Metagenics®

Genetic Potential Through Nutrition

Synergistic Solutions for Pain, Stress & Hormones

Combining Chiropractic Care and Natural Medicines for Better Patient Outcomes

Erica Smith. BHSc (Comp Med), AdvDipNat, AdvDipMedHerb.
Dr Andrea Huddleston. MRepMed, MWomHMed, BSc Chiro, B Chiro.

1

Complex chronic pain and suffering

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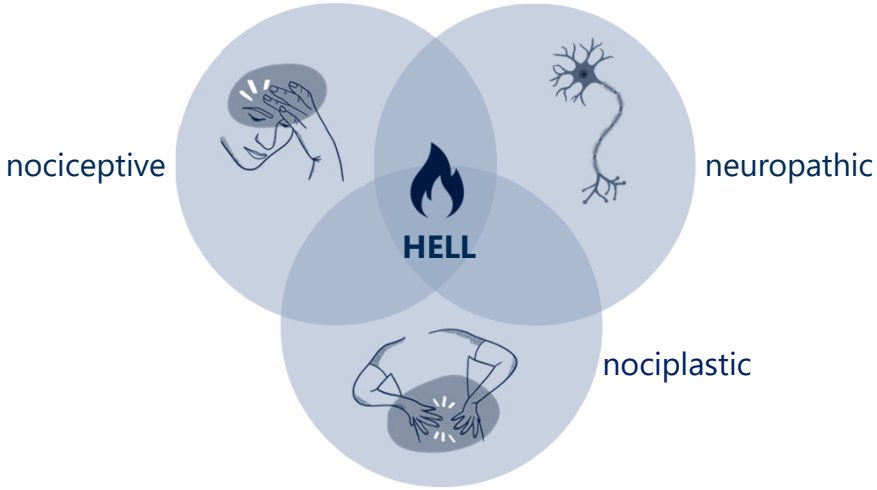
Chronic pain is complicated and complex



Ingraham P. The three basic types of pain. 2019 [Internet] https://www.painscience.com/articles/pain-types.php

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Complex chronic presentation

- Pain persists >3 months
- Associated with distress and/or disability

Clinical challenges:

- Severity disproportionate to the underlying cause
- Exaggerated by coexisting conditions
- Prescription medication risks

Treede RD, et al. Pain. 2019;160(1):19-27. doi: 10.1097/j.pain.0000000000001384;
Geneen LJ, et al. Cochrane Database Syst Rev. 2017;4(4):CD011279. doi: 10.1002/14651858.CD011279.pub3;
Mao J. BMJ. 2017 Feb 17;356:j741. doi: 10.1136/bmj.j741

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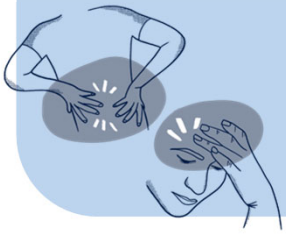
Each journey to chronic pain is complex



Injury/infection evolves to **complex disease state** — e.g. Sprain → complex regional pain syndrome, Shingles → post-herpetic neuralgia

A symptom of underlying degenerative disease — e.g. Osteoarthritis, spinal stenosis, compression fractures

Primary sign of condition — e.g. Fibromyalgia, trigeminal neuralgia

Mao J. BMJ. 2017 Feb 17;356:j741. doi: 10.1136/bmj.j741

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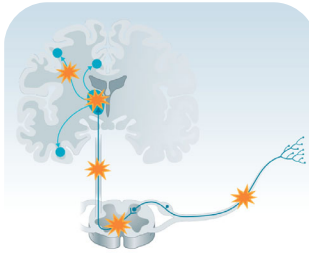
Chronic pain amplification



Hyperactivated non-neuronal cells;
Mast cells
Astrocytes
Microglia

Neuroinflammation
Pain neurotransmission
Pain sensitivity

Opioid receptors

Central sensitisation

Nociplasticity:
Cells that fire together, wire together

Finnerup NB, et al. Physiological reviews. 2021;101(1):259-301. doi.org/10.1152/physrev.00045.2019;
Petrosino S, et al. Int J Mol Sci. 2020;21(24):9526. doi: 10.3390/ijms21249526

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Medical pain management

Medication	Indications	Risks/adverse effects
Paracetamol	Mild – moderate pain, fever, or with other analgesia for stronger pain.	**Rare:** Allergic reaction (rash or swelling), blood disorders. High doses may cause liver and kidney damage.
NSAIDs	Pain, inflammation, fever (headache, menstrual cramps, muscle strain).	**Common:** Nausea, indigestion. **Less common:** May cause gastrointestinal (GI) bleeding, kidney problems, asthma.
Antiepileptics e.g. gabapentin	Nerve pain (neuralgia), fibromyalgia.	**Gabapentin:** Light-headedness, tired or drowsy, unusually overactive, agitation, change in weight, constipation, diarrhoea.
Antidepressants e.g. SSRIs	Depression, grief, Post traumatic stress disorder (PTSD).	**SSRIs:** Nausea, vomiting, diarrhoea, altered appetite, sleep problems, anxiety, dizziness, fever, joint aches, sexual problems.
Opioids e.g. morphine, tramadol	Severe acute pain (post-surgery or injury), chronic pain with cancer.	**Common:** Nausea, vomiting, constipation, drowsiness. **Risks:** Dependence, accidental overdose, hospitalisation and death.
Muscle relaxants e.g. orphenadrine	Muscle spasm associated with fibrositis, whiplash injuries, prolapsed disc, headache, hiccups.	**Common:** Dry mouth. **Less common or rare:** GI cramps, constipation, blurred vision, confusion, light-headed, fatigue, headache, muscle weakness, dilated pupils.
Corticosteroids e.g. prednisolone	Chronic inflammation (e.g. arthritis).	**Common:** Insomnia, weight gain, indigestion, hyperhidrosis.

SSRI: Selective serotonin reuptake inhibitor

Health Direct. Pain relief medications. [Internet]. Available from: https://www.healthdirect.gov.au

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Medical pain management

O'Connor AB. Pharmacoeconomics. 2009;27(2):95-112. doi: 10.2165/00019053-200927020-00002

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Why prescribe complementary medicine supplements?

Naturally:

1. Reduce reliance on medical analgesia
2. Assist healing and tissue restoration
3. Offer health-conscious alternatives
4. Support between visits
5. Amplify patient outcomes

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What's the alternative?

A better analgesic relieves pain and improves a patient's overall quality of life,

without

risking serious adverse effects

or the potential for abuse.

Eke-Okoro UJ, et al. J Clin Pharm Ther. 2018 Aug;43(4):460-466. doi: 10.1111/jcpt.12703

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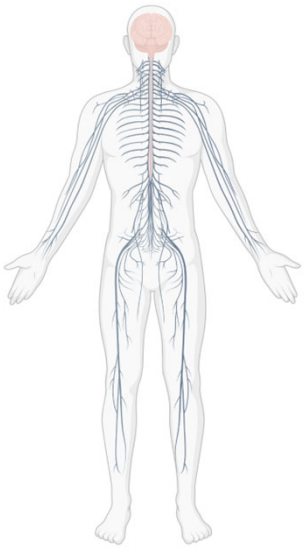
Chiropractic adjustment pain pathways



Supraspinal

- Changes in pain-related brain activity
- Activation of descending inhibitory systems

Spinal mechanisms

- Inhibition of central sensitisation
- Inhibition of temporal summation
- Segmental inhibition of nociceptive practices

Peripheral mechanisms

- Decreased inflammatory cytokine response
- Decreased peripheral oxidative stress

Adapted from: Gevers-Montoro C, et al. Eur J Pain. 2021; 25(7):1429-1448. doi: 10.1002/ejp.1773;
Image created by Biorender.com

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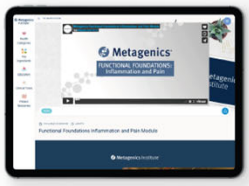
What Metagenics offers chiropractors

TruQuality™

Metagenics Institute™



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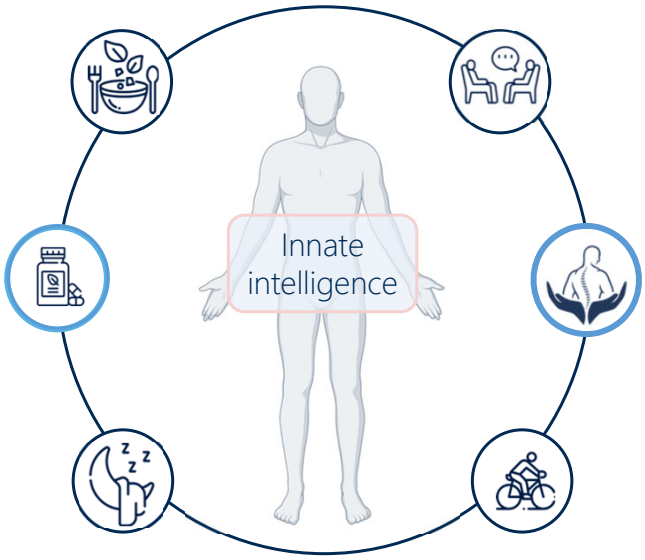
Natural medicines and chiropractic care enhance patient outcomes



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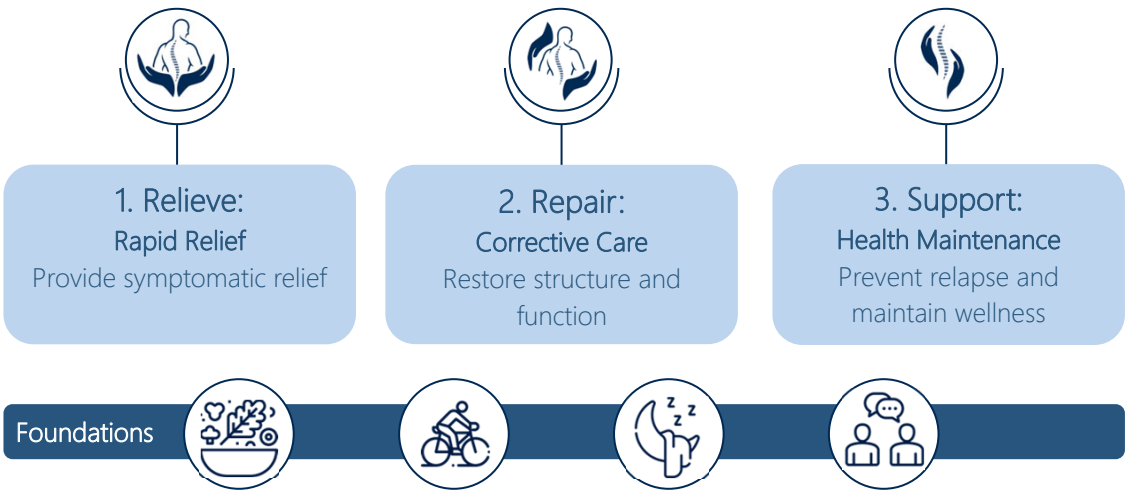

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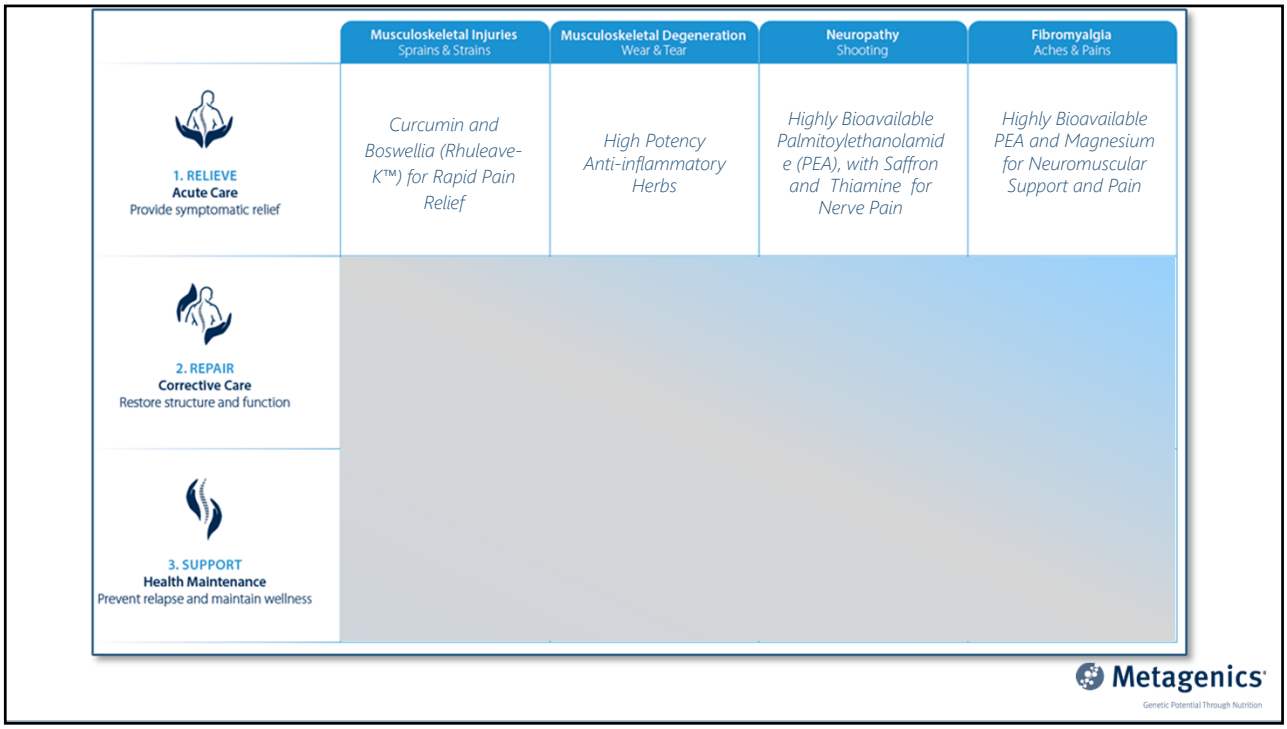
Musculoskeletal Injuries
Sprains & Strains
Musculoskeletal Degeneration
Wear & Tear
Neuropathy
Shooting
Fibromyalgia
Aches & Pains
1. RELIEVE
Acute Care
Provide symptomatic relief
Curcumin and Boswellia (Rhuleave-K™) for Rapid Pain Relief
High Potency Anti-inflammatory Herbs
Highly Bioavailable Palmitoylethanolamide (PEA), with Saffron and Thiamine for Nerve Pain
Highly Bioavailable PEA and Magnesium for Neuromuscular Support and Pain
2. REPAIR
Corrective Care
Restore structure and function
3. SUPPORT
Health Maintenance
Prevent relapse and maintain wellness
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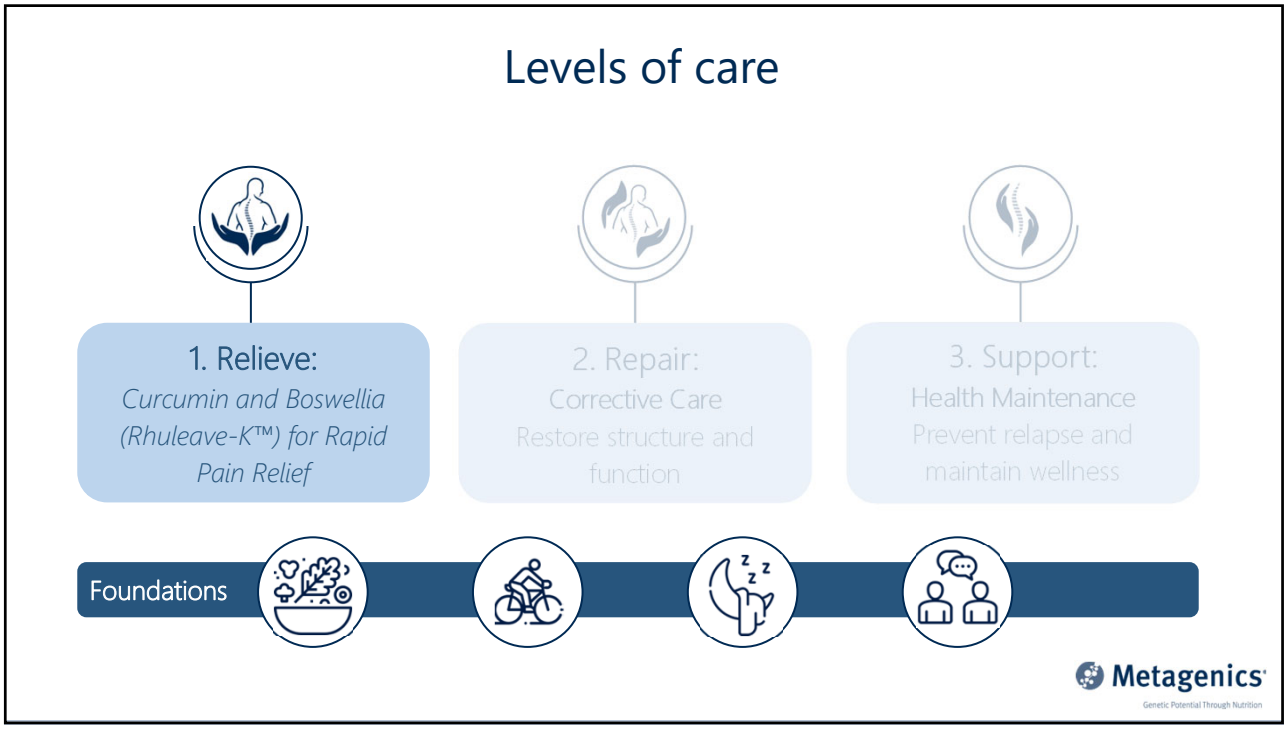
Levels of care
1. Relieve:
Curcumin and Boswellia (Rhuleave-K™) for Rapid Pain Relief
2. Repair:
Corrective Care
Restore structure and function
3. Support:
Health Maintenance
Prevent relapse and maintain wellness
Foundations
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COMPARATIVE RISK ASSESSMENT	NSAIDs	Paracetamol
Safe upper daily limits	**Always check label:** e.g., Ibuprofen: 1,200 mg/d; Aspirin: 4,000 mg/d	**Always check label:** e.g., Adult: 650-1,000 mg every 4-6 hrs. Do not exceed 4 g/d
Acute toxicity (overdose)	Adult: > 6 g dose → Risk of GI bleed, MI, stroke	Adult: 7.5-10 g/d → 4 stages of toxicity
Increased risks with chronic use (i.e. >3 doses weekly for longer than 3 months)	• GI mucosal erosion/bleeding • CV, hepatic, renal and haematologic risks • Multiple drug interactions • Paracetamol: in-utero neuro-development risks	
Contraindications (typical – always check label)	• Salicylate hypersensitivity • Severe hepatic or renal dysfunction • Third trimester of pregnancy	• Paracetamol hypersensitivity • Severe hepatic or renal dysfunction

Abbreviations: mg/d or g/d: Milligrams or grams per day; GI: Gastrointestinal; MI: Myocardial infarction; CV: Cardiovascular.

References on next slide

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COMPARATIVE RISK ASSESSMENT	NSAIDs	Paracetamol	Curcumin / Boswellia
Safe upper daily limits	**Always check label:** e.g., Ibuprofen: 1,200 mg/d; Aspirin: 4,000 mg/d	**Always check label:** e.g., Adult: 650-1,000 mg every 4-6 hrs. Do NOT exceed 4 g/d	Curcumin: 12 g/d Boswellia: 1,000 mg/d
Acute toxicity (overdose)	Adult: > 6 g dose → Risk of GI bleed, MI, stroke	Adult: 7.5-10 g/d → 4 stages of toxicity	No toxicity known. May induce mild GI symptoms e.g., nausea
Increased risks with chronic use (i.e. >3 doses weekly for longer than 3 months)	• GI mucosal erosion/bleeding • CV, hepatic, renal and haematologic risks • Multiple drug interactions • Paracetamol: in-utero neuro-development risks		No ill effects of chronic use reported
Contraindications (typical – always check label)	• Salicylate hypersensitivity • Severe hepatic or renal dysfunction • Third trimester of pregnancy	• Paracetamol hypersensitivity • Severe hepatic or renal dysfunction	• Allergy/hypersensitivity • Avoid boswellia in pregnancy • *Caution* with anti-platelet medications

References on next slide

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Comparative risk assessment

- Turmeric. In: Natural Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1995-2018 [updated 2021 Jun 15; cited 2021 Jun 30]. Available from: http://www.naturaldatabase.com. Subscription required to view.
- Boswellia. In: Natural Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1995-2018 [updated 2017 Jul 11; cited 2018 Jul 17]. Available from: https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=63. Subscription required to view.
- Ghlichloo I, Gerriets V. Nonsteroidal anti-inflammatory drugs (NSAIDs) [Updated 2022 May 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK547742/
- Agrawal S, Khazaeni B. Acetaminophen toxicity. [Updated 2022 Apr 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441917/
- McCrae JC, Morrison EE, MacIntyre IM, et al. Long-term adverse effects of paracetamol - a review. Br J Clin Pharmacol. 2018 Oct;84(10):2218-2230. doi: 10.1111/bcp.13656

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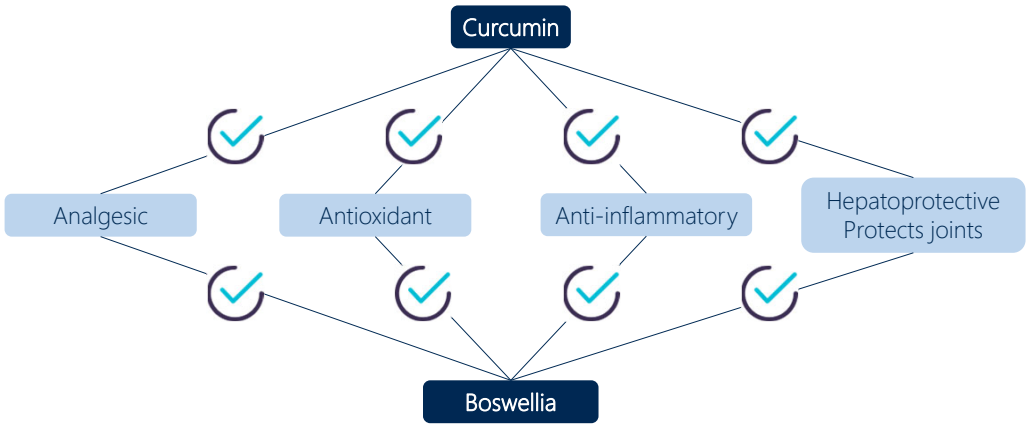
Synergistic partners in pain relief



Haroyan A, et al. BMC Complement Altern Med. 2018;18(1):7. doi: 10.1186/s12906-017-2062-z;
Mahdian D, et al. Iran J Basic Med Sci. 2020;23(11):1374-1381. doi: 10.22038/ijbms.2020.42115.9957

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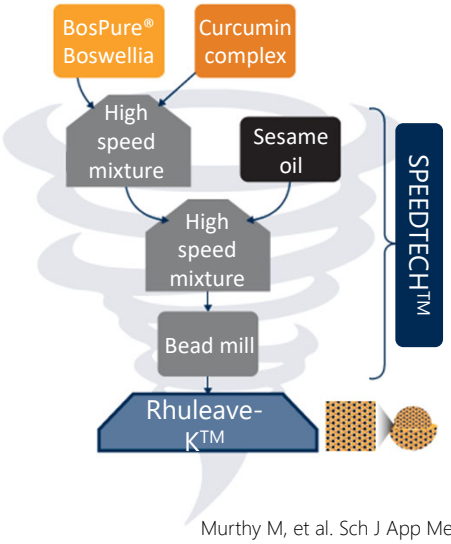
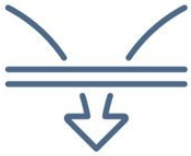
SPEEDTECH™ ensures rapid relief



Lipid matrix

Micronisation

SPEEDTECH™ absorption



Time efficient
Starts to work in 1 hour

Murthy M, et al. Sch J App Med Sci. 2022 Mar;3:311-26. doi:10.36347/sjams.2022.v10i03.008

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Rhuleave-K™ for acute pain

n=232
exercise-induced musculoskeletal pain
~80% pain

Murthy M, et al. Sch J App Med Sci. 2022 Mar;3:311-26. doi:10.36347/sjams.2022.v10i03.008

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Rhuleave-K™ for acute pain

n=232
exercise-induced
musculoskeletal pain
~80% pain

Rhuleave-K™
1,000 mg dose

or

Placebo

Every 30m
over 6h

Murthy M, et al. Sch J App Med Sci. 2022 Mar;3:311-26. doi:10.36347/sjams.2022.v10i03.008

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23

Rhuleave-K™ for acute pain

n=232
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Placebo

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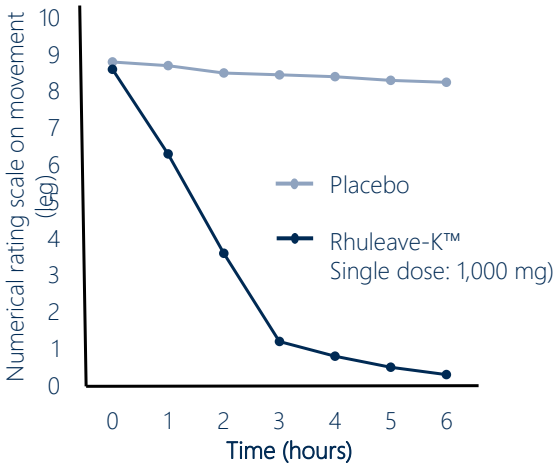

Murthy M, et al. Sch J App Med Sci. 2022 Mar;3:311-26. doi:10.36347/sjams.2022.v10i03.008

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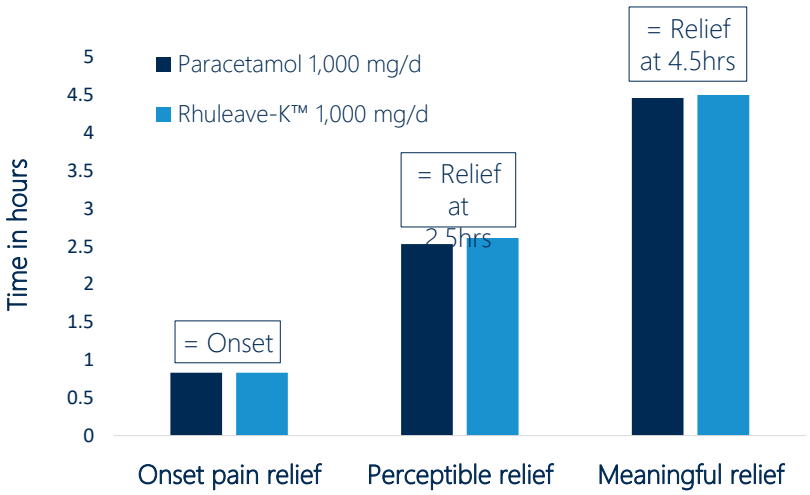
Head-to-head with paracetamol

n = 88
exercise-induced
musculoskeletal pain



Rudrappa GH, et al. Medicine (Baltimore). 2020 Jul 10;99(28):e20373. doi: 10.1097/MD.0000000000020373

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A sense of (pain) relief

Rhuleave-K™
reduced affective score **8.57 times**
more effectively than paracetamol*

Statistically significant (p = 0.027).

*as measured on McGill pain questionnaire

Rudrappa GH, et al. Medicine (Baltimore). 2020 Jul 10;99(28):e20373. doi: 10.1097/MD.0000000000020373

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Curcumin and Boswellia (Rhuleave-K™) for Rapid Pain Relief

Ingredients

Curcumin

Boswelia serrata (Bospure® Boswellia)

(Rhuleave-K™)

Clinical applications:
- Soft tissue injury (sprains, strains)
- Musculoskeletal pain
- Headaches
- Period pain
- Add on for chronic pain/pain flare ups

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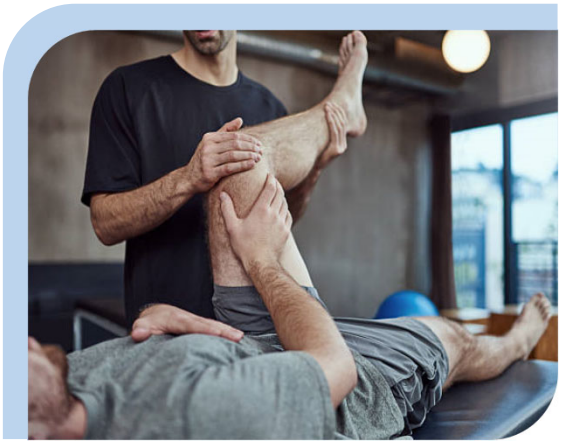
Curcumin and Boswellia (Rhuleave-K™) for Rapid Pain Relief



Clinical Applications
- Acute soft tissue injury (sprains, strains)
- Musculoskeletal pain
- Headaches
- Period pain
- Add on for chronic pain/pain flare ups

Plus:
- Delayed onset muscle soreness (DOMS)
- Dental pain
- Post-surgical recovery

→ *Whenever rapid pain relief is required*

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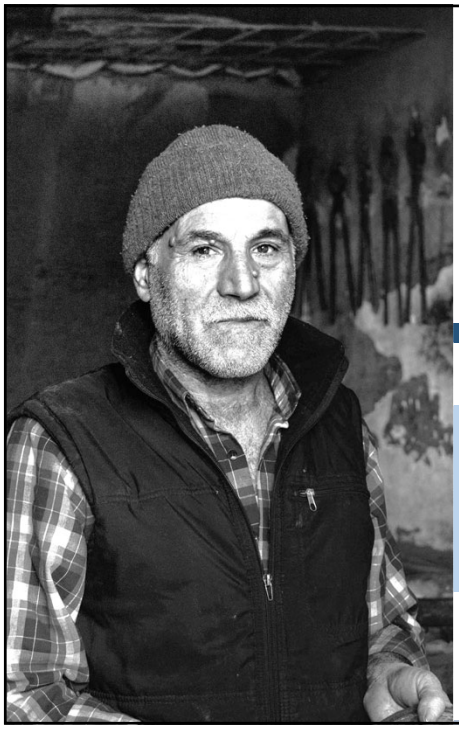

Clinical feedback

David* was hospitalised with lung inflammation and COVID-related breathing problems.

He was sent home to self-manage with NSAIDs and Paracetamol. Instead, he took ***Curcumin and Boswellia (Rhuleave-K™) for Rapid Pain Relief*** and within two days he was feeling 80% better.

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* Name changed for confidentiality purposes

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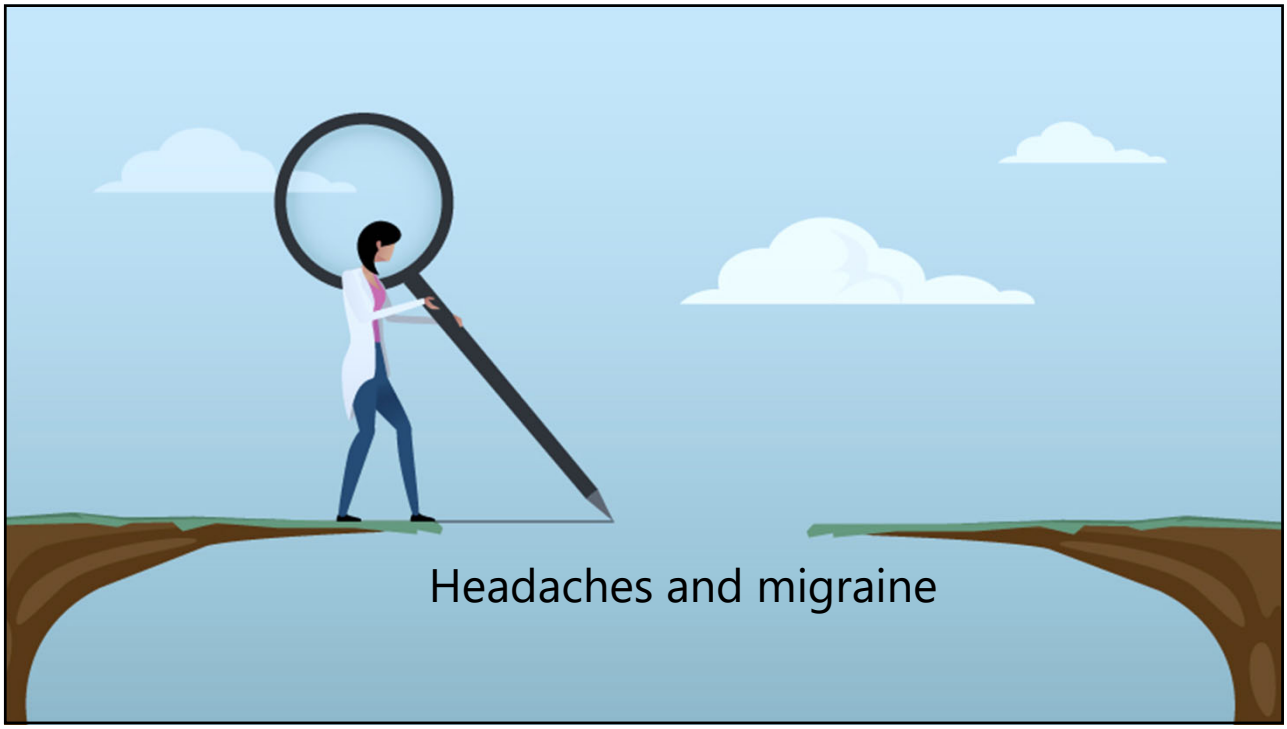

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Hormones & Pain

Major pain control mechanisms are present in the steroidogenic pathway

These hormones regulate:

- Immune modulation
- Anti-inflammatory actions
- Cell protection
- Tissue regeneration
- Glucose control
- Modulation of the CNS receptors
- Nerve conduction

Aloisi, A. M., & Bonifazi, M. 2006. Sex hormones, central nervous system and pain.Hormones and Behavior, 50(1), 1-7. https://doi.org/10.1016/j.yhbeh.2005.12.002

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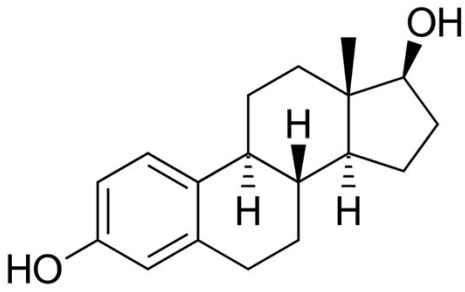
Oestrogen



Oestrogen influences pain processing

Excessive, unregulated oestrogen:

- Higher pain responses
- Inflammatory cascades
- Autoimmune diseases

Aloisi, A. M., & Bonifazi, M. 2006. Sex hormones, central nervous system and pain.Hormones and Behavior, 50(1), 1-7. https://doi.org/10.1016/j.yhbeh.2005.12.002

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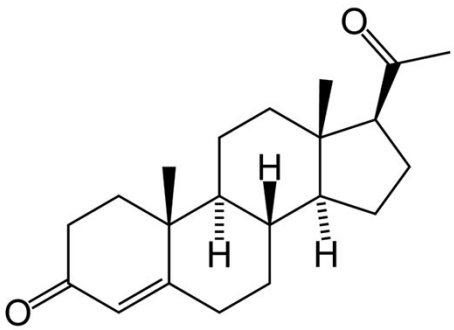
Progesterone



Progesterone influences pain processing

Progesterone:

- Dampens inflammation
- Inhibits pro-inflammatory cytokines
- Promotes cellular repair
- Neuroprotective role

Hall, O., Klein, S. Progesterone-based compounds affect immune responses and susceptibility to infections at diverse mucosal sites. *Mucosal Immunol* **10**, 1097–1107 (2017).

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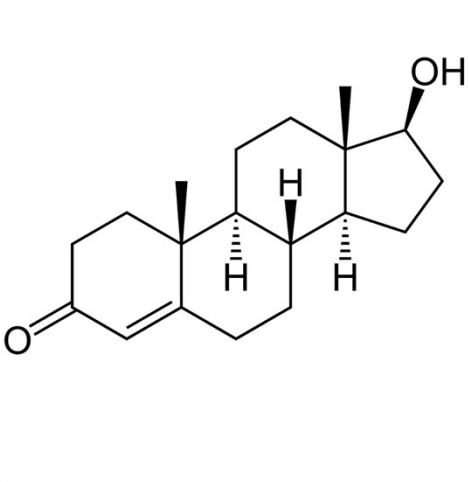
Testosterone



Testosterone influences pain processing

Testosterone:

- Anti-nociceptive
- Downregulates oestrogen receptors
- Decreases pain sensitivity
- Opioids suppress testosterone

Basaria, Shehzad et al. "Effects of testosterone replacement in men with opioid-induced androgen deficiency: a randomized controlled trial." *Pain* vol. 156,2 (2015): 280-288.

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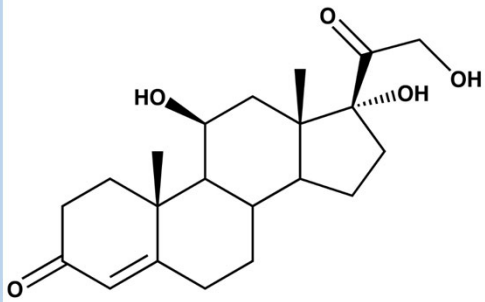
Cortisol



Cortisol influences pain processing

Cortisol:

- Different influences in acute and chronic pain
- Unmodulated inflammation
- Conditions the patient to a sensitised physiological response to pain
- Increases visceral pain

Hannibal KE, Bishop MD. Chronic stress, cortisol dysfunction, and pain: a psychoneuroendocrine rationale for stress management in pain rehabilitation. *Phys Ther*. 2014;94(12):1816-1825.

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Aaron's Story

Aaron, 41, firefighter
*shared with permission

- Congenital adrenal hyperplasia
- L5/S1 Disc Herniation
- Chronic, debilitating pain
- Low testosterone
- Elevated oestradiol
- Unrelenting stress

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"Hormone levels are biomarkers of chronic pain"

- Tennant, 2011

Tennant, F. 2011. Hormone therapies: newest advance in pain care. Practical Pain Management 11:98–105.

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Hormonal migraines

Menstrual headaches & migraines are different

- Typically, more severe
- More resistant to conservative measures
- More resistant to analgesics
- Tend to last longer

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Hormonal migraines

Why are they so complex?

Dr Andrea

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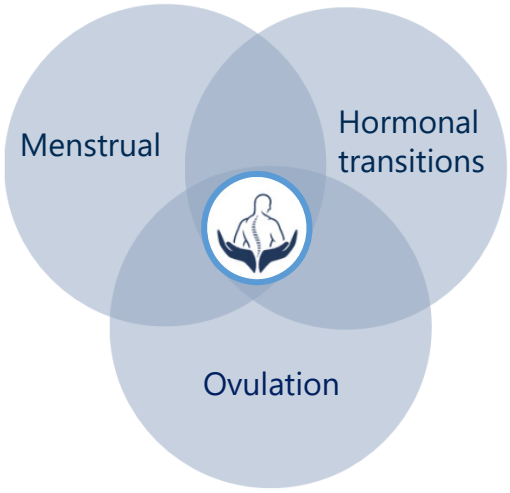
Types of hormonal migraines



Dr Andrea

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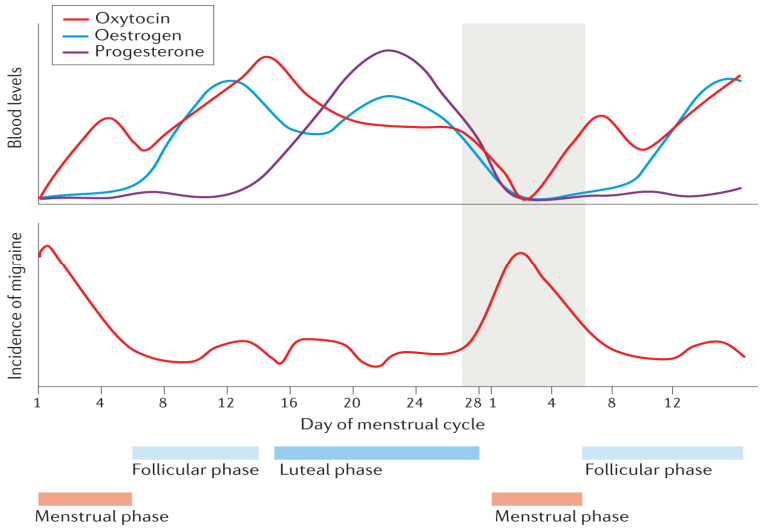
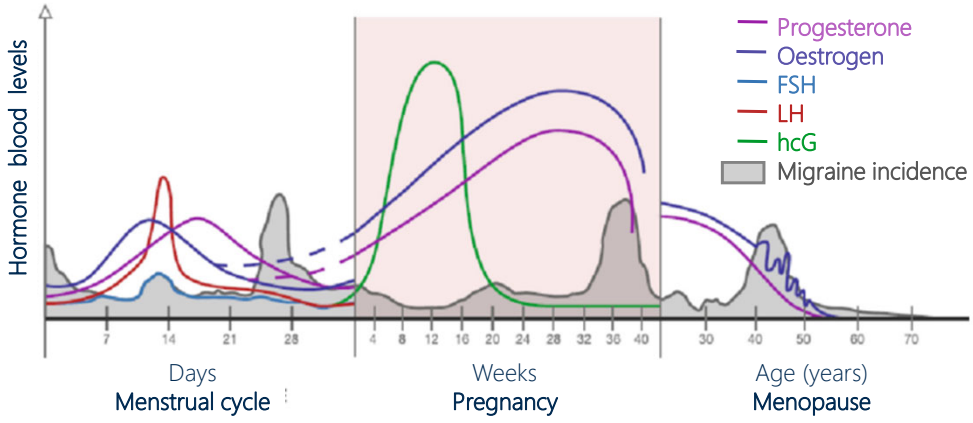
Cyclic hormonal dips can trigger migraine



Krause DN, et al. Nat Rev Neurol. 2021;17(10):621-633. doi: 10.1038/s41582-021-00544-2.

41

Hormonal dips can trigger migraine



Afridi SK. Migraine: navigating the hormonal minefield. Pract Neurol. 2020 Apr;20(2):115-121. doi: 10.1136/practneurol-2019-

42

Perimenopausal distress

Fluctuating oestrogen levels

Shorter menstrual cycles

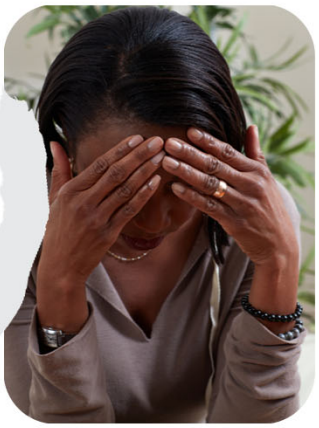
Hormonal fluctuations

Heavier menstruation, leading to iron deficiency

Increased prostaglandins

Disrupted sleep

Severe headaches



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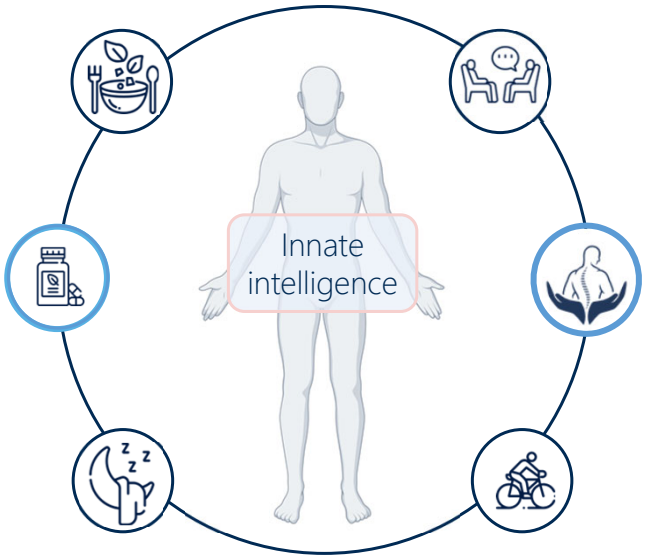
Management strategies



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Women's health support

1. Relieve:
Acute Care
Provide symptomatic relief

2. Repair:
Corrective Care
Restore structure and function

3. Support:
Health Maintenance
Prevent relapse and maintain wellness

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Balancing hormones for migraines

	Soy, Methylating Nutrients and BCM-95™ Turmeric to Clear Oestrogen	*Vitex, Ginger and Withania to Increase Progesterone*	*Oestrogen Lifting Herbs*
	Supports normal hormonal detoxification and oestrogen metabolism.	Relieves premenstrual symptoms. Reduces menstrual irregularity.	Manages menopausal symptoms. Supports female hormonal balance during menopause.
Consider for:	*Menstrual migraine*	*Perimenopausal migraine*	*Menopausal migraine*

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Vitex, Ginger and Withania to Increase Progesterone

Ingredients

- *Withania somnifera*
- *Vitex agnus-castus*
- *Zingiber officinale*
- Vitamin B6 (Pyridoxine hydrochloride)
- Vitamin E (Tocopherols concentrate – mixed (low alpha type))
- Zinc (Zinc amino acid chelate; Meta Zn® - Zinc bisglycinate)

Clinical applications

- Perimenopausal migraine
- Premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD)
- Subclinical hypothyroidism

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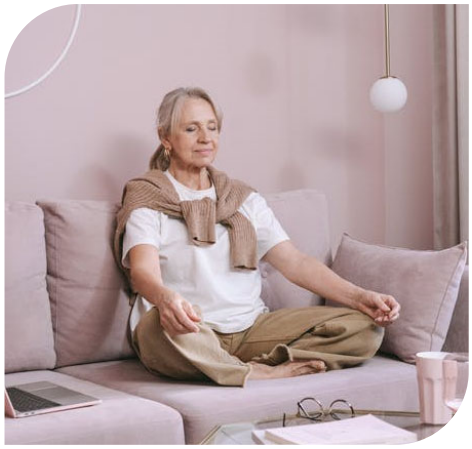
Oestrogen Lifting Herbs



Ingredients

- *Rehmannia glutinosa* (Rehmannia)
- *Cornus officinalis* (Asiatic cornelian cherry)
- *Dioscorea oppositifolia* (Chinese yam)
- *Ziziphus jujuba var. spinosa* (Zizyphus)
- *Paeonia suffruticosa* (Tree peony)
- *Poria cocos* (Poria)
- *Alisma orientale* (Water plantain)
- *Anemarrhena asphodeloides* (Anemarrhena)

Clinical applications

- Menopausal symptoms

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Magnesium for migraine

600 mg/day of magnesium
decreases migraine severity and frequency

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Nattagh-Eshtivani E, et al. Biomed Pharmacother. 2018 Jun;102:317-325. doi: 10.1016/j.biopha.2018.03.059

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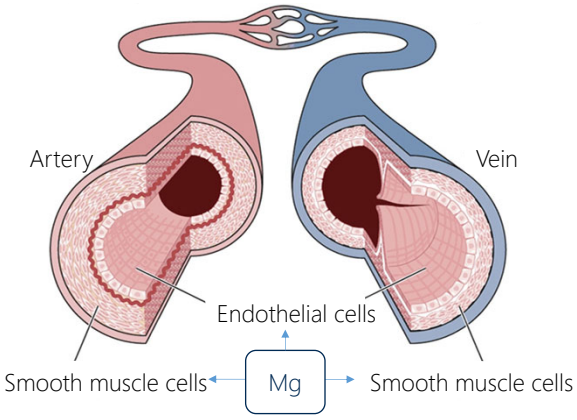
Magnesium is required for neuromuscular, circulatory and nervous systems



Mg regulates:
- Endothelial function
- Vasodilation (smooth muscle)
- Skeletal muscle contraction
- Inflammatory tone
- Nerve transmission
- Neuromuscular conduction
- Blood pressure

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Gröber U, et al. Nutrients. 2015;7(9):8199-226. doi: 10.3390/nu7095388

50

Highly Bioavailable PEA and Magnesium for Neuromuscular Support and Pain

Ingredients

Meta Mag® - magnesium bisglycinate

Palmidrol (PEA – Palmitoylethanolamide) (Levagen+™)

Clinical applications:

- Neuromuscular pain
- Chronic jaw pain and lower back pain
- Migraine and headaches
- Fibromyalgia

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Choosing the right magnesium for your patient

STRESS

- Healthy stress response
- Nervous system support

- 350 mg Meta Mag® Magnesium
- 3 g Taurine
- 2 g Glutamine
- 275 mg Potassium citrate

ENERGY

- Mental fatigue
- Physical fatigue

- 200 mg Meta Mag® Magnesium
- 1.2 g Acetyl-L-Carnitine
- 1 g Tyrosine
- Selenium, iodine and zinc

SLEEP

- Healthy sleeping patterns and sleep quality
- Restores circadian rhythm

- 300 mg Meta Mag® Magnesium
- Lutein and Zeaxanthin
- 400 mg Ornithine
- Sensoril™ Ashwagandha

PAIN

- Pain relief
- Neuromuscular function

- 210 mg Meta Mag® Magnesium
- 300 mg PEA (Palmitoylethanolamide) (Levagen+™)

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Magnesium for neuromuscular pain

Condition	Mg dose/form	Duration	Outcome
Muscle cramps during pregnancy (n=86)	300 mg/d Mg diglycinate	4 weeks	**Reduced leg cramp frequency and intensity by 50%.** Significantly more effective than placebo ($p<0.05$).
Chronic leg cramps (n=29)	300 mg/d Mg citrate	6 weeks	**Reduced leg cramps by 78%**, compared to 54% in placebo ($p<0.30$).
Fibromyalgia (n=60)	300 mg/d Mg citrate	8 weeks	Tender points reduced from 15/18 to 12/18 ($p<0.032$). **FIQ scores reduced from 35.41** to **23.64** ($p<0.008$).
Migraine (n=30)	600 mg/d Mg citrate	12 weeks	**Reduced migraine frequency 33%** vs placebo 16% ($p<0.005$). **Reduced migraine intensity 47%** vs placebo 0% ($p<0.001$).
Migraine (n=81)	600 mg/d Mg citrate	12 weeks	From week 9, **migraine frequency reduced 41.6%** vs placebo 15.8% ($p<0.05$). Magnesium group had fewer days with migraines and reduced use of pharmaceutical relief ($p<0.025$).

References on next slide

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53

Magnesium for neuromuscular pain

- Supakatisant C, et al. Oral magnesium for relief in pregnancy-induced leg cramps: a randomised controlled trial. Matern Child Nutr. 2015 Apr;11(2):139-45. doi: 10.1111/j.1740-8709.2012.00440.x
- Roffe C, et al. Randomised, cross-over, placebo-controlled trial of magnesium citrate in the treatment of chronic persistent leg cramps. Med Sci Monit. 2002;8(5):CR326-330
- Bagis S, et al. Is magnesium citrate treatment effective on pain, clinical parameters and functional status in patients with fibromyalgia? Rheumatol Int. 2013 Jan 1;33(1):167-72
- Köseoglu E, et al. The effects of magnesium prophylaxis in migraine without aura. Magnes Res. 2008 Jun 1;21(2):101-8
- Peikert A, et al. Prophylaxis of migraine with oral magnesium: results from a prospective, multi-center, placebo-controlled and double-blind randomized study. Cephalalgia. 1996 Jun;16(4):257-63

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Levels of care

1. Relieve:

Highly Bioavailable PEA and Magnesium for Neuromuscular Support and Pain

2. Repair:

Corrective Care

Restore structure and function

3. Support:

Health Maintenance

Prevent relapse and maintain wellness

Foundations

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Fibromyalgia

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PEA for fibromyalgia

n = 359

	Baseline	Clinical protocol (15 months)			Outcomes
Pain (VAS)	75.84	10 days	20 days	14 months	**52.49** (p<0.001)
Quality of Life (FIQ)	68.4	1,800 mg/d PEA	1,200 mg/d PEA	600 mg/d PEA	**49.1** (p<0.001)

VAS: Visual analogue scale
FIQ: Fibromyalgia impact questionnaire

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Schweiger V, et al. CNS Neurol Disord Drug Targets. 2019;18(4):326-333. doi: 10.2174/1871527318666190227205359

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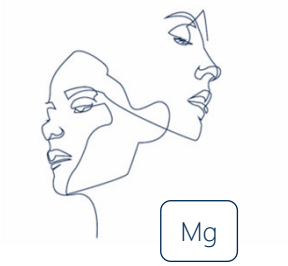
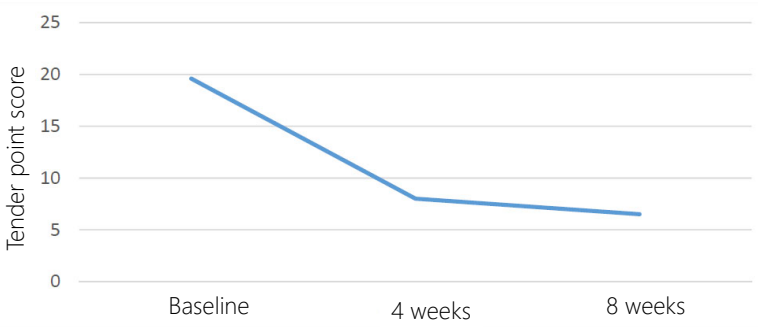
600 mg/d of magnesium reduces tender point scores



Mg

Significant improvement in myalgia within 48 hours



Daily dose of 600 mg/d magnesium + 2,400 mg/d malic acid

(n=15)

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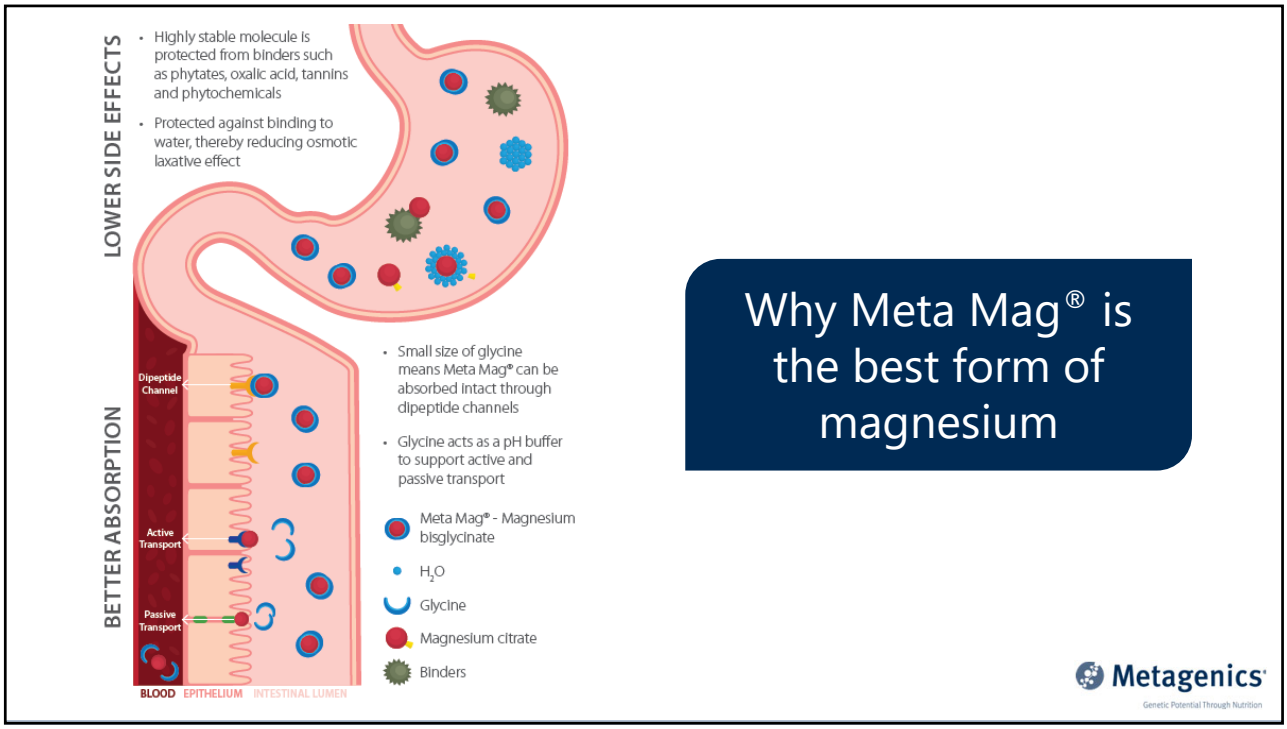
Abraham GE, et al. J Nutr Med. 1992;3:49-59. doi:

58


LOWER SIDE EFFECTS
Highly stable molecule is protected from binders such as phytates, oxalic acid, tannins and phytochemicals
Protected against binding to water, thereby reducing osmotic laxative effect
BETTER ABSORPTION
Dipeptide Channel
Active Transport
Passive Transport
BLOOD
EPITHELIUM
INTESTINAL LUMEN
Small size of glycine means Meta Mag® can be absorbed intact through dipeptide channels
Glycine acts as a pH buffer to support active and passive transport
Meta Mag® - Magnesium bisglycinate
H_2O
Glycine
Magnesium citrate
Binders
Why Meta Mag® is the best form of magnesium
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Matthew*,
Case study
48
Presenting with back pain since accident 30 years ago
* Name changed for confidentiality purposes
MetaClinic

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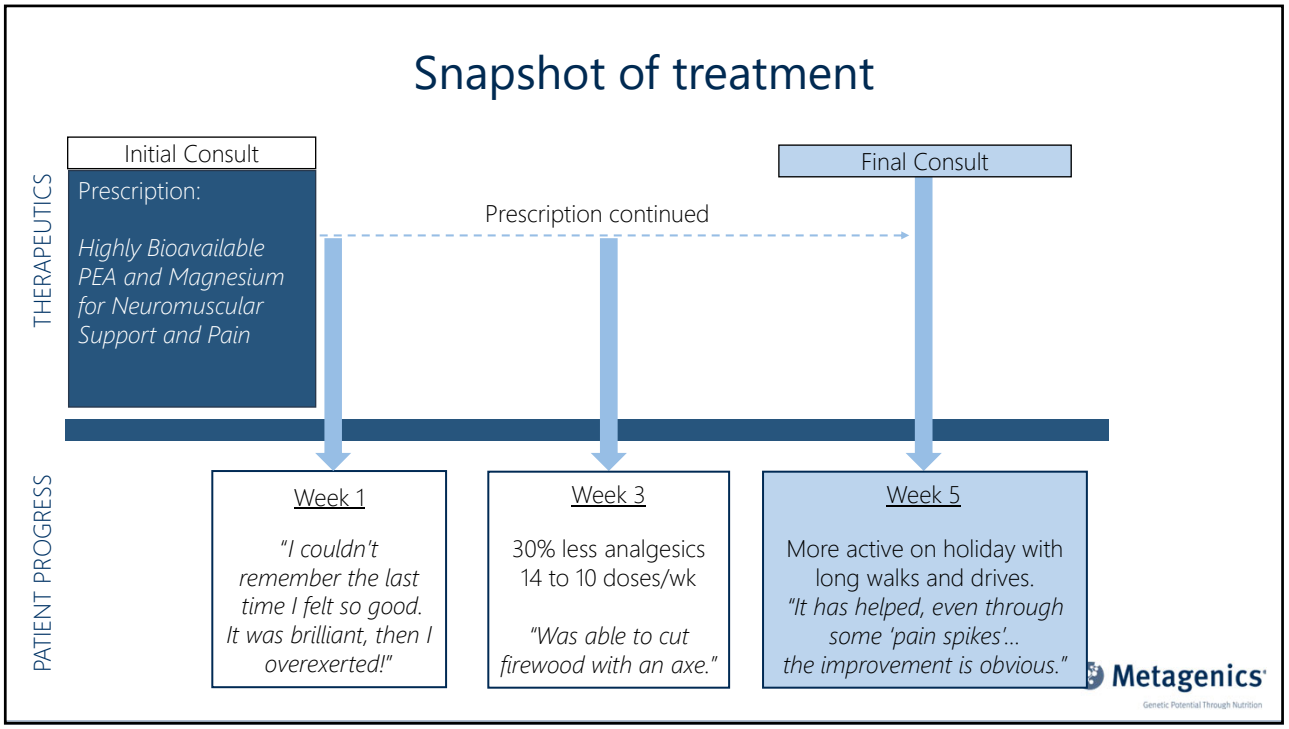
Snapshot of treatment
THERAPEUTICS
Initial Consult
Prescription:
Highly Bioavailable PEA and Magnesium for Neuromuscular Support and Pain
Prescription continued
Final Consult
PATIENT PROGRESS
Week 1
"I couldn't remember the last time I felt so good. It was brilliant, then I overexerted!"
Week 3
30% less analgesics 14 to 10 doses/wk
"Was able to cut firewood with an axe."
Week 5
More active on holiday with long walks and drives.
"It has helped, even through some 'pain spikes'... the improvement is obvious."
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Case study
Matthew, 48
Presentation & History
Progress
10
9
8
7
6
5
4
3
2
1
0
16
14
12
10
8
6
4
2
0
30%
Pain severity /10
Sleep quality /10
Weekly medication doses
Baseline
Week 3
Week 5
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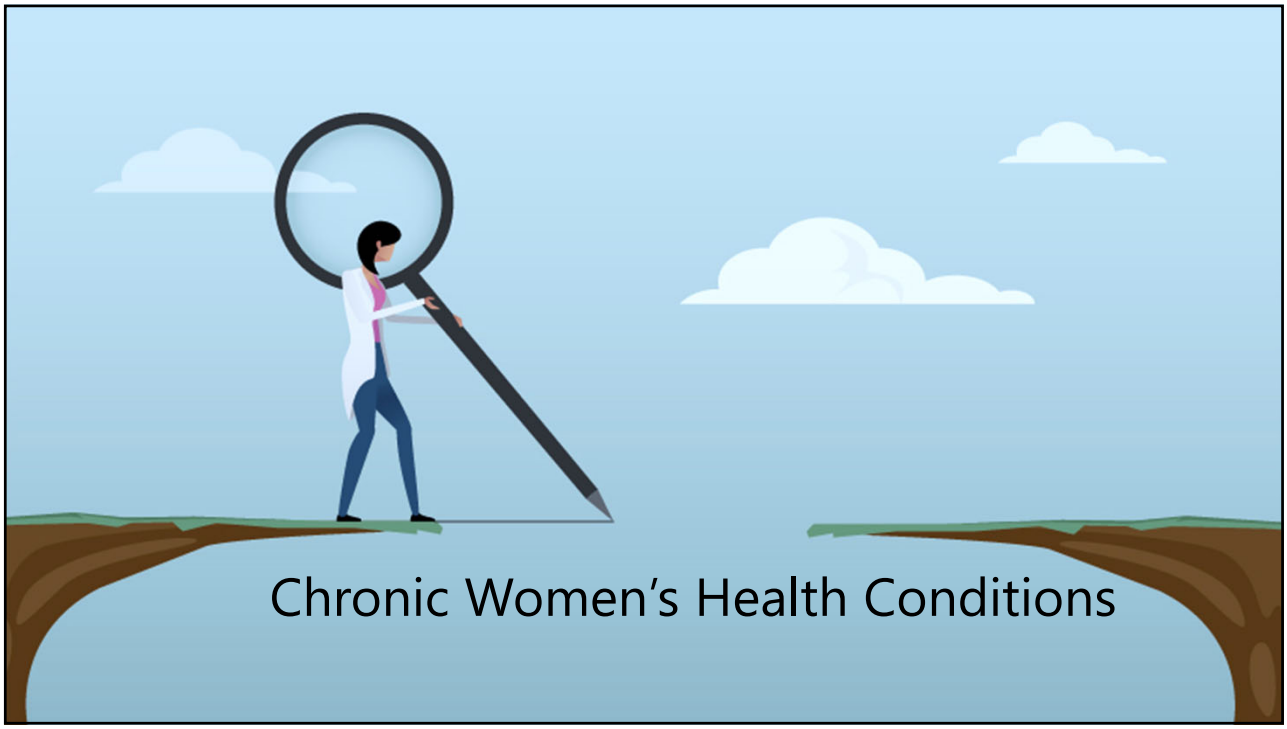

63

Dysmenorrhoea

90% of female patients experience period pain

Contributing factors:

- Pelvic biomechanics
- Hormonal balance
- Stress
- Diet
- Lifestyle

Ju H, Jones M, Mishra G. The prevalence and risk factors of dysmenorrhea. Epidemiol Rev. 2014;36:104-13. doi: 10.1093/epirev/mxt009. Epub 2013 Nov 26. PMID: 24284871.

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Clinical feedback

Heather* experiences dysmenorrhea and finds ibuprofen is the only thing that provides relief.

"I took two *Curcumin and Boswellia (Rhuleave-K™) for Rapid Pain Relief* ...in just under an hour the pain had considerably reduced. I took another two at this point and the pain reduced even further. I was able to carry on with normal activities which usually I'd only be able to do after taking ibuprofen. [I'm] impressed!"

* Name changed for confidentiality purposes

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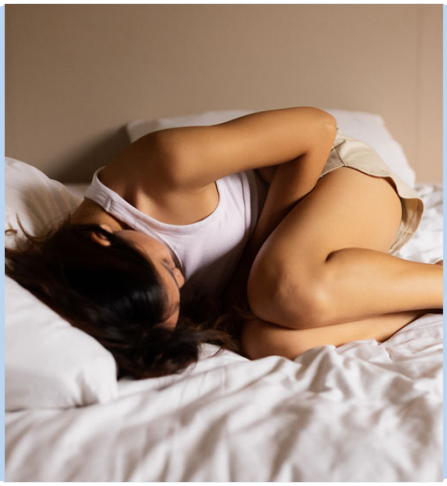
Endometriosis



10%-15% of reproductive aged women

Considerations
- Immune mediated
- Chronic inflammation
- Hormonal imbalances
- Autoimmune factors
- Pelvic biomechanics
- High rate of comorbidities

Christ JP, et al. Incidence, prevalence, and trends in endometriosis diagnosis: a United States population-based study from 2006 to 2015. Am J Obstet Gynecol. 2021 Nov;225(5):500.e1-500.e9. doi: 10.1016/j.ajog.2021.06.067. Epub 2021 Jun 17. PMID: 34147493.

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Chronic Pelvic Pain

1 in 7 women will develop chronic pelvic pain

Considerations

- High rate of comorbidities
- Strong association with previous physical and emotional trauma
- Associated with mood disorders
- Central sensitisation
- Involves most body systems

Dydyk AM, Gupta N. Chronic Pelvic Pain. 2022 May 29. In: StatPearls (FL): StatPearls Publishing; 2022

67

"Hormone levels are biomarkers of chronic pain"

Tennant, 2011

Tennant, F. 2011. Hormone therapies: newest advance in pain care. Practical Pain Management 11:98–105.

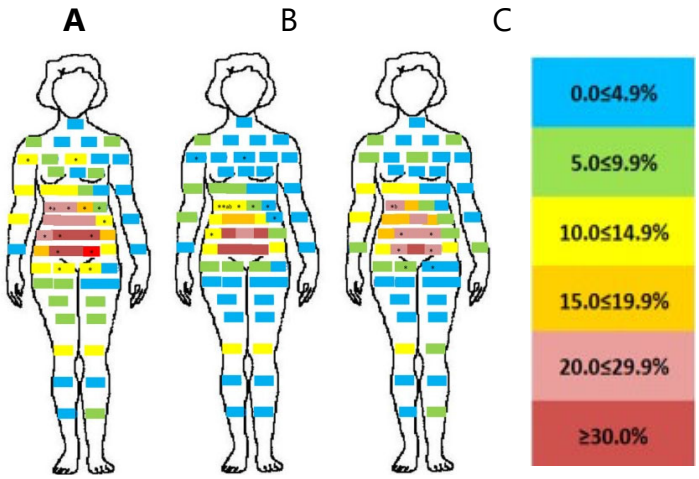
68

Gynaecological pelvic pain mapping

A. Endometriosis (n=190)

B. Other gynaecological condition (n=147)

C. Normal pelvis (n=136)



Schliep KC, et al. Hum Reprod. 2015;30(10):2427-38. doi: 10.1093/humrep/dev147.

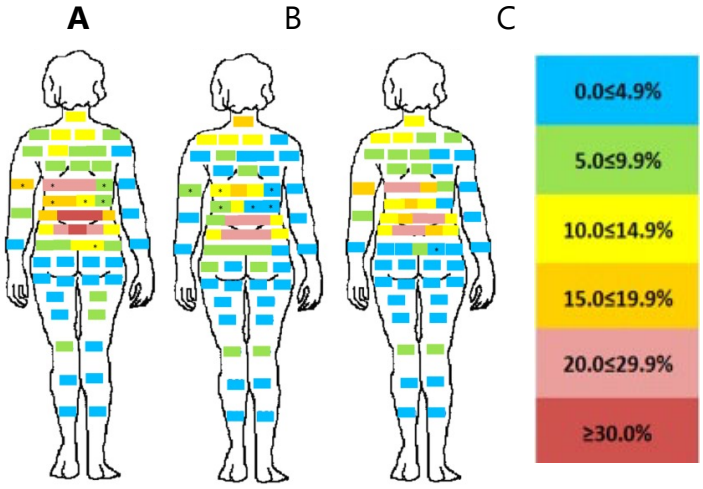
69

Gynaecological pelvic pain mapping

A. Endometriosis (n=190)

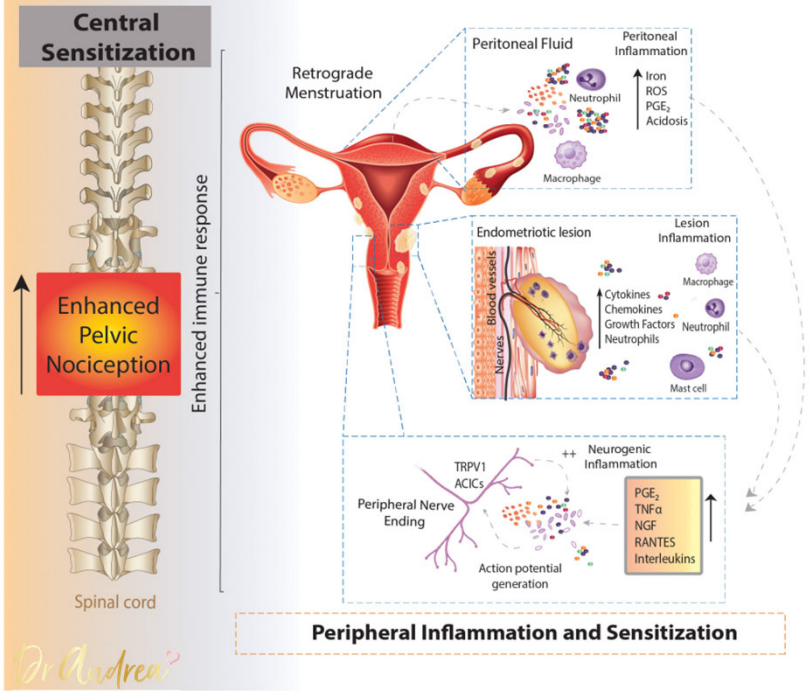
B. Other gynaecological condition (n=147)

C. Normal pelvis (n=136)



Schliep KC, et al. Hum Reprod. 2015;30(10):2427-38. doi: 10.1093/humrep/dev147.

70



Endometriosis: inflammatory & neurogenic pain

Maddern J, et al. Front Cell Neurosci. 2020; 14:590823. doi: 10.3389/fncel.2020.590823.

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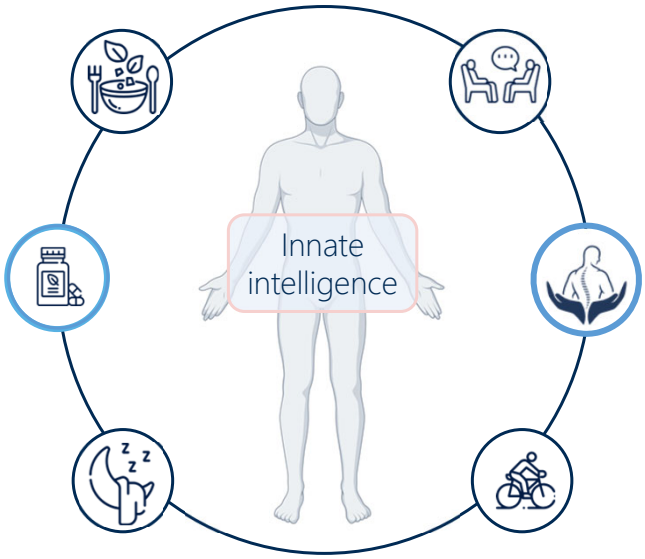
Management strategies



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1 in 20 Australians suffer from nerve pain?

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Levels of care

1. Relieve:
Highly Bioavailable Palmitoylethanolamide (PEA), with Saffron and Thiamine for Nerve Pain

2. Repair:
Corrective Care
Restore structure and function

3. Support:
Health Maintenance
Prevent relapse and maintain wellness

Foundations

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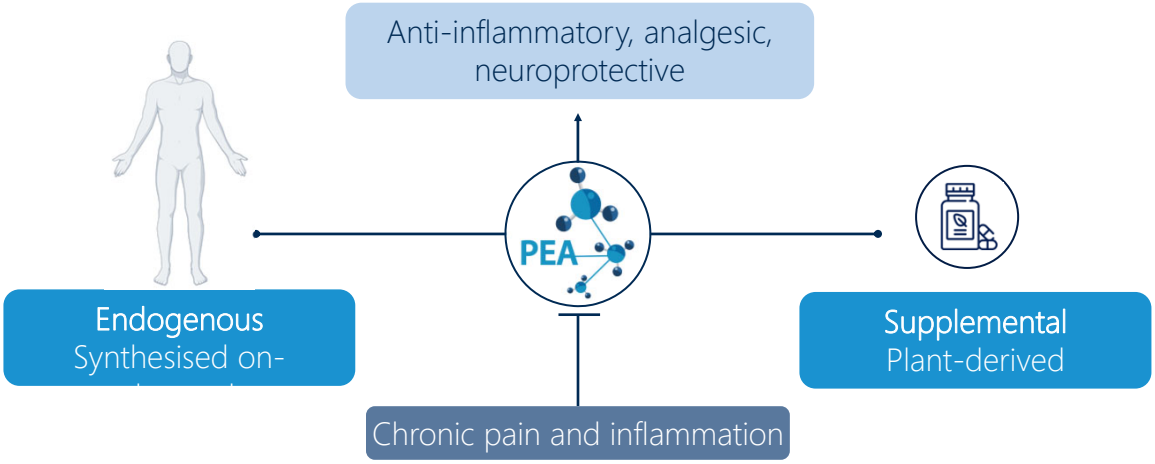
What is palmitoylethanolamide (PEA)?



Clayton P, et al. Int J Mol Sci. 2021;22(10):5305. doi: 10.3390/ijms22105305;
Petrosino S, et al. Int J Mol Sci. 2020;21(24):9526. doi: 10.3390/ijms21249526

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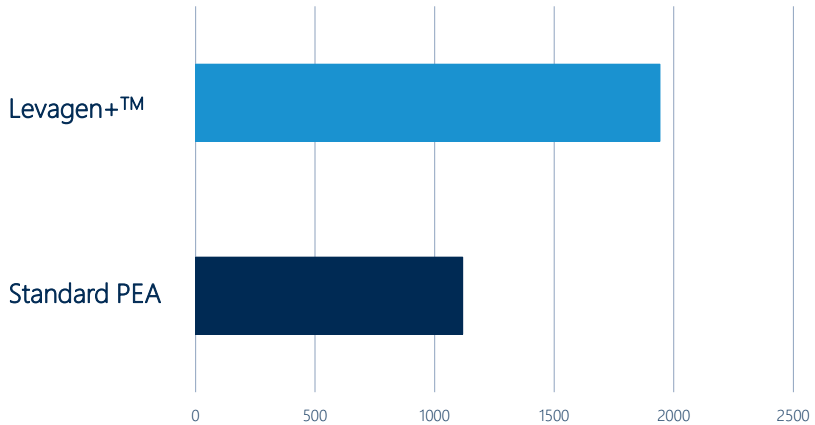
PEA absorption enhanced with Levagen+™



Total absorption area under curve (0-4 hours) pmol/mL

Levagen+™ uses LipiSperse® technology for enhanced absorption, making it 70% better absorbed

Briskey D. J Nutraceuticals Food Sci. 2020 May;5(2)3. doi: 10.36648/nutraceuticals.5.2.3

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PEA for neuropathic pain

Condition	PEA dose	Duration	Outcome
Lumbosciatica	300 mg/d vs. 600 mg/d vs. placebo	3 weeks	Subjective pain scores reduced: **300 mg/d: 65% to 35%** **600 mg/d: 71% to 21%** Placebo: 66% to 46% ($p<0.05$).
Lumbosciatica	600 mg/d with conventional treatments	30 days	Mean pain scores **reduced 70% to 34%** ($p<0.0001$).
Lumbosciatica	600 mg/d with or without conventional treatments	30 days	Pain scores reduced: **Male: 72.2% to 34.4%.** **Female: 67% to 33%.**
Traumatic and diabetic neuropathy	1,200 mg/d	50 days	Subjective pain scores reduced: **82% to 58%** ($p<0.001$). Neuropathic symptoms decreased: **5.2 ± 1.5 to 3.8 ± 2.1** ($p<0.025$).
Chemotherapy, trigeminal neuralgia, cervical spondylosis	1,062 mg/d of PEA for 10 days, then 708 mg/d	8 weeks	Pain frequency and intensity scores reduced: **71% to 21%** ($p<0.001$). Significant and prolonged reduction of neuropathic symptoms (burning, numbness and paraesthesia, $p<0.0001$) after discontinuation.
Lower back pain	1,200 mg/d added to ongoing opioid analgesia	6 months	Increased reduction in back pain intensity. 63% patients reported **reduced pain scores by 30%.**

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References on next slide

77

PEA for neuropathic pain

- Guida G, et al. [A multicenter clinical study of palmitoylethanolamide in chronic neuropathic pain: compression lumboischialgia]. Dolor. 2010;25(1):35–42
- Domínguez CM, et al. N-palmitoylethanolamide in the treatment of neuropathic pain associated with lumbosciatica. Pain Manag. 2012 Mar;2(2):119-24. doi: 10.2217/pmt.12.5
- Morera C, et al. Sex differences in N-palmitoylethanolamide effectiveness in neuropathic pain associated with lumbosciatalgia. Pain Manag. 2015;5(2):81-7. doi: 10.2217/pmt.15.5
- Cocito D, et al. Short-term efficacy of ultramicronized palmitoylethanolamide in peripheral neuropathic pain. Pain Res Treat. 2014;2014:854560. doi: 10.1155/2014/854560
- Chaurasia ID, Vinayak K, Tiwari S, Malpani P, Behram S, Koshariya M. Therapeutic potential of palmitoylethanolamide in the management of neuropathic pain. Rom Neurosurg. 2018;32(4):654-61. doi:10.2478/romneu-2018-0085
- Passavanti MB, et al. The beneficial use of ultramicronized palmitoylethanolamide as add-on therapy to tapentadol in the treatment of low back pain: a pilot study comparing prospective and retrospective observational arms. BMC Anesthesiol. 2017 Dec 19;17(1):171. doi: 10.1186/s12871-017-0461-9

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PEA for neuromuscular pain

Cohort	PEA dose	Duration	Outcome
Chronic jaw pain (n=24)	Week 1: 900 mg/d Week 2: 600 mg/d	2 weeks	Pain intensity scores significantly reduced **from 69.9% down to 7.6%** whilst ibuprofen reduced pain from 68.4% to 37.4% ($p<0.0001$).
Lumbar pain with nerve compression (n= 636)	300 mg/d or 600 mg/d	3 weeks	300 mg/d reduced pain scores from 65% to 36%. **600 mg/d reduced pain scores from 71% to 21%.** Placebo decreased from 66% to 46% ($p<0.05$).
Lower back pain (n=55)	1,200 mg/d + opioid analgesia	6 months	63% patients reported **PEA further reduced pain scores by 30%.** Reduced neuropathy (burning pain, numbness, hyperalgesia). Reduced opioid pain relief requirement ($p<0.001$). Classification shifted from severe to moderate pain ($p<0.01$).
Fibromyalgia (n=80)	1,200 mg/d for 4 weeks, 600 mg/d for 8 weeks alongside pregabalin and SNRI.	12 weeks	Pain significantly reduced when combined with pharmaceuticals. **Tender points reduced from 8/18 to 4/18 sites** ($p<0.0001$). **Pain scores (1/10) reduced from 4.0 to 3.0** ($p<0.001$).
Migraine (n=20)	1,200 mg/d PEA alongside NSAIDs, as required	12 weeks	Significantly reduced subjective pain scores from **Males: 75% to 53%, and females: 79% to 63% ($p<0.02$).** Significantly reduced number of migraine attacks per month ($p<0.0002$).

References on next slide

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PEA for neuromuscular pain

- Marini I, et al. Palmitoylethanolamide versus a nonsteroidal anti-inflammatory drug in the treatment of temporomandibular joint inflammatory pain. J Orofac Pain. 2012 Apr 1;26(2):99
- Guida G, et al. La palmitoiletanolamida (Normast) en el dolor neuropatico cronico por lumbociatalgia de tipo compresivo: estudio clinico multicentrico [A multicenter clinical study of palmitoylethanolamide in chronic neuropathic pain: compression lumboischialgia]. Dolor. 2010;25(1):35–42
- Passavanti MB, et al. The beneficial use of ultramicronized palmitoylethanolamide as add-on therapy to tapentadol in the treatment of low back pain: a pilot study comparing prospective and retrospective observational arms. BMC Anesthesiol. 2017 Dec 19;17(1):171. doi: 10.1186/s12871-017-0461-9
- Del Giorno R, et al. Palmitoylethanolamide in fibromyalgia: results from prospective and retrospective observational studies. Pain Ther. 2015 Dec;4(2):169-78. doi:10.1007/s40122-015-0038-6
- Chirchiglia D, et al. Effects of add-on ultramicronized N-palmitolethanolamide in patients suffering of migraine with aura: a pilot study. Front Neurol. 2018 Aug 17;9:674. doi:10.3389/fneur.2018.00674

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PEA safe and effective with medication

Condition	Medication	PEA Dose	Duration
Anticancer drug-induced neuropathic pain	Methotrexate, tramadol, pregabalin	1,200 mg/d	15+ weeks
Burning mouth syndrome	Gabapentin	1,200 mg/d	12 weeks
Fibromyalgia	Duloxetine, gabapentin	600 mg/d	12 weeks
Lower back pain	Oxycodone	1,200 mg/d	4 weeks
	Tapentadol	1,200 mg/d	24 weeks
Major depressive disorder	Citalopram	1,200 mg/d	6 weeks
Migraine with aura	NSAIDs	1,200 mg/d	12 weeks
Multiple sclerosis	IFN-β1	600 mg/d	52 weeks
Parkinson's disease	Levodopa	600 mg/d	12 weeks
		300 mg/d	52 weeks
Prophylaxis treatment for nummular headache	Topiramate	600 mg/d	16 weeks
Trigeminal neuralgia	Carbamazepine	1,200 mg/d	6 weeks

PEA: Palmitoylethanolamide
IFN-β1: Interferon-beta-1

References on following slide

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PEA safe and effective with medication

- Hesselink JM, et al. Therapeutic utility of palmitoylethanolamide in the treatment of neuropathic pain associated with various pathological conditions: A case series. J Pain Res. 2012;5:437–442. doi:10.2147/JPR.S32143.
- Chirchiglia D, et al. Add-on administration of ultramicronized palmitoylethanolamide in the treatment of new-onset burning mouth syndrome. Int Med Case Rep J. 2019 Feb 15;12:39–42. doi:10.2147/IMCRJ.S194403.
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PEA amplifies analgesia efficacy

1 + 1 = 4 x greater pain relief (than either alone)

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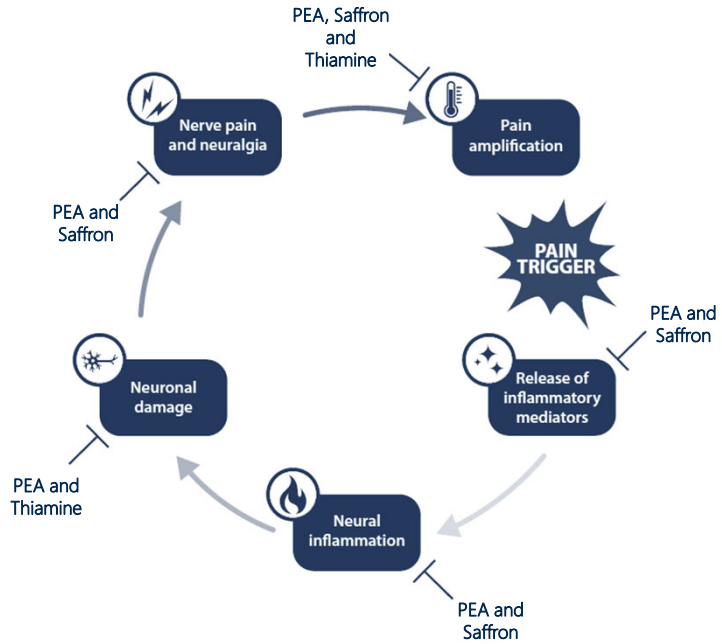

Highly Bioavailable Palmitoylethanolamide (PEA), with Saffron and Thiamine for Nerve

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Highly Bioavailable Palmitoylethanolamide (PEA), with Saffron and Thiamine for Nerve Pain

Ingredients

Palmidrol (PEA – Palmitoylethanolamide) (Levagen+™)
Crocus sativus (Saffron) (affron®)
Thiamine (Vitamin B1)

Clinical applications:

- Neuralgia and neuropathic pain
- Sciatica and compression neuropathy
- Neurodegenerative conditions
  - Parkinson's Disease
  - Multiple sclerosis
  - Alzheimer's Disease

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PEA for migraine

Migraine with aura (n=20); average 3 attacks monthly

Intervention:
1,200 mg/d PEA
+ NSAIDs (as required) for 90 days

Results:
60 days: Significantly *reduced* pain intensity
90 days: Overall; ½ the frequency, with reduced duration, and NSAID requirement

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Chirchiglia D, et al. Front Neurol. 2018 Aug 17;9:674. doi:10.3389/fneur.2018.00674

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Levels of care

1. Relieve:
Rapid Relief
Provide symptomatic relief

2. Repair:
Corrective Care
Specialised Pro-Resolving Mediators

3. Support:
Health Maintenance
Prevent relapse and maintain wellness

Foundations

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Specialised pro-resolving mediators (SPMs)

Endogenous
Synthesised from omega-3

Supplemental
LIPINOVA-11TG™

SPMs

Resolution of inflammation
Tissue remodeling
Immune regulation

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Saqib U, et al. Oncotarget. 2018;9(25):17937-17950. doi:10.18632/oncotarget.24788

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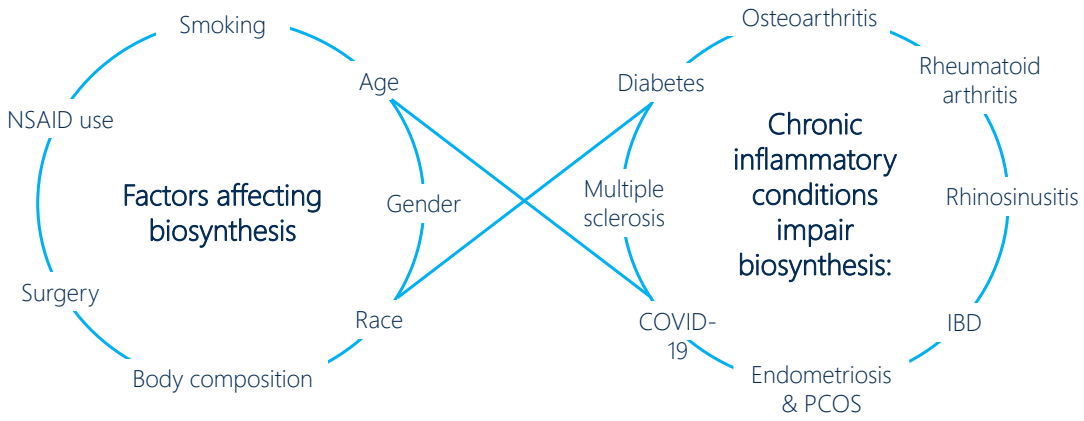
Impaired SPM biosynthesis is common



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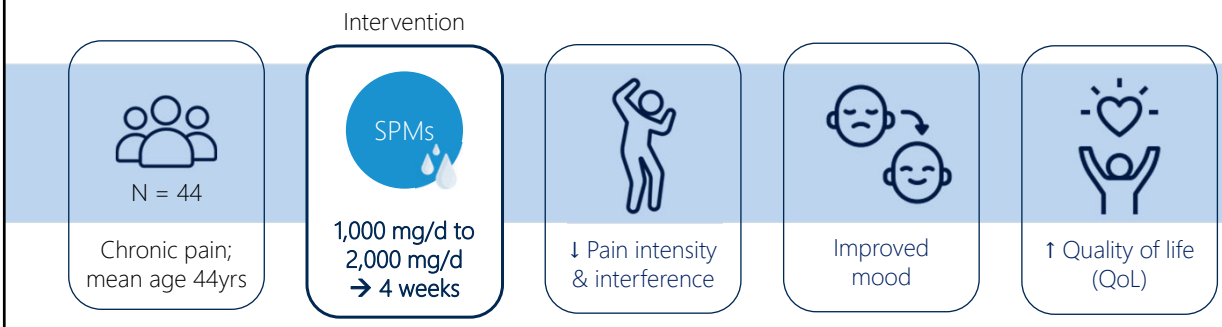
SPMs resolve pain *and* suffering



Callan N, et al. J Transl Med. 2020 Oct;18:401. doi: 10.1186/s12967-020-02569-5

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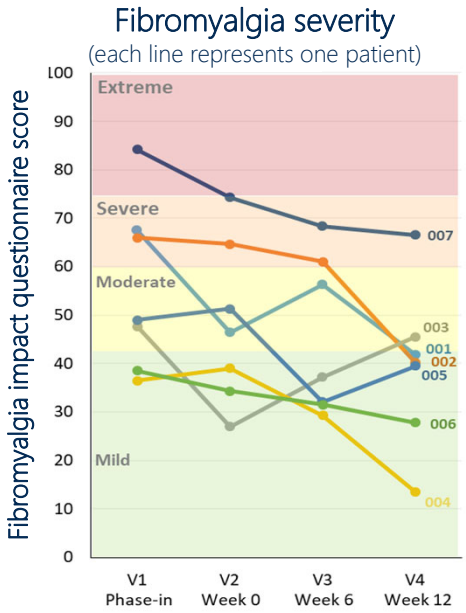

Supplemental SPMs improved fibromyalgia

- 87% response rate
- Improvements in physical function
- Symptoms worsened after supplements ceased in some patients
- Lower CIRS score indicative of better outcomes (patient 004)
- No reported side effects

O'Connor A, et al. Poster presented at the 10th Linus Pauling Institute International Conference, Corvallis, RA. August 2019.bbb

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Levels of care

1. Relieve:
Rapid Relief
Provide symptomatic relief

2. Repair:
Corrective Care
Specialised Pro-Resolving Mediators

3. Support:
Health Maintenance
High Purity, Low Reflux, Concentrated Fish Oil

Foundations

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Choosing SPMs or fish oils

	SPMs REPAIR	Omega-3 (EPA / DHA) SUPPORT
Indications	• Chronic or unresolved inflammation • Autoimmune conditions • Metabolic dysfunction • Acute inflammation with urgency of circumstance (e.g. athlete, profession needing return of function, etc.)	• Omega-3 replenishment • Inflammation with low omega-3 intake • Healthy ageing and wellbeing • Cardiovascular risk mitigation • Brain health and cognition • Increased requirement (e.g. pregnancy) • Mood or psychiatric conditions
Consider when:	• Low EPA/DHA intake • Ageing • Metabolic dysfunction • Obesity • Unresolved inflammatory trigger (e.g. stealth infection, biotoxin, etc.)	• Low EPA/DHA intake • Genetic susceptibility

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Specialised Pro-Resolving Mediators

Ingredients

Concentrated omega-3 triglycerides containing:
- 17-HDHA
- 18-HEPE
- 14-HDHA

Eicosapentaenoic acid (EPA)

Docosahexaenoic acid (DHA)

Clinical applications:
- Promotes resolution of inflammation
- Anti-inflammatory
- Analgesic

High Purity, Low Reflux, Concentrated Fish Oil

Ingredients

Concentrated omega-3 triglycerides
- Eicosapentaenoic acid (EPA)
- Docosahexaenoic acid (DHA)

Clinical applications:
- Cognition and brain function
- Inflammatory conditions
- Pregnancy and lactation
- Cardiovascular disease
- Nervous system support

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Consider this…

Which is TRUE regarding 20% of the population currently living with chronic pain?

- Over 20% also have mental health disorders
- About 50% are prescribed antidepressants
- That suicidal ideation is 2-3 times higher than the general population
- All of the above

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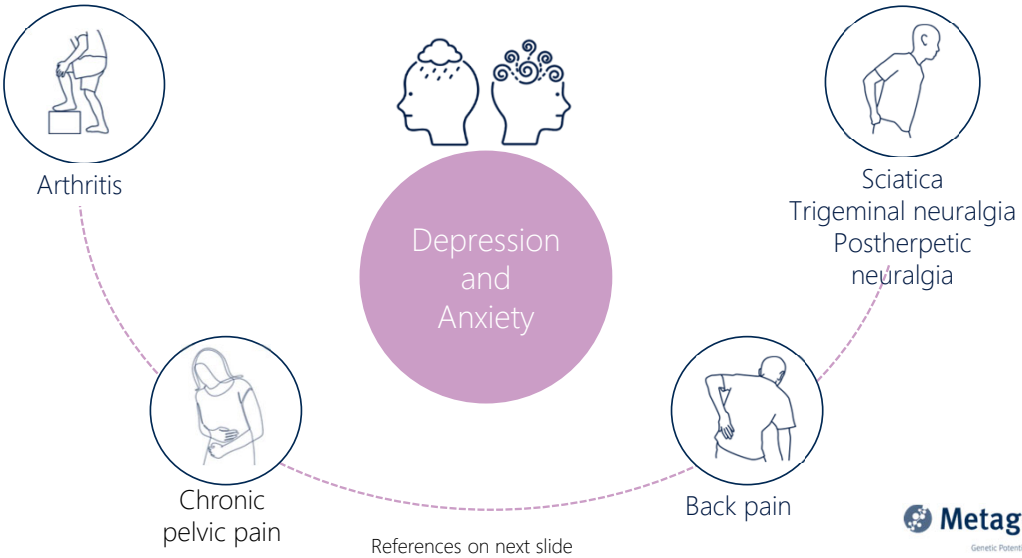
Complex chronic pain and mood



References on next slide

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Complex chronic pain and mood

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Choosing the right magnesium for your patient

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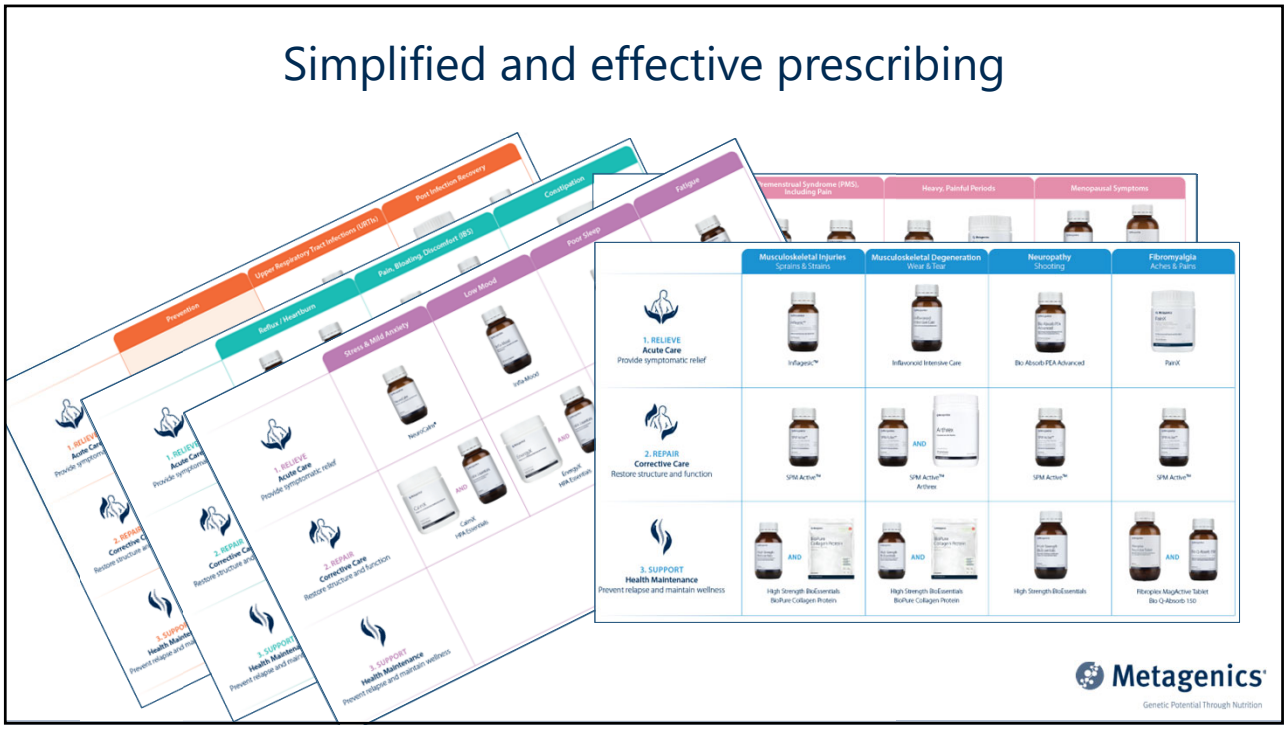
Simplified and effective prescribing
Musculoskeletal Injuries
Sprains & Strains
Musculoskeletal Degeneration
Wear & Tear
Neuropathy
Shooting
Fibromyalgia
Aches & Pains
1. RELIEVE
Acute Care
Provide symptomatic relief
2. REPAIR
Corrective Care
Restore structure and function
3. SUPPORT
Health Maintenance
Prevent relapse and maintain wellness
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A Simple Guide to Healthy Living - Patient Brochure

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Erica Smith. BHSc (Comp Med), AdvDipNat, AdvDipMedHerb.
Dr Andrea Huddleston. MRepMed, MWomHMed, BSc Chiro, B Chiro.

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