

FACT SHEET

Natural Products: Phytotherapy and Aromatherapy

- Barbara Riedl, MD: Psychotherapy & Psychosomatic Medicine, 4P- Private Practice, Burgdorf, Switzerland
- Christine Huber, MD: Institute for Complementary & Integrative Medicine, University Hospital, Zurich, Switzerland
- Beatrix Falch, MSc PhD: Division of Natural Chemistry & Phytopharmacy, University of Applied Sciences, Zurich, Switzerland
- Heather Tick, MD: Departments of Family Medicine, Anesthesiology & Pain Medicine, University of Washington, Seattle, WA
- Florian Reisig, MD: Department of Anesthesiology & Pain Medicine, Inselspital, University Hospital, Bern, Switzerland.

Medicinal Herbs and Their Extracts as Part of Integrative Treatment for Patients with Chronic Non-Malignant Pain

The medicinal use of plants, phytotherapy, has been used empirically since mankind has existed and has been recorded in the writings of many ancient cultures for at least five thousand years. It is often forgotten that plant-based medicine is a link between standard modern medicine and many ancient healing practices. Plants have been the foundation of much of modern-day pharmacology and the therapeutic effects of many plants have been proven through clinical and pharmacological research.

Phytotherapy may use the entire plants, plant parts or their preparations derived through various procedures such as essential oils, liquid or dried extracts and decoctions. Phytotherapy may include only a single plant or mixtures of plants and extracts. These products may be delivered through many routes: orally in tablets, capsules, tinctures or teas, topically on skin or mucous membranes, or inhaled. Aroma-therapy uses aromatic substances derived from plants and is a subdomain of phytotherapy.

"Integrative medicine" refers to a holistic medical practice, striving to create an inclusive space where the choice of treatment options combines standard medical practices with nonstandard care and disciplines that might even include ancient practice traditions. The choice of treatment options is based on the patient's medical needs and preferences. There is a robust basic science literature for many integrative medicine practices, which demonstrates plausible mechanisms for the desired outcomes. Many of these practices impact epigenetics and the autonomic nervous system allostatic mechanisms^{i,ii}. There is increasing interest in expanding the clinical evidence base for integrative options for care including phytotherapy.

Phytotherapy is an integral part of integrative medicine as well as foundational to many developments in standard modern medicine. A well-known example for drug development based on phytotherapy is the successful development by Bayer AG of acetylsalicylic acid, the painkiller of the 19th and 20th centuries, which was based on the derivatives of salicylic acid extracted from white willow bark. Willow bark (Salix alba) was intensively used in Europe since the mid-18th centuryⁱⁱⁱ, but the first records of the medical use – together with myrtle (Myrtus communis) – date back to 1543 AD in the Ebers Papyrus: "to relieve inflammatory conditions and painful symptoms"^{iv}. White willow bark is still available as an herbal supplement and causes fewer gastrointestinal adverse effects than its pharmacologic cousin.

Regarding nociceptive pain of the musculoskeletal system with primary or secondary inflammation, oral herbal medicines such as devil's claw extract (Harpagophytum procumbens^v, frankincense (Boswellia serrata)^{vi} and turmeric (Curcuma longa)^{vii,viii} are nowadays clinically established and approved through clinical studies as well. For the painful muscle spasticity in multiple sclerosis, a preparation of tetrahydrocannabinol (THC) and cannabidiol (CBD) from Cannabis sativa was developed with good efficacy (p = 0.0002)^{ix}. On the other hand, a general use of medicinal cannabis for central and peripheral neuropathic pain or chronic pain is currently not advisable due to the psychotropic side effects of THC (Number needed to treat (NNT) 24 and number needed to harm (NNH) 4)^x.

Research into medical cannabinoids is currently focusing on CBD, which has anti-inflammatory properties in animal models. A positive impact on neuroinflammatory pathomechanisms, such as glial cell activation and resulting disturbed intersynaptic glutamate homeostasis, is postulated. The underlying mechanism is essential to understand both central pain sensitization and chronification^{xi} – as well as the cause for neurodegenerative diseases^{xii}.

For the treatment of peripheral neuropathic pain, high dose capsaicin patches (8%) are standard care, though pooled NNT 10.6 is low^{xiii} and NNH 2.5 for adverse skin reactions is high^{xiv}. Capsaicin mouthwash solution (0.02%) also seems to produce a relevant pain reduction in "burning mouth syndrome" by desensitizing the TRPV1 receptor as well^{xv}.

Phytotherapeutics are effectively used to treat various neuro-psycho-vegetative symptoms accompanying chronic pain, as many patients suffer from extensive intolerance of standard care drugs. Taking a more detailed patient history often reveals an association between chronic pain and other "central sensitivity syndromes"xvi. Which then also suggests a significant nociplastic pain component as one feature a generalized amplification of perceptionxvii. Lavender oil (Lavandula angustifolia) is used for anxious^{xviii} and St. John's wort (Hypericum perforatum) for depressive symptoms^{xix}, which can be recorded and monitored easily and systematically with the PHQ-4 guestionnaire. A moderate effect of chamomile (Matricaria chamomilla L.) has been found for both symptom complexes^{xx}; the same applies to Withania somnifera, which originates from Ayurvedic medicine, even if the specific mechanism of action is still unclear^{xxi}. Ginkgo biloba is in use for relieving neurosensory symptoms, well proven

e.g. for patients with dementia^{xxii} and peppermint oil (Mentha piperita) (10%) for chronic, primary headache^{xxiii} as well as for irritable bowel syndrome (NNT 7)^{xxiv}. Valerian (Valeriana officinalis) and hops (Humulus lupulus) are clinically established for the treatment of sleep disorders^{xxv}.

Both doctors and non-medical practitioners usually recommend oral preparations. Aromatherapeutics and locally applied phytotherapeutics are possible parts of body-centred treatments (ergotherapy / physiotherapy) and are additionally used by other advanced nurse practitioners – typically in oncology and palliative care. In addition to pharmacological effects, the local application of plant products or aromatherapeutics integratively helps to boost self-awareness, self-care, mindfulness and enjoyment of life, i.e. well-proven components of a successful multimodal pain therapy^{xxvi,xxvii}.

Most preparations can be obtained without a prescription, empowering the patient to independently address their symptoms, e.g. with ointments or tea infusions. Many of the teas, creams and ointments have as part of their effects, the sensory experience of drinking the tea or applying the topical preparation. In the long run, the planning of a patient owned medicinal herbal garden/balcony can be encouraged. This would be an extended approach with regional plants in order to integrate further meditative and body-centred elements into self-treatment.

An "anti-inflammatory" lifestyle^{xvvii} entails dietary adjustments (e.g. weight loss in the case of obesity, Mediterranean cuisine, herbals with bittering agents and use of omega-3 fatty acids^{xvix}) and regulatory measures: daily structure, sleep hygiene, stress reduction, relaxation techniques, meditation and mindfulness exercises (e.g. MBSR, Body Mind Medicine, "Shinrin Yoku" aka forest bathing) as well as regular physical exercise adapted to the underlying disease^{xvx}. It is a subsequent continuation of treatment concepts that are linked by (medicinal) plants. Last but not least, the use of herbal preparations and a dietary adjustment can promote a better understanding of the long term dependency between human beings and nature itself, in terms of a sustainable lifestyle and responsible use of available resources worldwide^{xxxi}.

References

¹Hansen MM, Jones R, Tocchini K. Shinrin-Yoku (Forest Bathing) and Nature Therapy: A State-of-the-Art Review. Int J Environ Res Public Health. 2017 Jul 28;14(8). pii: E851.

- ¹Goldstein DS. Concepts of scientific integrative medicine applied to the physiology and pathophysiology of catecholamine systems. Compr Physiol. 2013 Oct;3(4):1569-610
- "Lichterman BL. Aspirin: The Story of a Wonder Drug. BMJ. 2004 Dec 11;329(7479):1408
- ¹⁴ Montinari MR, Minelli S, De Caterina R. The first 3500 years of aspirin history from its roots A concise summary. Vascul Pharmacol. 2019 Feb;113:1-8.
- ^vMenghini L, Recinella L, Leone S et al. Devil's claw (Harpagophytum procumbens) and chronic inflammatory diseases: A concise overview on preclinical and clinical data. Phytother Res. 2019 Sep;33(9):2152-2162
- ^{vi} Cameron M, Chrubasik S. Oral herbal therapies for treating osteoarthritis. Cochrane Database Syst Rev. 2014 May 22:2014(5):CD002947.
- ⁴¹Daily JW, Yang M, Park S. Efficacy of Turmeric Extracts and Curcumin for Alleviating the Symptoms of Joint Arthritis: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. J Med Food. 2016 Aug; 19(8):717-29.
- ^{vii} Gaffey A, Slater H, Porritt K, Campbell JM. The effects of curcuminoids on musculoskeletal pain: a systematic review. JBI Database System Rev Implement Rep. 2017 Feb;15(2):486-516
- ^{ix} Novotna A, Mares J, Ratcliffe S et al. A randomized, double-blind, placebo-controlled, parallel-group, enriched-design study of nabiximols* (Sativex(®)), as add-on therapy, in subjects with refractory spasticity caused by multiple sclerosis. Eur J Neurol. 2011 Sep;18(9):1122-31.
- *Goel A. Review: In chronic noncancer pain, cannabinoids reduce pain (NNT 24) but increase adverse events (NNH 6). Ann Intern Med. 2018 Dec 18;169(12):JC62.
- ^{xi} Ji RR, Nackley A, Huh Y, Terrando N et al. Neuroinflammation and Central Sensitization in Chronic and Widespread Pain. Anesthesiology. 2018 Aug;129(2):343-366.
- ^{xii} Clark IA, Vissel B. Excess cerebral TNF causing glutamate excitotoxicity rationalizes treatment of neurodegenerative diseases and neurogenic pain by anti-TNF agents. J Neuroinflammation. 2016 Sep 5;13(1):236
- ^{xiii} Finnerup NB, Attal N, Haroutounian S, McNicol E et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol. 2015;14:162-73.
- ³⁰ Mason L, Moore RA, Derry et al. Systematic review of topical capsaicin for the treatment of chronic pain. BMJ. 2004 Apr 24;328:991.
- ^{xv} Jankovskis V, Selga G. Vitamin B and Zinc Supplements and Capsaicin Oral Rinse Treatment Options for Burning Mouth Syndrome. Medicina (Kaunas). 2021 Apr 17:57(4):391
- ^{xxi} den Boer C, Dries L, Terluin B et al. Central sensitization in chronic pain and medically unexplained symptom research: A systematic review of definitions, operationalisations and measurement instruments. J Psychosom Res. 2019 Feb;117:32-40

- ^{xvi} Nijs J, Lahousse A, Kapreli E et al. Nociplastic Pain Criteria or Recognition of Central Sensitization? Pain Phenotyping in the Past, Present and Future. J Clin Med. 2021 Jul 21;10(15):3203
- ^{xvii} Donelli D, Antonelli M, Bellinazzi C et al. Effects of lavender on anxiety: A systematic review and meta-analysis. Phytomedicine. 2019 Dec;65:153099
- ^{ac} Zirak N, Shafiee M, Soltani G et al. Hypericum perforatum in the treatment of psychiatric and neurodegenerative disorders: Current evidence and potential mechanisms of action. J Cell Physiol. 2019 Jun;234(6):8496-8508
- **Amsterdam JD, Li Y, Soeller I, Rockwell K, et al. A randomized, double-blind, placebo-controlled trial of oral Matricaria recutita (chamomile) extract therapy for generalized anxiety disorder. J Clin Psychopharmacol. 2009 Aug;29(4):378-82
- ^{xxi} Speers AB, Cabey KA, Soumyanath A et al. Effects of Withania somnifera (Ashwagandha) on Stress and the Stress- Related Neuropsychiatric Disorders Anxiety, Depression, and Insomnia. Curr Neuropharmacol. 2021;19(9):1468-1495.
- ^{xxii} Spiegel R, Kalla R, Mantokoudis G et al. Ginkgo biloba extract EGb 761® alleviates neurosensory symptoms in patients with dementia: a meta-analysis of treatment effects on tinnitus and dizziness in randomized, placebo-controlled trials. Clin Interv Aging. 2018 Jun 13;13:1121-1127.
- xxiii Goebel H, Heinze A et al. [Peppermint oil in the acute treatment of tension-type headache].in German Schmerz. 2016 Jun;30(3):295-310.
- X^{XII} Ingrosso MR, Ianiro G, Nee J et al. Systematic review and meta-analysis: efficacy of peppermint oil in irritable bowel syndrome. Aliment Pharmacol Ther. 2022 Sep;56(6):932-941.
- xxx Salter S, Brownie S. Treating primary insomnia the efficacy of valerian and hops. Aust Fam Physician. 2010 Jun;39(6):433-7.
- ^{xxvi} Tick H, Nielsen A, Pelletier KR et al. Pain Task Force of the Academic Consortium for Integrative Medicine and Health. Evidence-Based Nonpharmacologic Strategies for Comprehensive Pain Care: The Consortium Pain Task Force White Paper. Explore (NY). 2018 May-Jun;14(3):177-211.
- xxxii Lin YC, Wan L, Jamison RN. Using Integrative Medicine in Pain Management: An Evaluation of Current Evidence. Anesth Analg. 2017 Dec;125(6):2081-2093
- ^{xvviii} Ford ES, Bergmann MM, Kröger J, Schienkiewitz A et al. Healthy living is the best revenge: findings from the European Prospective Investigation Into Cancer and Nutrition-Potsdam study. Arch Intern Med. 2009 Aug 10;169(15):1355-62.
- xxx Daien C, Czernichow S, Letarouilly JG et al. Dietary recommendations of the French Society for Rheumatology for patients with chronic inflammatory rheumatic diseases. Joint Bone Spine. 2022 Mar;89(2):105319.
- ^{xxx} Gautam S, Tolahunase M, Kumar U et al. Impact of yoga based mind-body intervention on systemic inflammatory markers and co-morbid depression in active Rheumatoid arthritis patients: A randomized controlled trial. Restor Neurol Neurosci. 2019;37(1):41-59.
- xxxx Kjærgård B, Land B, Bransholm Pedersen K. Health and sustainability. Health Promot Int. 2014 Sep;29(3):558-68