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COMPLEMENTARY AND ALTERNATIVE MEDICINE FOR PAIN MANAGEMENT IN CANCER PATIENTS

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Abstract

The field of Natural Health Sciences and Occult sciences is getting high attention and gaining importance in treatment of several diseases that are not responding the traditional practice. However, the lack of extensive research and data supporting these fields is preventing them from becoming accepted method of treatment. Complementary and Alternative Medicine is not mysterious but science itself. In the last decade there is substantial research in these areas like aura, bio energy or electromagnetic energy, radiation energy from bodies and techniques to measure these energies leading to wider acceptance. Holistic Healing is the practice of health that considers the entire person and all of the factors affecting the person and it is based on foundational principles of Aurveda, Traditional Chinese Medicine and Herbal medicine. Holistic medicine uses Mind and Body techniques, Natural products, Energy and Spiritual healing. Survey released by National Center for Complementary and Alternative Medicine (NCCAM-NIH) revealed that 56% of population in US and in advanced countries uses CAM. Randomized Clinical studies conducted with 189 Patients undergoing standard chemotherapy, placebo or Reiki found that Energy healing (Reiki) was statistically significant in raising the comfort and well-being of patients post-therapy. Further, in the systematic review of 5 randomized clinical trials, two studies reported statistically significant reductions in pain when Reiki was used in addition to opioid agents. Additionally, energy healing on oncology patients undergoing infusion, showed 50% reduction in mean pain scores after each treatment. The investigations suggested that the sessions were considered helpful to improve well-being (70%), relaxation (88%), and pain relief (45%). Similarly, in another cross over study, it was shown that in all sixteen cancer patients included in energy healing sessions, fatigue decreased, and quality of life was significantly improved with the reiki sessions compared with rest. Recent studies demonstrated that acupuncture was significantly associated with reduced cancer pain and can decrease the use of analgesics with moderate certainty of evidence. In addition, biology based practices like Herbal, probiotics and vitamins are also used to reduce pain. These methods are accepted by various professional certification agencies like National Certification Center of Energy Practitioners (NCCOEP) and Alliance of Energy practitioners (NAOEP) that is serving as resource for research and literature support. In summary, the complementary and alternative medicine field is upcoming and gaining acceptance as therapeutic method to increase patient confidence and reduce impact of ailment.

Keywords: Pain Management, Cancer, Energy Healing, Acupuncture, Natural Products, Reiki, Complementary and Alternative medicine.

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Introduction

The pain management strategies include pain medicines, physical therapies and complementary therapies such as mind and body techniques acupuncture and massage including community support groups. Studies

suggest that a person's quality of life is influenced by their perception and by the way they cope emotionally with pain. The pain can be acute, a normal response to an injury or medical condition or it can be chronic, and that lasts for long time to heal. The pain may range from small ache to sharp excruciating pain which is localized to one part or widespread to entire body. The most common causes of pain in human beings include injury, medical conditions like cancer, arthritis, back problems and surgery.

Body responds to threats by several protecting mechanisms and Pain is one of them. The body contains pain receptors (nociceptors), free endings of nerves and the number of receptors varies. Skin has lots of receptors

and responds quickly and the gut has very few it takes time to respond for a pain like stomach ache. This is a reflex reaction that prevents further damage occurring and is controlled by thalamus.

People use analgesics as pain medicines like Paracetamol, Aspirin [1], Non-Steroidal Anti Inflammatory Drugs (NSAIDs) along with Opioids. Pain medicines like Aspirin and other NSAIDs help to reduce inflammation and fever/by blocking chemicals called prostaglandins that cause inflammation, swelling and make nerve endings sensitive, which can lead to pain anesthetics [2].

Many treatments are available to help manage pain by nonmedical methods. The methods can be used individually or in a combination. These methods range from using heat or cold packs, Physical Therapy, Acupuncture [3] Massage, Meditation and Yoga [4]. Additionally, psychological therapy like Cognitive Behavior Therapy (CBT) also will be used for self-management of pain.

In this paper, a comprehensive review was presented on how complementary and alternative medicine approaches like Reiki, Biofield, Acupuncture and Natural products are used to comfort cancer patients and reduce pain.

Discussion

i) **Holistic, Alternative, Complementary and Integrative Medicine:** Hippocrates, the father of the modern medicine said that the healing power of nature believed in self-healing and the environment, diet and lifestyle can contribute to ill health. Holism or holistic is the concept of emphasizing the importance of the whole body and the interdependence of its parts. Holistic Healing is the practice of health that considers the entire person and all of the factors affecting the person. Holistic healing seeks to maintain or restore balance among (and within) the various dimensions of the individual and the part can never be well unless the whole is well (Socrates). Complementary and Alternative healthcare and medical practices are a group of healthcare and medical practices that are not usually considered as part of conventional medicine. However, the methods that are proven safe and effective are gaining acceptance in mainstream medical practice. This parallel medical system has five major domains like 1) Alternative medical systems 2) Mind and Body intervention 3) Biologically based treatment, 4) Manipulative and body based methods and 5) Energy therapies (Fig.1). Alternative medicine is generally combined with complementary medicine to form a common term Complementary and Alternative Medicine (CAM).

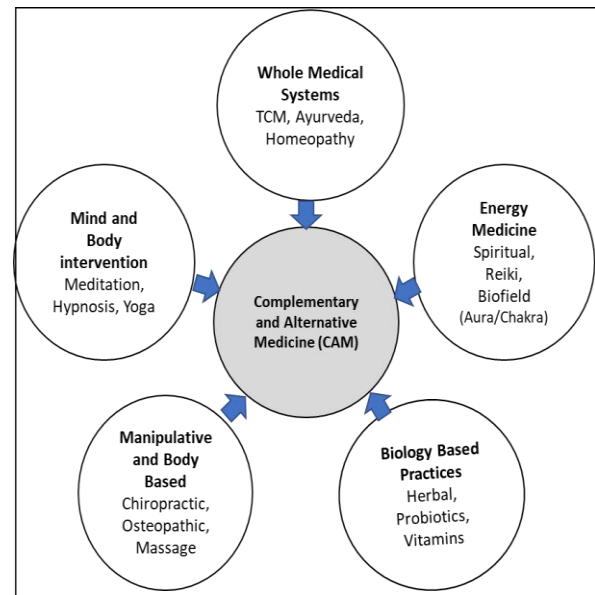


Figure 1: Domains of Complementary and Alternative medicine and medical practices

Methods used in CAM system

Traditional Chinese Medicine (TCM) is ancient system of healing from 200 BC and other countries like Korea, Japan, India and Vietnam have developed their own systems. This medicine emphasizes proper balance or disturbance in Qi or vital energy in health and disease. The treatment includes usage of Acupuncture, Herbal medicine, and Massage, along with Reiki and Qi Gong, forms of energy therapy. Complementary and alternative medicine systems include Ayurveda, which originated in India 5,000 years ago and the treatment encompasses Yoga, Meditation, Massage, Diet, and Herbs, Additionally, Homeopathy developed by Samuel C Hahnemann exploits the usage of microdoses of a substance to stimulate the disease symptoms in bodies for self-healing (Principle of Similar). Conventional medicine relies on research, safety, and carefully validated clinical trials. However, CAM treatments lack that research foundation and testing and are scientifically not proven.

Integrative medicine is a partnership between the patient and the doctor who decides the appropriate use of conventional and CAM to help heal exploiting the body's innate healing process. The treatment considers all factors influencing health and disease including mind and spirit. Several studies are in progress to evaluate the safety and efficacy of many CAM practices to provide clarity on using these methods (Fig. 2). Manipulative practices include methods that are based on manipulation or movement of the body, like chiropractors working on the relationship between structure and function for treating spinal cord problems. Similarly, massage therapists manipulate soft tissues of the body for normalization of the tissues.

Conventional Medicine	Alternative Medicine	Complementary Medicine	Integrative Medicine	Functional Medicine
				
Focus on Disease Treats symptoms at organ level	Used in place of conventional medicine. Treats symptoms using medicines closer to nature	Hybrid method of Conventional and Alternative medicine	Combination of Conventional and Alternative medicine in a coordinated process	Treats patient as a whole and not disease. Addresses functional imbalances of disease
Western, uses drugs, surgery, radiation	Not scientifically proven. Non-mainstream practice		Safe and Patient focused. Evidence based	Scientificallly based on Systems Biology

Concept from healingclinic.com

Figure 2:Differences between Conventional and non-conventional methods (CAM) used for treatment of diseases

Reiki was discovered by a Buddhist monk named Usui. The practice of Reiki was brought to Hawaii and USA in the 1970s by Hawayo Takata, a Japanese-Hawaiian woman [5]. Reiki supports the individual's energy to become "restored, free-flowing or balanced and one is more likely to feel relaxed and the body's own innate healing abilities are 'jump-started' and utilized for healing" [6]. The therapist will access universal energy sources that can strengthen the body's ability to heal itself, reduce inflammation, and relieve pain and stress [7].

Energy Therapy is based on energy fields within the body or those from other sources (Electromagnetic). The practitioners of Energy healing use Qi Gong, Reiki, Prana, and Therapeutic Touch to manipulate biofields by applying pressure or manipulating the body by placing the hands in or through these fields for the treatment of asthma, cancer, or pain management. Hypnosis is an altered state of consciousness. Energy Centers in the body are formed where 72,000 nadis (nerves) come together and unite. It is believed that they run along the length of the spinal cord in the body, from the pelvic base to the top of the head. Changes in Chakra frequencies result in ailments (Fig. 3)

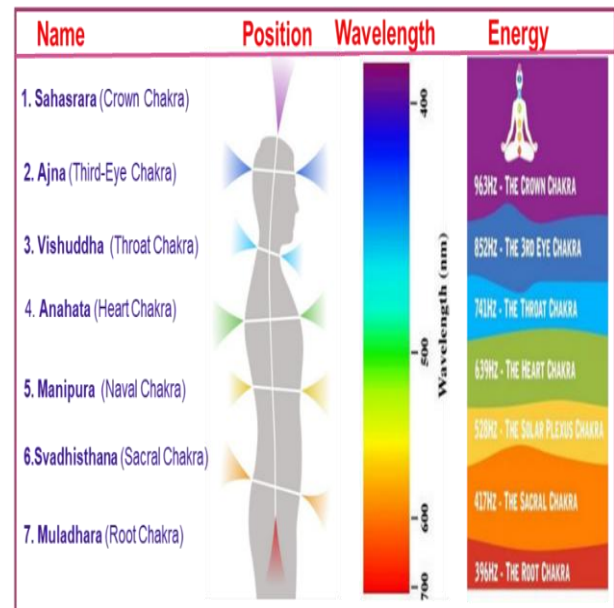


Fig.3: Relationship between the position of Nerve Junctions Chakra, Wavelength and Energy Bio field Reader (BFR) is used to measure bio energy that processes live-stream video, video files, and digital images. This is a great tool to assess changes in the bio field as they happen.BFR is used successfully in healing, reflexology, EFT, or one of the many other complementary therapies [8]. Similarly, the Universal Aura scanner is also used to measure Geopathic Stress, Human Energy and Paranormal Energy [9].

Growth of CAM internationally:

Even though there is no unequivocal evidence, several governments like India licensed Ayurveda (Panchakarma and Massage), Siddha, Unani, and Homeopathy and established medical colleges to generate specialists in this field (AYUSH, Govt. of India) [10]. Over the last decade, the U.S. population has shown a steady and substantial increase in the use of CAM. As per the estimates carried out in 2007 overall prevalence of use at 38.3% of adults (83 million persons) and 11.8% of children (8.5 million children under age 18 years) [11] was observed. Further, 75 US medical schools out of 130 are offering courses in Integrative Medicine. CAM (40), Traditional medicine [25], Acupuncture [22], Meditation [21], and Spirituality (18) are top 5 courses [12]. CAM therapies are used by 20–50% of the population in Europe [13] and an Australian survey in 1992/1993 found that 48.5% of the population used at least one non-medically prescribed alternative therapeutic modality [14]. The average prevalence of use of CAM in the UK from data collected across 13 surveys was 20.6% (range 12.1-32%). The average referral rate to CAM was 39% (range 24.6-86%), and CAM was recommended by 46% of physicians (range 38-55%) [15].

a. Complementary and Alternative Medicine for pain management:

Any type of pain can affect a person's life by not being able to do the job well or conduct day-to-day activities. Pain may also cause trouble in sleeping and eating. Pain is the

condition for which people tend to use complementary and integrative health approaches. This includes different pains like musculoskeletal pain (back, neck, joint) or linked with specific conditions (arthritis). Pain is a vital response to actual or potential tissue injury. If the acute pain becomes chronic pain it may lead to biological changes in the central nervous system as well as changes in peripheral tissues.

Growing evidence suggests that CAM may help in the treatment and management of pain. Now that self-management of chronic pain is recognized as a treatment strategy, it is important to understand how to best integrate effective complementary approaches into care and how to optimize interventions for individuals and groups (Fig.4)

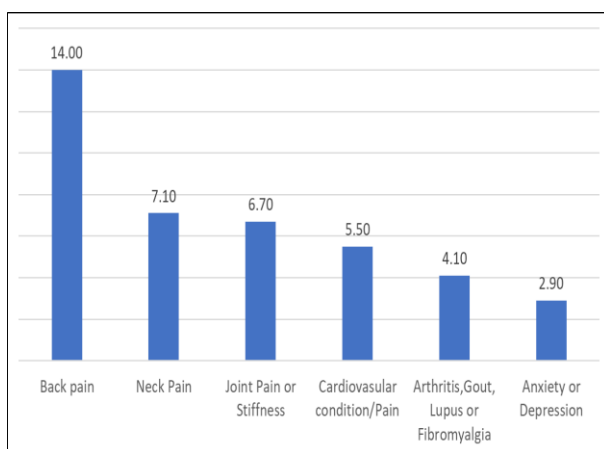


Fig 4: Complementary Health Approaches used for different pain conditions. Values shown are Percent population used. (NCCIH, 2012).

Data presented in the graph indicates ~32% usage of CAM mainly to treat different pain conditions [16]. The CAM methods draw attention away from the pain and release muscle tension caused by pain. They can help the patient relax by releasing natural opioids within the body that can enhance the effects of pain medicine and medical therapies.

b. Pain in cancer patients:

An extensive and methodical search of the literature published between September 2005 and January 2014 using the databases PubMed, Medline, Embase, CINAHL, and Cochrane reported on the prevalence of cancer pain in an adult population, has revealed that pain prevalence rates were 39.3% after curative treatment, 55.0% during anticancer treatment and 66.4% in advanced, metastatic, or terminal disease [17]. In cancer patients, the pain is experienced because the cancer has already spread in the body. Further, the pain may be an early indication of bone cancer or testicular cancer. Back pain is common in people with colorectal cancer, pancreatic cancer, or ovarian cancer. Those with brain tumors often complain of a headache that doesn't go away. The cancer itself or different factors, like the type of cancer, its stage, surgery, treatment, or tests can cause pain. Pain from the cancer

can result from a growing tumor pressing on nerves, bones, or organs. If a tumor spreads to the spine, it can press on the nerves of the spinal cord and lead to its compression causing back and/or neck pain, and sometimes it is severe. Pain may also be experienced in an arm or leg. Coughing, sneezing, or other movements often make the pain worse. Bone pain can happen when cancer starts in or spreads to the bones. Surgery is often part of the treatment for cancers that grow as solid tumors. Depending on the kind of surgery, some amount of pain is usually expected and can last from a few days to weeks. Phantom pain is a longer-lasting effect of surgery, resulting from the removal of an organ (arm, leg, or breast) during the cancer treatment. Pain can also result as a side effect of chemotherapy (Peripheral neuropathy and mouth sores) and radiation therapy the pain can even make some people stop treatment. Some tests used for cancer diagnostics and to evaluate treatment progress may be painful.

Complementary and Alternative Medicine for Pain Management

a) Reiki/Energy healing for Pain:

Patients with cancer experience several chemotherapy-related side effects, like fatigue, nausea and vomiting, pain, insomnia and dyspnea, hair loss, cognitive dysfunction, and alterations in sexual functioning which can have a significant effect on comfort and well-being during and after cancer treatment. Increasing patient comfort and well-being during the chemotherapy process is a goal of all oncology specialists, and emphasis has been placed on the use of complementary and alternative medicine (CAM) to achieve this goal. Several facilities offer Reiki as an adjunct therapy for patients with cancer. The Norris Cotton Cancer Center in Lebanon, New Hampshire, USA, offers Reiki therapy to all infusion clinic patients.

The Investigation in an outpatient chemotherapy infusion center was conducted to determine whether the provision of Reiki therapy during outpatient chemotherapy is associated with increased comfort and well-being [20]. The studies used double-blind, randomized clinical controlled trials using 189 patients. The patients receiving chemotherapy were randomly placed into one of three groups. Patients received standard care, a placebo, or an actual Reiki therapy treatment. A demographic tool and pre-and post-tests were given before and after chemotherapy infusion. The trials showed that Reiki therapy was statistically significant in raising the comfort and well-being of patients post-therapy, the sham Reiki placebo was statistically significant. Patients in the standard care group did not experience changes in comfort and well-being during their infusion session. In contrast, the findings also indicated that the presence of an RN providing one-on-one support during chemotherapy was influential in raising comfort and well-being levels, with or without an attempted healing energy field. As

there are multiple parameters are used and all seem to have the same effect the trial was inconclusive.

The medical team at San Giovanni Battista Hospital, Turin, Italy investigated the effect of Reiki in the treatment of anxiety, pain, and global wellness in cancer patients. These studies were conducted between 2003 and 2005, along with a second wider 3-year study. The study subjects included 118 patients (67 women and 51 men; with a mean age of 55 years). The nurses collected the patient's personal data and clinical history before starting each session. Each session lasted about 30 min; pain and anxiety scores were recorded using a Visual Analog Scale (VAS), together with a description of the physical feelings the patients perceived during the session. All 118 patients received at least 1 Reiki treatment (total number, 238). In the subgroup of 22 patients who underwent the full cycle of 4 treatments, the mean VAS pain score decreased from 4.4 to 2.32 ($P = .091$). These studies showed that the reiki sessions were felt helpful in improving pain relief and reducing anxiety [21].

The effective management of cancer pain is a common problem in palliative care and high doses of opioids are often used for treatment that cause multiple side effects, that are difficult to manage. An Initial single arm clinical study employing twenty volunteers experiencing pain for a variety of reasons (e.g., cancer, arthritis, chronic back problems) were provided with a Reiki treatment and Pain was measured using both a visual analogue scale (VAS) and a Likert scale. Measures of pain were obtained immediately before and after the Reiki treatment and the results showed a highly significant improvement in pain control (reduction of 2.25 on the VAS and 1.25 on the Likert Scale) following the Reiki treatment [22]. Based on these results, a Phase II clinical Trial of Reiki for the Management of Pain was conducted in Advanced Cancer Patients. This trial compared pain, quality of life, and analgesic use in a sample of patients with cancer pain using 24 patients who received either standard opioid management plus rest or standard opioid management plus Reiki. Participants either rested for 1.5 hr on Days 1 and 4 or received two Reiki treatments (Days 1 and 4) one hour after their first-afternoon analgesic dose. Visual analog scale (VAS) pain ratings, blood pressure, heart rate, and respirations were obtained before and after each treatment/rest period. Analgesic use and VAS pain scores were reported for 7 days. Participants from the group using standard opioid management plus Reiki experienced improved pain control on Days 1 and 4 following treatment, compared to the group resting for 1.5 h on Days 1 and 4, and improved quality of life, but no overall reduction in opioid use [23].

b) Biofield therapy in clinical studies-Identification of Biomarkers

Biofield is a term coined during the NIH Health Conference in 1992 and defined as a mass less field, not necessarily electromagnetic, that surrounds and permeates living

bodies and affects the body bio field therapy is non-invasive and explicitly works with the bio field of both the practitioner and client to stimulate a healing response in the client [24]. Bio field therapies are widely used in patients suffering from cancer and those receiving palliative care. Systematic reviews of clinical trials of biofield therapies have been conducted for all biofield therapies tested or for specific conditions like cancer [25] and cancer pain [26]. More than 15 clinical trials have been conducted with biofield therapies in patients with cancer, both during and after conventional biomedical treatment, and focused on studies as adjunctive care to reduce symptoms of pain, fatigue, anxiety, and depression. Most significantly, in the high-quality studies biofield therapy for cancer-related symptoms has shown clinically significant reductions in depression and persistent fatigue, as well as positive effects on clinically relevant biological markers like diurnal cortisol variability in fatigued breast cancer patients as compared to mock treatments or standard care and in cervical cancer patients [27]. Biofield treatment has also improved depressive symptoms and prevented the drop in natural killer cell cytotoxicity otherwise seen in the relaxation therapy and usual care comparison groups [28].

The impact of bio field therapies on tumor markers and other clinical biomarkers has been minimally studied, bio field therapy on multiple tumor types, with reports of inhibition of DNA synthesis and mineralization in osteosarcoma, inhibition of cell cycle and induction of apoptosis in prostate cancer cells [29] and inhibition of migration and invasion of breast cancer cells [30] have been identified.

c) Acupuncture for Cancer Pain:

Cancer is the second leading cause of death with an annual death rate of 10.0 million in 2020 pain is one of the most common symptoms of cancer and about more than 70% of individuals with advanced cancer suffer from moderate to severe pain [31]. The World Health Organization has recommended the appropriate use of opioids to reduce pain, but the opioid crisis [32] has drastic challenges in pain management and this warranted a need for non pharmacological treatments. Acupuncture has been widely used for the control of chronic pain [33]. Recent studies demonstrated that acupuncture was significantly associated with reduced cancer pain and can decrease the use of analgesics with moderate certainty of evidence and approximately one in 10 cancer survivors have used acupuncture in the United States.

Eight randomized controlled trials (RCTs) with a total of 530 patients with moderate to severe pain compared the efficacy of acupuncture and sham acupuncture. Three methods of acupuncture including manual acupuncture, electro acupuncture, and auricular acupuncture were included RCT studies. NRS score for pain Alleviation is measured as an outcome of these studies [34].

The results showed that acupuncture could effectively relieve the cancer pain intensity compared to sham acupuncture or wait-list control. No serious treatment-related adverse events were observed. The certainty for evidence was moderate.

RCT	Number of participants / Studies	Effect Size (Mean Difference)	Certainty of Evidence (Grade)
Acupuncture / sham acupuncture	226/172 (7 studies)	-1.39 points (-2.15, -0.63)	Moderate
Acupuncture / Wait list	151/104 (3 studies)	-1.63 points (-2.14, -1.13)	Moderate
Manual acupuncture / sham		-0.88 points (-1.75, -0.01)	Moderate
Manual acupuncture / wait-list	129/81 (2 studies)	1.62 points (-2.37, -0.86)	Low
Manual acupuncture plus analgesic /analgesic only	32/32 (1 study)	-0.83 points (-1.36, -0.30)	Low
Electroacupuncture/ sham	52/52 (2 studies)	-0.84 points (-2.43, 0.75)	Moderate
Electroacupuncture/ Wait list	22/23 (1 study)	-2.00 points (-3.11, -0.89)	Low
Electroacupuncture plus analgesic /analgesic only	80/80 (2 studies)	-1.27 points (-2.93, 0.39)	Low
Acupuncture plus analgesic /analgesic only	112/112 (3 studies)	-1.12 points (-2.19, -0.06)	Low

Table 1: Summary of randomized controlled studies conducted with patients with severe or moderate cancer pain and the outcome is pain reduction.

Based on the RCT studies and systematic reviews published in JAMA Oncology in 2020 [35], searching several databases and websites for evidence on using acupuncture for the treatment of cancer pain, the international multidisciplinary panel consisting of 13 Western medicine oncologists, Chinese

medicine/acupuncture clinical practitioners made following recommendations to treat cancer pain using acupuncture [34].

- (1) A strong recommendation of acupuncture rather than no treatment to relieve pain in patients with moderate to severe cancer pain
- (2) a strong recommendation of acupuncture in breast cancer patients to relieve their aromatase inhibitor-induced arthralgia
- (3) a weak recommendation for the combination treatments with acupuncture to reduce pain intensity, decrease the opioid dose, and alleviate opioid-related side effects in moderate to severe cancer pain patients who are using analgesics

Current oncology guidelines recommend acupuncture for cancer pain, fatigue, and hot flashes [35] further, a newly released guideline from the Society for Integrative Oncology and ASCO recommends acupuncture for aromatase inhibitor-related joint pain, musculoskeletal pain, and general cancer pain [37].

d) Natural Products for Cancer pain therapy:

Different types of pain-killing medicines are used currently to treat cancer pain including opioids and most of these cause harmful side effects to cancer patients. Hence, there is an urgency to find alternative naturally occurring products for cancer pain relief. Natural products (NPs) are strong candidates for the development of new drugs for the treatment of chronic pain, such as cancer pain. In a recent survey of literature using PubMed, Scopus and Web of Science (from inception to June 2018), identified 15 natural products for the treatment of cancer pain and suggested that these NPs have targets in central and peripheral nervous systems.

Morphine was one of the first NP compounds isolated from opium in a pure form in the early 19th century and is used as a standard pain killer especially for cancer patients. Since the discovery of morphine, NPs have played an essential role as strong candidates for the development of new drugs for the treatment of chronic pain, such as cancer pain [38]. Mono and Di Terpenes, Alkaloids, Flavonoids, and Cannabinoids are potential chemical compounds present in natural products that reduce inflammation, increase oxidation, and reduce tumor size.

Evaluation of the effect of Carvacrol (5-isopropyl-2-methylphenol), a phenolic monoterpene, found in several species of the genera *Origanum*, *Lippia*, and *Satureja* that act on hyperalgesia and nociception induced by sarcoma 180 in mice revealed that it significantly reduced cancer nociception activating central nervous system (CNS) areas involved in the pain inhibitory descending pathway, as well as decreasing tumor size, what contributed to reduce pain [3]. Similarly, α -Terpineol (TP), a monoterpene from *Eucalyptus* was found to have an antinociceptive effect mediated by peripheral mechanisms in a cancer pain model induced by sarcoma 180. This is mediated by the reduction of iNOS levels and maintenance of GSH levels,

contributing to the reduction of nociceptive responses induced by tumor cells [40].

Resiniferatoxin, a natural diterpene structurally related to phorbol esters present in 3 species of Euphorbia, works as the most potent endogenous and synthetic agonist for the Transient receptor potential vanilloid 1 (TRPV1), a non-selective calcium-ion channel. Studies showed that a single dose of Resiniferatoxin has completely abolished the hyperalgesia induced by osteosarcoma for several days and prevented the establishment of thermal hyperalgesia [41]. This compound also showed an analgesic effect on bone cancer pain in dogs.

Morin, a bioflavonoid found in several species of herbs and fruits, has antioxidant and anti-inflammatory properties. A study conducted in a bone cancer model in rats showed that treatment with morin attenuates the behavioral hypersensitivity of animals and the morin antinociceptive effects on bone cancer pain may be associated with CB2 receptor activation in the spinal cord [42].

Several studies have demonstrated that gelsemine, an alkaloid, has a variety of biological actions, such as antinociceptive and antitumor properties. In a model of tumor pain induced by Walker 256 carcinoma cells, it is found that gelsemine promoted potent antinociception due to the spinal activation of α 3-glycine receptors, an important therapeutic target for the treatment of chronic pain [43].

Natural products	Source	Model	Results	Mechanisms of action proposed
Terpenes				
Carvacrol	Genus Origanum, Lippia and Satureja	Cancer pain induced by S180 (i.pl.)	↓ Hyperalgesia and nociception and palpation induced nociception; ↓ tumor growth	Activation of pain inhibitory descending pathway; modulation of IL-10 and GABA receptors
α -Terpineol	Eucalyptus	Cancer pain induced by S180 (i.pl.)	↓ Hyperalgesia and nociception and	↓ iNOS; ↑ GSH

			palpation induced nociception; ↓ oxidative stress	
Resiniferatoxin	Species of Euphorbia	Osteosarcoma induced by NCTC 2472 cells	↓ Thermal Hyperalgesia	↓ microglia (Iba-1), ↓ astrocytes
Resiniferatoxin	Species of Euphorbia	Bone cancer pain	Analgesic effect of a single intrathecal injection	(GFAP), ↓ HDAC1 and TRPV1 antagonist
Flavonoids				
Morin	Several species of herbs and fruits	Bone cancer pain induced by Walker 256	Antinociceptive; ↓ astrocyte activation and neuroinflammation	↓ TNF- α , IL-1 β , IL-6 and ↑ IL-10; ↓ mRNA of GFAP; agonist of CB2
Gelsemine	Genus Gelsemium of the family Loganiaceae	Bone cancer pain induced by Walker 256	↓ Mechanical allodynia	Activation of spinal α 3; glycine receptors

Table 2: Evaluation of different types of Natural products in clinical trials on various models of cancer pains and mechanism of action of natural products tested [44].

Finally, the cannabinoids, derived from the Cannabis sativa plant, were identified as potential adjuvants in the configuration of cancer pain. cannabidiol (CBD) derived from the Cannabis sativa L., popularly known as “marijuana”, belongs to a family of compounds known as cannabinoids and has shown potential for pain relief. One of the mechanisms of action of these compounds is through the endocannabinoid system (CB1 and CB2 receptors), which contributes to inhibiting the release of neurotransmitters such as glutamate and GABA [44].

In summary, the compounds obtained from plant species have been shown to be promising candidates for the development of new therapies for cancer pain. The diversity of targets range from these is inhibition of pro-inflammatory cytokines or enhancement of anti-inflammatory cytokines and reduction of oxidative stress

modulation to central mechanisms such as opioid system modulation and inhibition of glutamatergic receptors.

Summary and Future Objectives

Discovering the mechanisms by which a complementary approach exerts its effects could help in the design of better treatments and predict which people are most likely to respond. Hence, there is a need for rigorous research on complementary and integrative health approaches for pain that span basic, mechanistic, translational, and clinical domains. As prioritized by NCCIH (NIH, USA) in its 2016 Strategic Plan, exploring the Science of Complementary and Integrative Health, the objectives to be prioritized for the use of CAM in non pharmaceutical pain management include-

- i) Identification of biological targets and pathways by which CAM approaches like natural products, mind and body interventions have clinical benefits
- ii) Investigating interactions of multiple non pharmacologic interventions (e.g., meditation and probiotics) to determine whether they can increase effect size and enhance resilience.
- iii) Developing and validating objective pain measures for complementary and integrative health approaches in the treatment of pain.

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Conflict of Interest

Author has no conflict of interest to disclose

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References

1. Aldred EM, Buck C, Vall K; Analgesia and relief of pain, Editor(s): Aldred EM, Buck C, Vall K. Pharmacology, Churchill Livingstone, 2009, p247-254,
2. Ricciotti E, FitzGerald GA. Prostaglandins and inflammation. *Arterioscler Thromb Vasc Biol.* 2011; 31(5):986-1000.
3. Wilkinson J, Faleiro R. Acupuncture in pain management. *Contin Educ Anaesth Crit Care Pain.* 2007;7(4):135-138
4. Urits I, Schwartz RH, Orhurhu V, Maganty NV, Reilly BT, Patel PM et al. A Comprehensive Review of Alternative Therapies for the Management of Chronic Pain Patients: Acupuncture, Tai Chi, Osteopathic Manipulative Medicine, and Chiropractic Care. *Adv Ther.* 2021; 38(1):76-78.
5. Toms R. Reiki therapy a nursing intervention for critical care. *Crit Care Nurs* 2011; 34: 213-217.
6. Moore A. Reiki energy medicine: enhancing the healing process. *Integrative Medicine Quarterly News* 2005; 2: 1-5
7. Brathovde A. Reiki for self-care of nurses and healthcare providers. *Holist Nurs Pract* 2006; 20: 95-101
8. Jain S, Hammerschlag R, Mills P, Cohen L, Krieger R, Vieten C, Lutgendorf S. Clinical Studies of Biofield Therapies: Summary, Methodological Challenges, and Recommendations. *Glob Adv Health Med.* 2015; 4(Suppl):58-66.
9. Mannem M. Improved universal aura scanner. World Wide patent application 2019; WO2019058184A1
10. Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homeopathy (AYUSH); Ministry of Health and Family Welfare, Govt. of India
11. Barnes PM, Bloom B, Nahin RL. Complementary and alternative medicine use among adults and children: United States, 2007. *National health statistics reports*;2008; 12: Hyattsville, MD: National Center for Health Statistics.
12. Cowen VS, Cyr V. Complementary and alternative medicine in US medical schools. *Adv Med Educ Pract.* 2015; 6: 113-117
13. Fisher P, Ward A. Medicine in Europe: Complementary medicine in Europe. *Brit Med.J.* 1994, 309: 107-111.
14. MacLennan AH, Wilson DH, Taylor AW. Prevalence and cost of alternative medicine in Australia. *Lancet* 1996, 347: 569-573.
15. Posadzki P, Alotaibi A, Ernst E. Prevalence of use of complementary and alternative medicine (CAM) by physicians in the UK: a systematic review of surveys. *Clin Med (Lond).* 2012;12(6):505-512.
16. Nahin RL. National Health Interview Survey 2012 data on diseases and conditions for which adults use complementary health approaches. 2016 Unpublished raw data
17. van den Beuken-van Everdingen MH, Hochstenbach LM, Joosten EA, Tjan-Heijnen VC, Janssen DJ. Update on Prevalence of Pain in Patients With Cancer: Systematic Review and Meta-Analysis. *J Pain Symptom Manage.* 2016;51(6):1070-1090.
18. Nowak, AK, Stockler, MR, Byrne, MJ. Assessing quality of life during chemotherapy for pleural mesothelioma: Feasibility, validity, and results using the European Organisation for Research and Treatment of Cancer Core Quality-of-Life Questionnaire and Lung Cancer Module. *Journal of Clinical Oncology*2004; 22: 3172-3180.
19. Kayl AE, Meyers CA. Side effects of chemotherapy and quality of life in ovarian and breast cancer patients. *Current Opinions in Obstetrics and*

- Gynecology 2006; 18: 24–28.
20. Catlin A, Taylor-Ford RL. Investigation of standard care versus sham Reiki placebo versus actual Reiki therapy to enhance comfort and well-being in a chemotherapy infusion center. *Oncol Nurs Forum*. 2011; 38(3):E212-220.
21. Birocco N, Guillaume C, Storto S, Ritorto G, Catino C, Gir N et al. The effects of Reiki therapy on pain and anxiety in patients attending a day oncology and infusion services unit. *Am J Hosp Palliat Care*. 2012;29(4):290-294.
22. Olson K, Hanson J. Using Reiki to manage pain: a preliminary report. *Cancer Prev Control* 1997; 1(2):108–113.
23. Olson K, Hanson J, Michaud M. A phase II trial of Reiki for the management of pain in advanced cancer patients. *J Pain Symptom Manage*. 2003;26(5):990-997.
24. Rubik B, Pavlek R, Greene E, Laurence D, Ward R, Al E. In: Rubik B, et al, editors. *Alternative medicine: expanding medical horizons: a report to the National Institutes of Health on alternative medical systems and practices in the United States*. Washington, DC: US Government Printing Office; 1995: p13-57.
25. Gonella S, Garrino L, Dimonte V. Biofield therapies and cancer-related symptoms: a review. *Clin J Oncology Nurs*. 2014;18(5):568-576.
26. Anderson JG, Taylor AG. Biofield therapies and cancer pain. *Clin J Oncology Nurs*. 2012;16(1):43-48.
27. Jain S, Pavlik D, Distefan J, Bruyere RL, Acer J, Garcia R, Coulter I, Ives J, Roesch SC, Jonas W, Mills PJ. Complementary medicine for fatigue and cortisol variability in breast cancer survivors. *Cancer*. 2012;118(3):777-787.
28. Wong J, Ghiasuddin A, Kimata C, Patelesio B, Siu A. The impact of healing touch on pediatric oncology patients. *Integr Cancer Ther*. 2013;12(1):25-30.
29. Yan X, Shen H, Jiang H, Zhang C, Hu D, Wang J, Wu X.. External Qi of Yan Xin Qigong induces G2/M arrest and apoptosis of androgen-independent prostate cancer cells by inhibit-ing Aki and NF-kappa B pathways. *Mol Cell Biochem*. 2008; 310: 227-234.
30. Yan X, Shen H, Jiang H, Hu D, Zhang C, Wang J, Wu X. External Qi of Yan Xin Qigong Induces induces apoptosis and inhibits migration and invasion of estrogen-independent breast cancer cells through suppression of Aki/NF-kB signaling. *Cell Physiol Biochem*. 2010;25(2-3):263-270.
31. Laird B, Colvin L, Fallon M. Management of cancer pain: basic principles and neuropathic cancer pain. *Eur J Cancer*. 2008;44(8):1078–1082.
32. Sharfstein JM, Olsen Y. Lessons learned from the opioid epidemic. *JAMA*. 2019;322(9):809–810.
33. Vickers AJ, Vertosick EA, Lewith G, MacPherson H, Foster NE, Sherman KJ, et al. Acupuncture for chronic pain: update of an individual patient data meta-analysis. *J Pain*. 2018;19(5):455–474
34. Ge L, Wang Q, He Y, Wu D, Zhou Q, Xu N, Yang K et al. Acupuncture for cancer pain: an evidence-based clinical practice guideline. *Chin Med* 2022; 17, 8 (2022).
35. He Y, Guo X, May BH, Zhang AL, Liu Y, Lu C, Mao JJ, Xue CC, Zhang H. Clinical Evidence for Association of Acupuncture and Acupressure With Improved Cancer Pain; A Systematic Review and Meta-Analysis. *JAMA Oncol*. 2020;6(2): 271-278
36. Lyman GH, Greenlee H, Bohlke K, Bao T, DeMichele AM, Deng GE et al. Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline. *J Clin Oncol*. 2018;36(25):2647-2655.
37. Mao JJ, Ismaila N, Bao T, Barton D, Ben-Arye E, Garland E et al. Integrative Medicine for Pain Management in Oncology: Society for Integrative Oncology-ASCO Guideline. *J Clin Oncol*. 2022; 40 (34):3998-4024
38. Li JW, Vederas JC. Drug discovery and natural products: end of an era or an endless frontier? *Science*. 2009; 10;325(5937):161-165
39. Guimarães AG, Serafini MR, Quintans-Júnior, LJ. Terpenes and derivatives as a new perspective for pain treatment: a patent review. *Expert Opin. Ther. Pat* 2014; 24: 243–265.
40. Dagne E, Bisrat, D, Alemayehu M, Worku, T. Essential oils of twelve Eucalyptus species from Ethiopia. *J. Essent. Oil Res*. 2000; 12: 467–470
41. Menéndez L, Juárez L, García E, García-Suárez O, Hidalgo A, Baamonde A. Analgesic effects of capsazepine and resiniferatoxin on bone cancer pain in mice. *Neurosci. Lett*. 2006; 393: 70–73.
42. Jiang W, Wang Y, Sun W, Zhang M. Morin suppresses astrocyte activation and regulates cytokine release in bone cancer pain rat models: antinociceptive effects of morin on bone cancer pain. *Phytother. Res*. 2017; 31: 1298–1304.
43. Zhang JY, Gong N, Huang JL, Guo LC, Wang YX. Gelsemine, a principal alkaloid from *Gelsemium sempervirens* Ait., exhibits potent and specific antinociception in chronic pain by acting at spinal $\alpha 3$ glycine receptors. *Pain* 2013; 154: 2452–2462.
44. Hashimoto-dani Y, Ohno-Shosaku T, Kano M. Endocannabinoids and synaptic function in the CNS. *Neuroscientist* 2007; 13: 127–137