in Chinese skullcap include flavans and flavonoids: baicalin, baicalein, wogonin antioxidants

Displays anti-inflammatory effects by reducing expression of nitric oxide, inducible NOS (iNOS), COX-2, PGE2), NF-kappaB and as well as inflammatory cytokines, such as IL-1beta, IL-2, IL-6, IL-12 and TNF-alpha

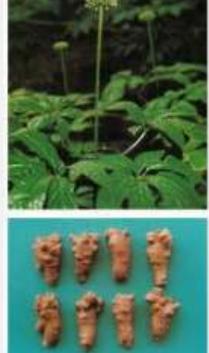


Kim EH. Anti-inflammatory effects of Scutellaria baicalensis extract via suppression of immune modulators and MAP kinase signaling molecules. J Ethnopharmacol. 2009 Nov 12;126(2):320-31.

Levy RM. Flavocoxid is as effective as naproxen for managing the signs and symptoms of osteoarthritis of the knee in humans: a shortterm randomized, double-blind pilot study. Nutr Res. 2009 May;29(5):298-304.

## Panax notoginseng/San qi Used in Yunnan Bai yao or Gunshot powder









## Effect of Panax notoginseng in patients with multiple fractured ribs and pulmonary contusions caused by 2008 Wenchuan earthquake.

#### Abstract

BACKGROUND: The aim of this study was to investigate whethe notoginseng (PN group) is superior to conventional treatment alo with multiple fractured ribs and pulmonary contusions.

PATIENTS AND METHODS: We retrospectively analyzed the m and pulmonary contusions with either conventional treatment (n pain scores and arterial oxygen saturation were measured at bas

This is an incredible trauma medicine! Shorter hospital stay, faster healing, less systemic analgesics. I've used it on my injuries many times

duration of mechanical ventilation, systemic analgesics, and hospital stay were also recorded.

**RESULTS:** VAS scores in the PN group were lower than in the CG group at 1 week (p < 0.01) and at 2 weeks (p < 0.05). Arterial oxygen saturation in both groups was higher after treatment than at baseline (p < 0.05), but there was no statistically significant difference between the 2 groups (p > 0.05). The duration of mechanical ventilation, systemic analgesics administration, and hospital stay in the PN group was remarkably decreased as compared to the CG group (p < 0.05).

**CONCLUSION:** Combining conventional treatment and P. notoginseng seems to be an efficient method that can improve the clinical symptoms of multiple fractured ribs and pulmonary contusions.

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PMID: 25592947 DOI: 10.1159/000370011

[PubMed - indexed for MEDLINE]

## **Clematis chinensis**

photo credit :http://gilpin.extension.colostate.edu/about-us/



### **Clematis...not just a pretty garden plant**

Clin Ther. 2007 May;29(5):862-873. doi: 10.1016/j.clinthera.2007.05.006.

Assessment of comparative pain relief and tolerability of SKI306X compared with celecoxib in patients with rheumatoid arthritis: a 6-week, multicenter, randomized, double-blind, doubledummy, phase III, noninferiority clinical trial.

Song YW<sup>1</sup>, Lee EY<sup>2</sup>, Koh EM<sup>3</sup>, Cha HS<sup>3</sup>, Yoo B<sup>4</sup>, Lee CK<sup>4</sup>, Baek HJ<sup>5</sup>, Kim HA<sup>6</sup>, Suh Y 2nd<sup>6</sup>, Kang SW<sup>7</sup>, Lee YJ<sup>8</sup>, Jung HG<sup>9</sup>.

Author information

#### Abstract

BACKGROUND: SKI306X, which consists of biologically active ingredients from Clematis mandeburica, Tricbosantbes kirilowii, and Prunell vulgaris, was developed and tested in preclinical trials in Korea. Those studies found that SKI306X was associated with an anti-inflammator and analgesic effect, and that it can delay the destruction of cartilage in rheumator arthritis (RA).

OBJECTIVE: The aim of this study was to compare the pain relief and tolerability of SKI306X and celecoxib in patients with RA.

**METHODS:** This study was a 6-week, multicenter, randomized, double-blind, double-dummy, Phase III, noninferiority clinical trial. Eligible patients were aged 18 to 80 years, had a history of RA with a disease duration of > or =3 months, and were functional American College of Rheumatology (ACR) class I, II, or III before entry. After a washout period of 2 weeks, patients were randomized to SKI306X 200 mg TID or celecoxib 200 mg BID for 6 weeks. The primary end point was a change in patient assessment of pain intensity using a visual analog scale (VAS). The secondary end points were a 20% improvement in response rate as defined by the ACR (ACR20) and the frequency of rescue medication use. Results after 3 and 6 weeks of treatment were compared with baseline and between treatment groups, and all patients were assessed for adverse events (AEs), clinical laboratory data, and vital signs. AEs were identified based on spontaneous reports by patients during interviews conducted by the investigators and the study coordinator.

**RESULTS:** Two hundred twenty-two Korean patients from 7 medical centers were assessed and 183 were enrolled and randomized to 1 of 2 treatment groups. Ninety-one patients (10 male, 81 female; mean [SD] age, 52.13 [12.64] years; mean [SD] duration of RA, 9.08 [10.23] years; no. [%] of ACR class I, II, and III, 13 [14.29], 44 [48.35] and 34 [37.36] patients, respectively) received SKI306X 200 mg TID and 92 patients (10 male, 82 female; mean [SD] age, 51.78 [10.94] years; mean [SD] duration of RA, 8.78 [7.78] years; no. [%] of ACR class I, II, and III, 14 [15.22], 44 [47.83], and 34 [36.96] patients, respectively) received celecoxib 200 mg BID. An analysis of the change in reported pain intensity as determined by VAS (mm) score between baseline and week 3 (mean [SD], 13.64 [16.62] vs 14.45 [15.89]), and between baseline and week 6 (18.4 [20.8] vs 17.9 [19.1], respectively) suggested that SKI306X was not inferior to celecoxib. The number of patients who achieved ACR20 response rate was not significantly different between the SKI306X group and the celecoxib group at week 3 (16/87 [18.4%] vs 24/87 [27.6%], respectively) and at week 6 (29/87 [33.3%] vs 29/87 [33.3%]). The frequency of rescue medication use was not significantly different between the SKI306X group and 22 (23.9%) patients in the celecoxib group and 22 (23.9%) patients in the celecoxib group. The most frequent drug-related AEs were epigastric pain (9/91 [9.9%]) in the SKI306X group and glutamyltranferase elevation (4/92 [4.3%]) in the celecoxib group. No significant between-group differences were observed in the prevalence of drug-related clinical- or laboratory-determined AEs.

CONCLUSION: The results of this study suggest that SKI306X was generally well tolerated and not inferior to celecoxib in regard to pain relief

Six weeks; 220 patients Formula as good as celecoxib side effects tolerable and better than celecoxib



## Rhizoma Corydalis spp.

The strongest herb for pain in the Chinese Materia Medica



- Called Yan Hu Suo in TCM
- Cousin to Opium Poppy
- Contains Corydaline & tetrahydropalmatine {THP) as its key ingredients

A new compound has been isolated dehydrocorybulbine

Rated 40% as powerful as morphine (Bensky)

Traditionally combined with many TCM herbs for arthralgia, myalgia and headaches

Photo is corydalis cava

# Chinese herbal compound relieves inflammatory and neuropathic pain

Source and Direct quote: https://www.google.com/search?q=Chinese+herbal+compound+relieves+inflammatory+ and+neuropathic+pain&rlz=1C1CHBF\_enUS720US720&oq=Chinese+herbal+compound+relieves+inflammatory+and+neuropathic+pain& aqs=chrome..69i57.3579j0j8&sourceid=chrome&ie=UTF-8

### Fairly recent new alkaloid

- "A compound derived from a traditional Chinese herbal medicine has been found effective at alleviating pain, pointing the way to a new nonaddictive analgesic for acute inflammatory and nerve pain, according to UC Irvine pharmacology researchers.
- January 2, 2014
- "Irvine, Calif., Jan. 2, 2014 A compound derived from a traditional Chinese herbal medicine has been found effective at alleviating pain, pointing the way to a new nonaddictive analgesic for acute inflammatory and nerve pain, according to UC Irvine pharmacology researchers.
- Working with Chinese scientists, Olivier Civelli and his UC Irvine colleagues isolated a compound called dehydrocorybulbine (DHCB) from the roots of the *Corydalis yanhusuo* plant. In tests on rodents, DHCB proved to diminish both inflammatory pain, which is associated with tissue damage and the infiltration of immune cells, and injury-induced neuropathic pain, which is caused by damage to the nervous system. This is important because there are no current adequate treatments for neuropathic pain.
- Moreover, the researchers found that DHCB did not generate the tolerance seen with continued use of most conventional pain relievers, such as morphine.
- "Today the pharmaceutical industry struggles to find new drugs. Yet for centuries people have used herbal remedies to address myriad health conditions, including pain. Our objective was to identify compounds in these herbal remedies that may help us discover new ways to treat health problems," said Civelli, the Eric L. & Lila D. Nelson Chair in Neuropharmacology. "We're excited that this one shows promise as an effective pharmaceutical. It also shows a different way to understand the pain mechanism."
- Study results appear in the Jan. 20 issue of Current Biology"

# Western, Eclectic and Rainforest herbs in the fight against pain

Topicals:

Capsaicin

Aconitum

Piscidia

Colocynthis

Bryonia

Camphor

Internal

\*Eschscholzia & other poppies

• Piscidia

- Indian pipe (monotropa)
- Erythrina
- DROP doses only:
  - Aconite
  - Bryonia
  - Colocynthis

## **Prepared Tuber of** *Aconite napellus*



- It derived the name Wolfbane in ancient times as arrows tipped with the juice of the plant were used to kill wolves.
- Most powerful topical herb for pain, yet...Handle with caution!
- Attributed to many accidental poisonings in China, even in Aconite harvesters!
- "...Though various species of aconite have been considered important medicinal plants by most traditions in areas where it grows, it has become a feared agent to avoid in much of the West. This is unfortunate, because in appropriate doses, aconite is generally very safe and has many beneficial actions. Thorough knowledge of the herb is essential to insure safety, but given this, it serves as a potent addition to the botanical armamentarium...."
- Quote from Dr E. Yarnell, ND, RH(AHG)
- <u>http://ndnr.com/pain-medicine/aconite-a-powerful-tool-or-an-agent-to-avoid/</u>
- Eclectic dose 1:10 aconite 1-8 minims/day
- (one minim is 1/480 of an ounce, or approximately 2 drops) so 2 to 16 drops per day = 1-8 minums

## **Aconitum Toxicity continued**

- Under the restrictions of the 1968 Medicines Act, aconite in lotion form must not exceed 1.3 parts of aconite to 100 parts of lotion.
- When used internally, the root undergoes a special process to detoxify it. The process involves soaking the roots whole in vinegar for one month, followed by a salt water soak for one month. The process is repeated several times.
- In this prepared form it is sold under the name 'Aconitum praeparata' or FU-ZI.
- These alkaloids and their metabolites act on voltage-sensitive sodium channels in excitable tissues (Friese et al., 1997).
- "...Fresh roots with their intact alkaloids are significantly more potent and have higher potential for toxicity than dried or cooked roots. Heat converts aconitine and mesaconitine to benzylaconine derivatives, which are significantly less potent and safer..."

Dr E. Yarnell, ND, RH(AHG)

http://ndnr.com/pain-medicine/aconite-a-powerful-tool-or-an-agent-to-avoid.."



### Aconitum in traditional Chinese medicine: A valuable drup or an unpredictable risk?

#### Author information

#### Abstract

Aconitum species have been used in China as an essential drug in Traditional Chinese Medicine (TCM) for 2000 years. Reviewing the clinical application of Aconitum, their pharmacological effects, toxicity and detoxifying measures, herb-herb interactions, clinical taboos, famous herbal formulas, traditional and current herbal processing methods based upon a wide range of literature investigations serve as a case study to explore the multidisciplinary implications of botanicals used in TCM. The toxicological risk of improper usage of Aconitum remains very high, especially in countries like China, India and Japan. The toxicity of Aconitum mainly derives from the diester diterpene alkaloids (DDAs) including aconitine (AC), mesaconitine (MA) and hypaconitine (HA). They can be decomposed into less or non-toxic derivatives through Chinese traditional processing methods (Paozhi), which play an essential role in detoxification. Using Paozhi, the three main forms of processed aconite -- yanfuzi, heishunpian and baifupian -- can be obtained (CPCommission, 2005). Moreover, some new processing techniques have been developed in China such as pressure-steaming. The current development of fingerprint assays, in particular HPLC, has set a good basis to conduct an appropriate quality control for TCM crude herbs and their ready-made products. Therefore, a stipulation for a maximum level of DDA content of Aconitum is highly desirable in order to guarantee the clinical safety and its low toxicity in decoctions. Newly developed HPLC methods have made the accurate and simultaneous determination and quantification of DDA content interesting.

#### PMID: 19651200 DOI: 10.1016/j.jep.2009.07.031

[Indexed for MEDLINE]



### **Topical Monkshood & the Eclectics**

- The famous Eclectic MD, Dr Ellingwood also found that it could be extremely useful in the relief of acute pain and suggests, "Perhaps the most immediate influence obtainable in acute pain is to put 5 drops each of Chloroform, and Aconite into the palm of the hand and hold it over the seat of pain for 2-3 minutes. The effect is instantaneous and marvelous."
- Dr Z has used Terebinthum, camphor, menthol and aconite with great success in many painful afflictions

Aconite has been used as a pain remedy wherever it is found. Headaches, rheumatic pains, arthritis, inflammatory pain, sciatica, pruritus ani, neuralgias and colicky pains have been treated historically with this plant (Felter, Eclectic mat med. pg 151,1922) (Sharp WHH: Aconite in neuralgia, *Eclectic Med J* p62, 1933 )



## **Topicals Aconite: A low dose anesthetic**



- Aconite first stimulates and later sedates the nerves connected to pain, touch and temperature,
- the initial tingling gives place to a long continued anesthetic action.
- Many of the eclectics drop dosed unprocessed aconite when used internally. Because of the potential toxicity of aconite, internal use is generally limited to very dilute preparations.
- A 1:10 tincture is prepared, then 5-10 drops are put into 120 ml (4 Oz) of water; ½ tsp should be given every half hour or 1 tsp every hour for pain. {REF http://ndnr.com/pain-medicine/using-low-dose-herbs-to-treat-pain/}

#### Ignavine: A novel allosteric modulator of the u opioid receptor.

#### Author information

#### Abstract

Processed Aconiti tuber (PAT) is used to treat pain associated with various disorders. Although it has been demonstrated that the κ opioid receptor (KOR) signaling pathway is a mediator of the analgesic effect of PAT, active components affecting opioid signaling have not yet been identified. In this study, we explored candidate components of PAT by pharmacokinetic analysis and identified ignavine, which is a different structure from aconitine alkaloids. A receptor binding assay of opioid receptors showed that ignavine specifically binds the μ opioid receptor (MOR), not the KOR. Receptor internalization assay in MOR-expressing cell lines revealed that ignavine augmented the responses produced by D-Ala(2)-N-Me-Phe(4)-Gly-ol(5)-enkephalin (DAMGO), a representative MOR agonist, at a low concentration and inhibited it at a higher concentration. Ignavine also exerted positive modulatory activity for DAMGO, endomorphin-1 and morphine in cAMP assay. Additionally, ignavine alone showed an analgesic effect in vivo. In silico simulation analysis suggested that ignavine would induce a unique structural change distinguished from those induced by a representative MOR agonist and antagonist. These data collectively suggest the possibility that ignavine could be a novel allosteric modulator of the MOR. The present results may open the way for the development of a novel pain management strategy.

PMID: 27530869 PMCID: PMC4987652 DOI: 10.1038/srep31748

[Indexed for MEDLINE] Free PMC Article

1.00

# Human Clinical study in epidural injection with lappaconitine for post-operative analgesia

- Zhongguo Zhong Xi Yi Jie He Za Zhi. 1995 May;15(5):274-6. Links
  - <u>Chen MG</u>, <u>Wang QH</u>, <u>Lin YB</u>.
  - Affiliated People's Hospital, Fujian College of TCM, Fuzhou.
  - This paper studied the effect and side-effect of Lappaconitine for post-operative analgesia with epidural injection. 50 patients who were operated in the upper abdomen with epidural anesthesia. These patients were randomly divided into 5 groups. The general condition of every group was similar. Group A, B, C was given Lappaconitine 4 ml, 8 ml, 12 ml individually for observation. Group D, E was given 0.9% NS 6 ml and morphine 2 mg individually as control. When the operation was finished the drug was injected into the epidural space with single blind method. The result showed the analgesia of the drug and its effective time was: group E > C > B > A > D. The analgesic effect of Group C was satisfactory. The efficacy and the maintenance time of A, B, C groups were significantly different from that of group D (P < 0.05, P < 0.01). Although the effect of group C was less potent than that of group E (morphine injection), there was no side-effect as morphine had. It suggested that Lappaconitine for post-operative analgesia with epidural injection is effective and safe.

### Clinical research on Gancao Fuzi decoction in treating osteoarthritis of knee joint

Author information

#### Abstract

**OBJECTIVE:** To explore the clinical curative effect of Gancao Fuzi Decoction in treating or mechanism on how to relieve the symptoms and signs of the disease.

## Oral prepared aconite with licorice

**METHODS:** 100 cases were randomly divided into treatment group with orally taken Gancao Fuzi Decoction and control group with orally taken Votalin sustained released tablets. Then the symptoms and signs of the disease were classified, and a table to record observations was designed. Two weeks later, statistical treatment was carried out basing on the observation and points in the table. And then the study drew comparisons before and after the treatment as well as between the two groups. Other evaluations were carried out among the patients with osteoarthritis of knee joint, including reactive protein C, blood sedimentation rate, interleukin-I, arthralgia, tendernese of joints, joint function, integrated therapy, adverse effects etc.

**RESULTS:** The total effective rate of the control and treated group were 88% and 92%, respectively. The symptoms, the physical sign score and the index of the laboratory had predominance statistical significant (P < 0.01) between the prior and after treatment and the latter was better, the effects of both groups were equal and had no statistical significance. The changes of the C-reactive protein and blood sedimentation in the control group were better than in the treated group.

**CONCLUSION:** Gancao Fuzi Decoction has the function of war-ming yang, expelling wind, eliminating dampness, removing swelling, relieving pain and improving joints indeed when treating osteoarthritis of knee joint.

PMID: 18973027

[Indexed for MEDLINE]



## Wintergreen

### (Gaultheria procumbens) fruiting

- Works well topically with arnica with TENS treatments for muscular & other pain disorders
- REFERENCES:

Kucera M. et al., Synergetic analgesic effect of the combination of arnica and hydroxyethyl salicylate in ethanolic solution following cutaneous application by transcutaneous electrostimulation. Arzneimittelforschung. 2003;53(12):850-6.

- Md State Med J. 1956 Jan;5(1):36-9.
- Chronic rheumatic disease; clinical evaluation of a topical methyl salicylate compound



## Topical capsaicin for pain management: therapeutic potential and mechanisms of action of the new high-concentration capsaicin 8% patch.

- The desensitizing effects of capsaicin are established for pain therapy.
- Binding to the TRPV1 receptors, and also High Voltage activated calcium channels, the net effect is the desensitization of the neurons which send pain signals is a reduction of substance P release. This hinders the ability to send neuralgic and other pain signals to the brain.
- Chronic exposure of neurons to capsaicin results in a cumulative depletion of substance P over a period of weeks, resulting in eventual pain relief, and also relief of neuropathic pruritis. \* +
- Also stimulation of the HVACC down regulates TRPV1
- But there's newer mechanism of actions that have emerged....

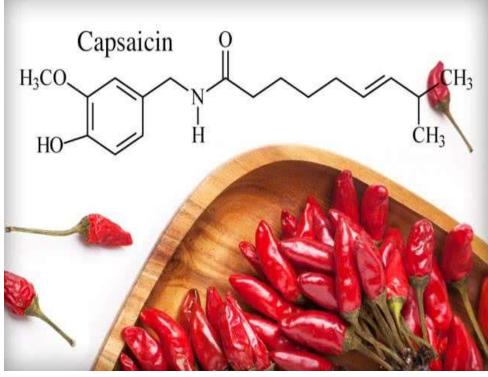


Image credit:https://www.cayennediane.com/what-are-capsaicinoids/

\*REF: Misery, Let al. Successful treatment of refractory neuropathic pruritus with capsaicin 8% patch: A bicentric retrospective study with long-term follow-up. Acta Derm. Venereol. 2015, 95, 864–865.

+ Anand, P. Topical capsaicin for pain management: therapeutic potential and mechanisms of action of the new high-concentration capsaicin 8% patch. Br. J. Anaesth. 2011, 107, 490–502

## **Capsicum New Mechanisms of pain control**

In addition to the depletion of substance P, some researchers have discovered that on-going treatment with capsaicin results in an irreversible destruction of primary afferent terminals related to the peripheral nerves, leading to analgesia. If the capsicum treatment is discontinued, the nerves can re-generate, leading to a return of sensation and pain

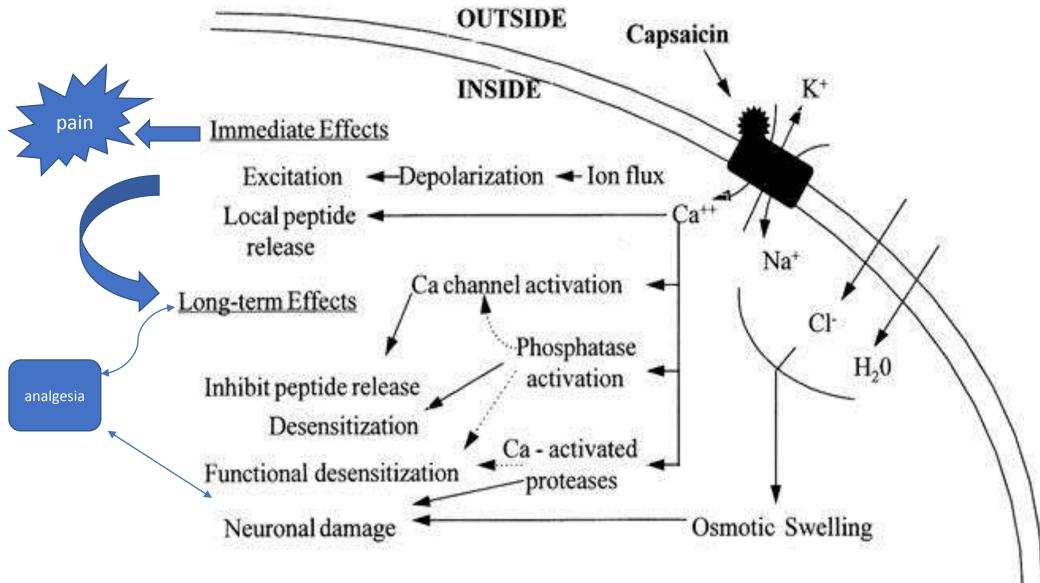
This is elucidated in the next slide

Capsaicin 8% is as good as oral pregabalin for neuropathic pain in clinical trials

Haanpaa, M. et al. *Capsaicin 8% patch versus oral pregabalin in patients with peripheral neuropathic pain*. Eur. J. Pain 2016, 20, 316–328.

- Pini A, Baranowski R, Lynn B (1990) Longterm reduction in the number of C-fibre nociceptors following capsaicin treatment of a cutaneous nerve in adult rats. Eur J Neurosci 2:89-9.
- Jancso G., Lawson SN Transganglionic degeneration of capsaicin-sensitive Cfiber primary afferent terminals. Neuroscience. 1990;39(2):501-11
- Nolano, M.; Simone, D.A.; Wendelschafer-Crabb, G.; Johnson, T.; Hazen, E.; Kennedy, W.R. Topical capsaicin in humans: Parallel loss of epidermal nerve fibers and pain sensation. Pain 1999, 81, 135–145.

## Mechanism of temporary destruction of nerve fibers by Capsicum: newer mechanism of action



Colocynthis as a "drop dose" botanical extract Image credit: https://www.alibaba.com/product-detail/Citrullus-colocynthis\_50021971833.html

Iran J Basic Med Sci. 2018 Apr;21(4):347-358. doi: 10.22038/IJBMS.2018.24026.6021.

## Medicinal herbs in the treatment of neuropathic pain: A review

#### Abstract

Chronic neuropathic pain is a common significant and debilitating problem that presents a major challenge to health-care. Despite the large number of available drugs, there are no curative conventional treatments for neuropathic pain. Nowadays, more attention has been focused on the herbal formulation in the field of drug discovery. Therefore, we performed an extensive review about herbal drugs and plants that exhibited protective effects on neuropathic pain. In this review, the beneficial effects of each plant in different neuropathic pain model, either in animals or in patients are reported. Moreover, the possible involved mechanisms for the protective effects are discussed. The more common plants which are used for the treatment of neuropathic pain are included as: *Acorus calamus, Artemisia dracunculus, Butea monosperma, Citrullus colocynthis, Curcuma longa, Crocus sativus, Elaeagnus angustifolia, Ginkgo biloba, Mitragyna speciosa, Momordica charantia, Nigella sativa, Ocimum sanctum, Phyllanthus amarus*, Pterodon pubescens Benth, Rubia cordifolia and Salvia officinalis. Furthermore, the most pathways which are known to be involved in pain relief by means of herbal remedies are anti-oxidant activity, anti-inflammatory, anti-apoptotic, neuroprotective and calcium inhibitory actions. In conclusion, this review suggests that some herbal plants can be suitable candidates for the treatment of neuropathic pain.

KEYWORDS: Analgesic; Antinociceptive; Chronic pain; Herbal medicine Neuropathic pain





#### Eschscholzia is a fast acting herb in known to reduce pain and anxiety Also, physicians are turning to Meconopsis spp. 'Blue'Himalayan Poppy

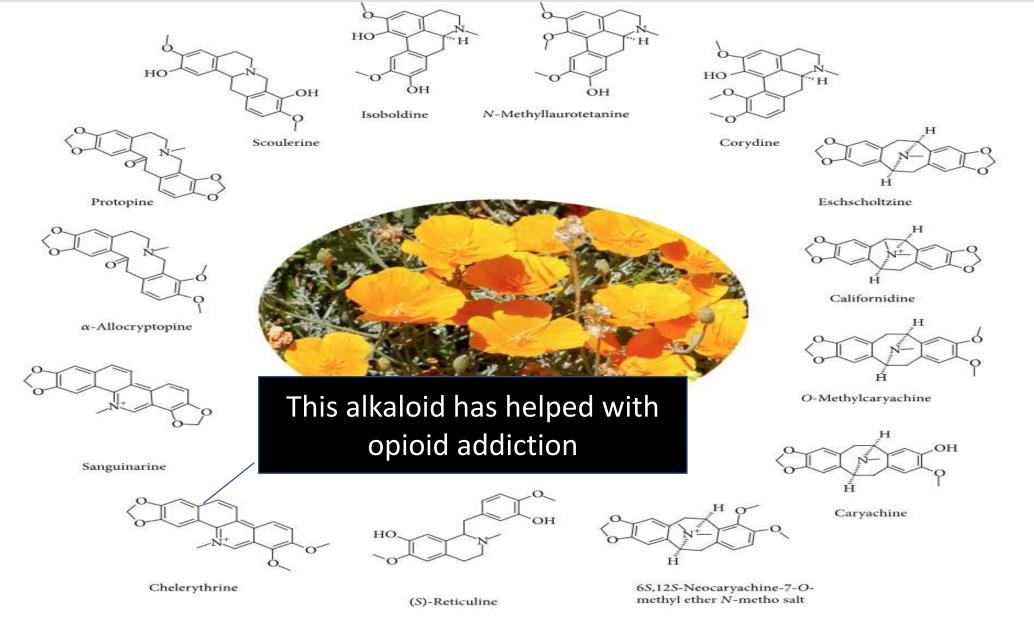
- California Poppy (*Eschscholzia californica*) is the official state flower of California.
- The plant, which grows to about

60 cm, has feathery foliage and velvety, goldenorange flower petals.

It is a member of the Papaveraceae. Older literature stated that it contained small traces of opium, but modern studies don't substantiate that

It does contain many other isoquinoline alkaloids which can interact with opioid receptors and ease opium withdrawal and helps pain through GABA and serotonin





#### Alkaloids identified in the aerial parts of Eschscholzia californica

SOUCE: https://www.hindawi.com/journals/bri/2015/617620/fig1/

## **History of Eschscholzia**

- California Poppy was a commonly used herb in native American and Hispanic societies, and gained considerable interest from medical practitioners in the late 1800's, when it was added to the Park-Davis drug catalog as "an excellent soporific (sedative sleep agent) and analgesic, above all harmless."
- Felter and Lloyd, the master writers of the Eclectic literature and Materia medica... considered *Eschscholzia* to be an "...analgesic and soporific without the dangers attending opiates, quieting pain and producing (a) calm sleep" (1893).
- Externally, the various Poppies can be used to treat pain and arrest local inflammation, used as a lotion, liniment, or plaster
- A more recent usage for *Eschscholzia* is in the treatment of heroin addiction and withdrawal. Donna Odierna, herbalist and director of the H.E.A.L.T.H. Needle Exchange clinic in Oakland, California, uses *Eschscholzia* as the primary ingredient in her clinic's "Kick Juice," along with smaller amounts of *Vitex agnuscastus, Avena sativa, Piper methysticum* and *Verbena officinalis*

(ref: https://wildrosecollege.com/encyclopaedia\_entry/poppy-californiaeschscholzia-californica/)

## **DrZ clinical anecdotes**

http://medcraveonline.com/IJCAM/IJCAM-11-00403.pdf recently published case anecdote by DrZ

#### • Stopping narcotic addiction with California poppy tincture

- 34 y/o female amputated her finger in a large metal door  $\rightarrow$  surgical repair successful
- Prescribed Oxycodone (OxyContin, Roxicodone)
- Became addicted and her social and emotional life became seriously affected
- DrZ read citation in Mills/Bone and ref by Fundythus et al. that plants with chelerythrine reduce morphine dependence (Eur J Pharmacol. 1996 Apr 11;300(3):173-81)
- DrZ attempted intervention & prescribed tincture of Eschscholzia 1:2 1 tsp q2hr waking
- Patient was able to escape the addiction of oxycodone over a period of 1 month
- Weaned off of Low dose Naltrexone (LDN) therapy with Eschscholzia
  - Recently, a patient at UBCNM Clinic with chronic pain due to RA was weaned off of Low dose Naltrexone (LDN) therapy with Eschscholzia and achieved better analgesia than with LDN
  - Sig was Eschscholzia tincture 1:2 sig:1 tsp QID waking

## Eschscholtzia

#### Neurophysiological effects of an extract of Eschscholzia californica Cham. (Papaveraceae)

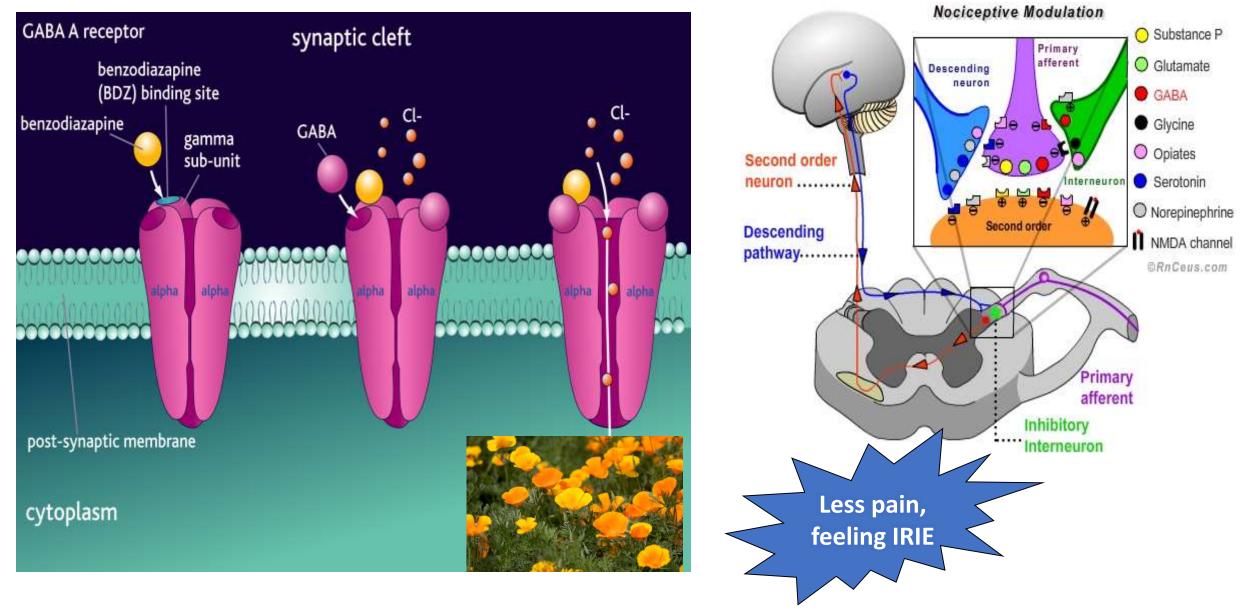
#### Author information

#### Abstract

#### Benzodiazepine receptors

An aqueous alcohol extract of Eschscholzia californica (Ec) has been evaluated for benzodiazepine, neuroleptic, antidepressant, antihistaminic and analgesic properties, in order to complete the study of the sedative and anxiolytic effects previously demonstrated. The plant extract did not protect mice against the convulsant effects of pentylenetetrazol, and did not cause muscle relaxant effects but appeared to possess an affinity for the benzodiazepine receptor: thus, flumazenil, an antagonist of these receptors, suppressed the sedative and anxiolytic effects of the extract. The Ec extract induced peripheral analgesic effects in mice but did not possess antidepressant, neuroleptic or antihistaminic effects.

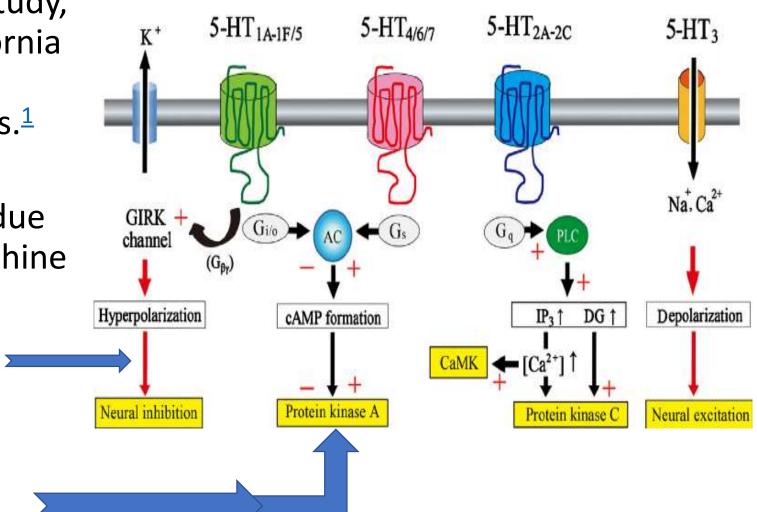
## Eschscholzia binds to benzodiazepine receptors BDZ and augments GABA's anxiolytic effects and GABA anti nociceptive /inhibitory effect on pain

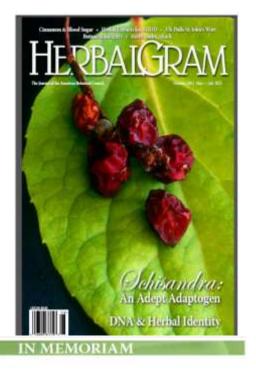


## https://www.ncbi.nlm.nih.gov/pubmed/16562853

- Neurological: In an *in vitro* study, 70% ethanol extract of California poppy was able to bind to 5-HT(1A) and 5-HT(7) receptors.<sup>1</sup>
- The activity on the 5-HT(1A) receptor was at least partly due to the presence of the aporphine alkaloid

Eschscholzia inhibits these pathways







Lloyd "Jamba" Scott 1937-2014



Jamaican Dogwood ("J dog"; Piscidia spp.) Photo: <u>www.EcoToursforCures.com</u> & Eileen Ruggiero

- Jamaican Dogwood was used by the ancient Arawaks & Maroons of Jamaica to stun fish prior to capturing; contains glycosides (Piscidin & Jamacin) & alkaloids (Erythraline)...
- Use with sciatic, neuralgia, toothaches menstrual cramps, acute sprains...
- Jamba taught me the Maroons often mixed it with Ganja as a topical poultice for pain and injury... {Bark used but eclectics used root bark}
- When he crossed over in 2014, Jamba was honored in HerbalGram for his contributions to herbal science...
- DrZ apprenticed with Jamba on over 30 trips to Jamaica since 1980 to learn about Jamaican herbs

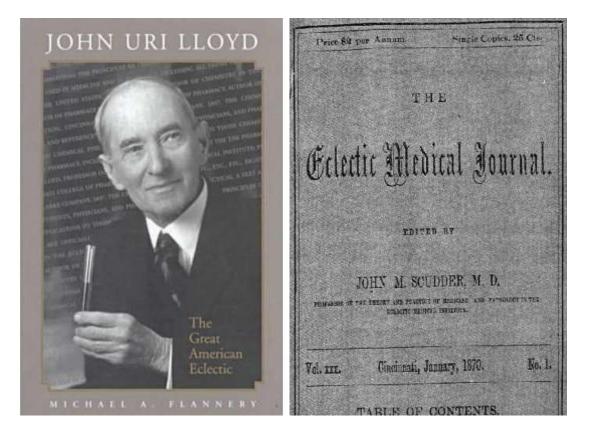
### Piscidia erythrina

Tincture workshop at Ecotours for Cures, Jamaica, WI



## The Eclectic MD's knew of and used Jamaican Dogwood for pain clinically over 100 years ago

- Used by M.D.'s in the late 1800's and early 1900's
- Popularized by Eclectic Physicians
- Use when opium was indicated, but could not be tolerated...
- Cancer pain, trigeminal pain, overcome spasm, sciatic, enteralgia, dysmenorrhea, the pain of fractures, neuralgia of the eyeball,
- It is also valuable to use in cough syrups instead of codeine to allay spasmodic coughs
- They used the 1:1 FE (1ml =1 gram JDog )
- Sig 60 drops FE prn Felter pp 548-49

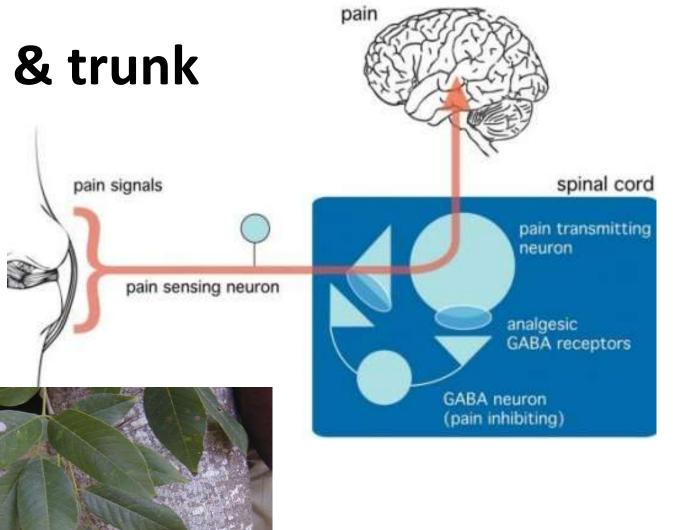


## **Piscidia erythrina** leaf & trunk

Photo by www.EcotoursForCures.com

- J Dog and Coral tree seem to work through GABA-A type receptors
- Modulate acetylcholine release, muscarinic receptor activation, augmentation of Ca2+ entry through L-type calcium channels, and calcium release from the intracellular stores.
- These findings provide further support for Piscidia & Erythrina's (next slide's)

traditional uses in tropical cultures





## **Erythrina spp.** (Coral tree, Mulungu, Hai Tong Pi)



- Erythrina, unlike its cousin Piscidia), is deciduous, although tropical in origin...
- It produces a profusion of pretty, reddish-orange flowers that are pollinated by hummingbirds at the ends of the tree's many branches. The tree is sometimes called "coral flower," as the flowers resemble the color of coral.
- It produces black seed pods containing large, red-and-black seeds, which are sometimes used by indigenous peoples to make necklaces and jewelry.
- Used topically and internally for pain and swelling in the joints and spasm and contraction of the muscles due to trauma or wind Cold Damp Invasion with Ramulus Cinnamoni cassiae.

## Molecular docking and analgesic studies of Erythrina variegata's derived phytochemicals with COX enzymes.

Author information

#### Abstract

Secondary metabolites from plants are a good source for the NSAID drug device appropriate doses noic extract of Erythrina variegata L. (Fabaceae) followed by molecular docking analysis. The analgesic activity of Erythrina variegata L. is evaluated by various methods viz., acetic acid-induced writhing test, hot plate and tail immersion test. Subsequently, molecular docking analysis has been performed to identify compounds having activity against COX-1 and COX-2 enzymes by using GOLD docking fitness. The result of preliminary phytochemical screening revealed that the extract contains alkaloids and flavonoids. In analgesic activity tests, the extract at the doses of 50, 100 and 200 mg/kg body weight (b.w.) produced a increase in pain threshold in a dose dependent manner. In acetic acid induced writhing test, the inhibitory effect was similar to the reference drug diclofenac sodium. The extract showed 18.89% writhing inhibitory effect at the dose 200 mg/kg b.w., whereas diclofenac sodium showed 79.42% inhibition of writhing at a dose of 10 mg/kg b.w. The results of tail immersion and hot plate test also showed potential analgesic activity of the extract which is also comparable to the standard drug morphine (5 mg/kg b.w.). Docking studies shows that phaseollin of Erythrina variegata L. has the best fitness score against the COX-1 which is 56.64 and 59.63 for COX-2 enzyme. Phaseollin of Erythrina variegata L. detected with significant fitness score and hydrogen bonding against COX-1 and COX-2 is reported for further validation.

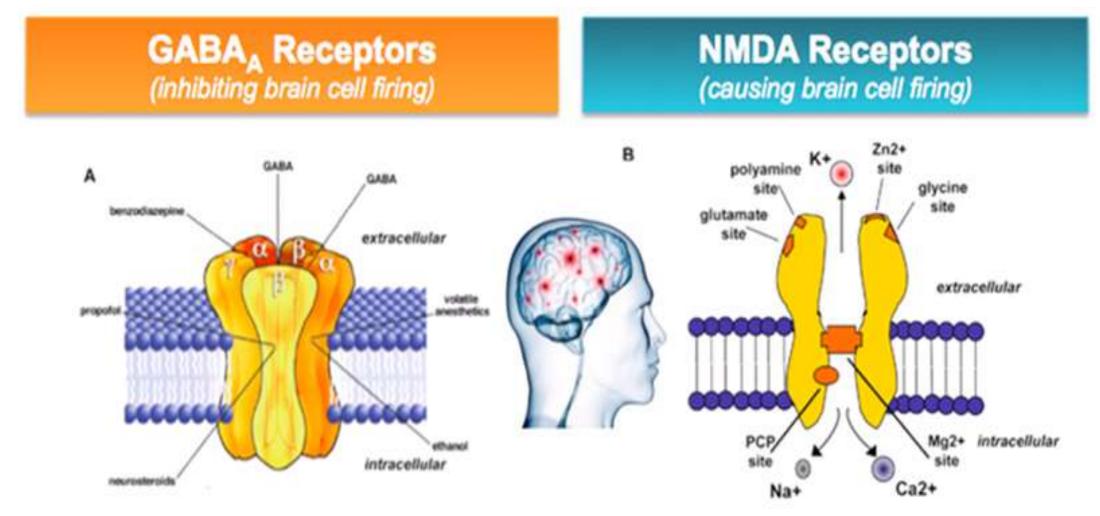
Comparable to morphine at the

KEYWORDS: Analgesic; COX-1; COX-2; Erythrina variegata L; GOLD; in silico drug discovery

PMID: 25489172 PMCID: PMC4248345 DOI: 10.6026/97320630010630

#### Free PMC Article

The effect of E. variegata against nociception induced by glutamate is of great interest since glutamate plays a significant role in nociceptive processing in both central and peripheral nervous systems [ref below].

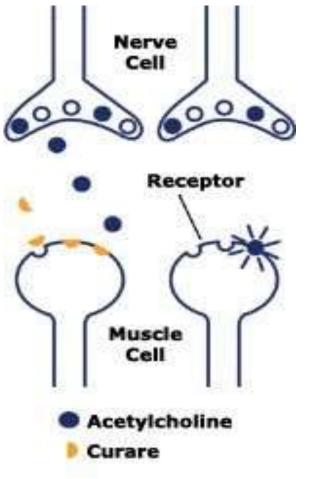


Ferreira J et al. Br J Pharmacol. 2004 141: 787 [PMID: 14967737 IMAGE:https://www.pinterest.com/pin/693202567613968840/

### **Erythrina spp.** variegata, mulungu, cristi-galli (Coral tree, Mulungu, Hai Tong Pi)

- Another alkaloid in mulungu (and other *Erythrina* plants), erysodine, has been documented with neuromuscular transitionblocking effects characteristic of curare...
- *Erythrina*; mulungu is documented with 20 isoquinoline alkaloids. Many of these have demonstrated piscicidal, anti-inflammatory, cardioactive, narcotic, and hypnotic activities.
- Researchers reported that mulungu extracts had an effect similar to the commonly-prescribed anti-anxiety drug diazepam.
- I use the 5:1 extract granules Called Hai Tong Pi available at many TCM apothecaries and on-line
- Make sure patient's try a little (1/8 tsp of the 5:1) as it is incredibly powerful
- I brought some if folks want to try some in their water





## Ghost pipe Monotropa uniflora

COMMON NAMES: Ice-plant, Bird's nest, Fit-plant, Ova-ova, Pipe-plant, etc.



- Ghost pipe lacks chlorophyll so it cant photosynthesize
- It taps into fungal mycorrhizae which have taped into living tree roots and parasitizes nutrients from both fungi and tree
- Also called corpse plant

# Older references to the plant in antiquarian medical literature....

- "…Instead of employing opium for restlessness, pain, nervous irritation etc, Bird's nest (Ghost pipe) is effective without any dulling properties.."Hutchens; Indian Herbology of North America, pg 39 1969
- "Action, Medical Uses, and Dosage.—Ice-plant root is a tonic, sedative, nervine, and antispasmodic. It has also been employed in *febrile diseases*, as a sedative and diaphoretic. The powder has been employed in instances of restlessness, pains, nervous irritability, etc., as a substitute for opium, without any deleterious influences..."
  - From King's American dispensary, pg 606



(photo credit US forest Service)

## From David Winston, AHG

DrZ in his clinic uses: Equal parts of 1:2 tinctures Monotropa Corydalis Piscidia Erythrina (use 6:1) **Eschscholzia** Albizzia DOSE: 60 gtt prn

"...It was used by native Americans and the Eclectic physician's for pain. It's action is similar in effect to Nitrous Oxide at the dentist, you are conscious and aware of pain, but distant from it, you know that it hurts, but simply don't care. The term that is used for this is antinociceptive, which means something that reduces sensitivity and threshold to painful stimuli. So Monotropa is primarily an antinociceptive, it raises the pain threshold. It is a very effective medicine combined 50/50 with Corydalis for cancer pain..." Winston, D Herbal therapeutics.net 10th edition page 130,2013

## **Supplements for Pain**

## Sales and Book Signing at Restorative Formulations booth after presentations