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- Read the enclosed course.
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#### Faculty

Chelsey McIntyre, PharmD, is a clinical pharmacist who specializes in drug information, literature analysis, and medical writing. She earned her Bachelor of Science degree in Genetics from the University of California, Davis. She then went on to complete her PharmD at Creighton University, followed by a clinical residency at the Children's Hospital of Philadelphia (CHOP). Dr. McIntyre held the position of Drug Information and Policy Development Pharmacist at CHOP until her move to Washington state in 2017, after which she spent the next six years as a clinical editor for Natural Medicines, a clinical reference database focused on natural products and alternative therapies. She continues to create rigorous professional analysis and patient education materials for various publications while also practicing as a hospital pharmacist. Her professional interests include provider and patient education, as well as the application of evidence-based research to patient care.

#### Faculty Disclosure

Contributing faculty, Chelsey McIntyre, PharmD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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#### Division Planners/Director Disclosure

The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

#### Audience

This course is designed for healthcare professionals involved in the care of patients with cancer who use or are interested in using alternative therapies.

#### Accreditations & Approvals



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(ANCC), to provide continuing education for the healthcare team.

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#### **Course Objective**

The purpose of this course is to provide healthcare professionals in all practice settings the knowledge necessary to increase their understanding of alternative therapies commonly used by patients with cancer.

#### Learning Objectives

Upon completion of this course, you should be able to:

- Review the common indications for complementary therapies during cancer treatment.
- 2. Discuss the evidence for the use of cannabis, aromatherapy, and bee-derived products for managing chemotherapy-related complications.
- 3. Weigh the risks and benefits of herbal therapies when used in patients with cancer.
- 4. Consider the evidence for vitamin and mineral supplements during cancer treatment.
- 5. Provide counseling points for the safe and effective use of health and wellness modalities in patients with cancer.

#### Pharmacy Technician Learning Objectives

Upon completion of this course, you should be able to:

- 1. Identify common natural medicines used during cancer treatment.
- 2. Outline alternative health and wellness modalities used by patients with cancer, including yoga, mindfulness, and acupoint therapy.



Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included

so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

# INTRODUCTION

Cancer, and the drugs used to treat it, can cause various complications that impact quality of life. As a result, many patients diagnosed with cancer may consider the use of additional, alternative treatment options at some point in their journey with their diagnosis. These types of alternative therapies often come in the form of natural medicines and health and wellness modalities.

# COMPLEMENTARY MEDICINE IN CANCER

The practice of incorporating alternative therapies into conventional treatments is referred to as complementary medicine. For many patients, complementary medicine provides the autonomy and joint decision-making that can often be missing after a cancer diagnosis [1].

Patients who express interest in considering an integrative, complementary approach to treatment may do so for a variety of personal reasons, including hesitation about participating in recommended conventional cancer treatments, concerns about adverse effects, and/or a desire to increase their odds of a positive outcome.

## COMMON INDICATIONS FOR COMPLEMENTARY THERAPY

There are many reasons for a patient to consider the use of complementary therapies while undergoing treatment for cancer. The most common reasons relate to the complications associated with chemotherapy and radiation treatment, such as nausea and vomiting, neuropathy, diarrhea, and oral mucositis. Other common reasons for the use of alternative therapies relate to the complications associated with cancer itself, including cachexia, fatigue, pain, and poor quality of life. For most of these indications, there are effective prescription treatments available. In such situations, those treatments should be recommended as the first-line option. However, if patients do not respond adequately to the recommended treatments or express a strong preference for the use of an alternative option, various complementary modalities may be considered. When used appropriately, these therapies can contribute to a higher level of patient satisfaction and quality of life.

# DISCUSSING COMPLEMENTARY THERAPIES WITH PATIENTS

It is critical for any patient interested in complementary medicine to understand that conventional treatments offer the best chance of survival. Thus, these treatments should be given priority over the consideration of any alternative therapies.

It is also crucial for patients to understand that some alternative therapies might interact with conventional treatments. This could cause conventional treatments to become less effective or more toxic. For example, some natural medicines carry the risk of drug interactions, some can alter immune system function, and some can increase a patient's bleeding risk.

If a patient is interested in an integrative therapy approach, then all alternative therapies should be discussed with a healthcare professional who is informed on the potential risks and benefits of these options. Patients should be appropriately counseled on the likelihood for risk associated with any therapies of interest. If the patient decides to implement an alternative therapy, the healthcare professional should be involved to ensure safety with implementation [1].

Each person brings with them a unique set of characteristics that impact the way they think about cancer, cancer treatment, the management of complications, and even life as a cancer survivor. These characteristics are both demographic and cultural in nature and include personal experiences, age, gender, sexuality, race, ethnicity, and socioeconomic status. Some patients may be predisposed to favor a complementary approach to care. The National Cancer Institute (NCI) provides guidance for culturally appropriate and respectful conversations about alternative therapies for cancer in its Communication in Cancer Care. The NCI also provides a more general resource to assist in counseling patients on the concerns associated with specific complementary therapies (*Resources*).

# NATURAL MEDICINES AS COMPLEMENTARY THERAPIES

As noted, some natural medicines can introduce safety concerns during cancer treatment. However, there are also many natural products that can be safely used in people with cancer. The evidence for safe and effective use of some of the more popular options is discussed here.

# AROMATHERAPY

Aromatherapy, or the inhalation of essential oils, is often promoted for a variety of physical, emotional, and spiritual purposes. While many people promote the use of aromatherapy in everyday life, it is also touted for use during cancer treatment [2]. Essential oils, which are derived from fruits, flowers, and/or seeds, contain the aromatic constituents of individual plants. The oil is usually inhaled by placing it into a device called a diffuser (which diffuses the oil into the air) or by placing it onto the skin or a piece of cotton near the nose [2].

Research on the use of aromatherapy varies significantly in quality and is hindered by difficulty with conducting high-quality placebo-controlled trials. Due to the distinctive smell of these oils, it can be nearly impossible to adequately blind a person to their treatment assignment. The control groups in these studies either employ no treatment at all or use an inert substance, such as water or a low-scent oil (e.g., coconut or jojoba oil).

Aromatherapy is generally considered safe when used in moderation. However, patients should be aware that essential oils are not intended to be taken by mouth. Certain essential oils have been associated with many serious adverse effects when ingested, including severe gastrointestinal upset, seizures, and kidney damage. Patients should also be counseled that, because essential oils are derived from plants, some people may experience a hypersensitivity reaction when these oils are placed on the skin.

Many oils are marketed for use as aromatherapy, some containing oil mixtures derived from multiple plants. Some of the more common aromatherapy oils include peppermint, lavender, lemon, bergamot, and bitter orange. However, most of these essential oils have been only minimally evaluated in clinical research. The most well-studied, particularly in the setting of cancer, are lavender and peppermint.

# Lavender

Research on the use of essential oil from lavender (*Lavandula angustifolia*) indicates that sessions lasting for up to 30 minutes may offer short-term benefits for patients with situational or chronic anxiety [3; 4]. Some studies have specifically assessed its impact on anxiety in people with cancer. A meta-analysis of the available research found that lavender oil aromatherapy provided short-term improvement in anxiety. However, it did not improve feelings of depression or overall psychological well-being [5].

Lavender oil aromatherapy has also been evaluated for the management of cancer-related pain, with disappointing results. Small clinical studies in patients with advanced or terminal cancer found that diffusing lavender oil did not improve pain scores. Similarly, providing a massage with lavender oil did not improve pain scores more than a massage without lavender oil [6; 7].

## Peppermint

The essential oil of peppermint (*Mentha piperita*) has also been widely used—and widely studied—as aromatherapy. Unlike lavender, which has most often been studied for the management of various forms of psychological distress, peppermint has received attention in relation to the management of gastrointestinal (GI) concerns. So far, clinical research suggests that it may be beneficial for chemotherapyinduced nausea and vomiting (CINV). One clinical study found that inhaling the scent of peppermint oil from a drop placed under the nose about every eight hours for five days after receiving chemotherapy can reduce the severity and frequency of nausea and vomiting [8]. A separate study also found that adding peppermint oil to a cool, damp washcloth that was placed onto the neck for about 30 minutes relieved nausea when compared with a washcloth that did not contain peppermint oil [9].

# **BEE-DERIVED PRODUCTS**

A variety of bee-derived (beehive) products have gained popularity for the management of healthrelated issues, a practice referred to as apitherapy. Honey represents the most common and wellknown apitherapy product. However, a number of other beehive products have also been used for the management of chemotherapy- and cancer-related complications.

## Honey

Honey has shown promise in the prevention and management of oral mucositis. Although not all studies agree, many do suggest that rinsing the mouth with honey or applying honey to oral lesions can reduce the severity of oral mucositis. Most of these studies have asked patients to rinse with, and then slowly swallow, about 20 mL of honey at least three times daily [10; 11]. As a result of these findings, clinical practice guidelines from the Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology (MASCC/ ISOO) suggest the use of honey for the prevention of oral mucositis in patients with head and neck cancer who are receiving radiation. No recommendation is made for patients with other forms of cancer [12].

There has also been interest in using honey for various chemotherapy-related complications; however, there is little to no evidence to support its use for these indications. Although honey is generally considered safe for use, patients with prediabetes or diabetes should be cautious about the amount of honey consumed each day. A dose of 20 mL of honey, the dose used in these clinical trials, contains approximately 22 grams of sugar.

## Propolis

Propolis is a resinous material used by honeybees to construct and maintain the hive. It is typically derived from the buds of poplar or conifer trees and is purported to have antimicrobial and antiinflammatory activity.

Similarly to honey, propolis has become a popular alternative therapy for oral mucositis, a use that is supported by the available research. Clinical studies have found that using a mouthwash containing propolis can reduce the severity of oral mucositis when compared with placebo. In most cases, the mouthwash was used to rinse the mouth for about one minute, three times daily [13; 14; 15].

There has also been interest in using propolis to improve quality of life and nutritional status during cancer treatment, although this has not been adequately assessed in clinical research.

Propolis is generally safe for most people to use either orally or topically. However, people with atopic disease may be more likely to experience an allergic reaction to propolis and should use these products with caution. In some cases, patients have experienced allergic contact dermatitis, including cheilitis, when propolis is used on or near the lips or mouth [16].

## Royal Jelly

Royal jelly is a milky, gelatinous secretion produced by nurse honeybees. This substance, which is intended to nurture developing honeybees, is generally high in water, proteins, carbohydrates, and lipids. Royal jelly has garnered interest for a wide range of chemotherapy-related complications. Unlike honey and propolis, it has not been extensively evaluated for oral mucositis. Instead, early research has focused on its ability to prevent or mitigate complications associated with tyrosine kinase inhibitors (TKIs).

One very small clinical study evaluated the potential for royal jelly to prevent TKI-induced liver or kidney damage, ultimately finding no benefit. In this same study, royal jelly also did not appear to prevent TKI-induced acral erythema (hand-foot syndrome). However, this study did identify a potential benefit in TKI-related fatigue [17; 18]. A separate, small study suggests that royal jelly may modestly reduce cancer-related fatigue [19].

As with propolis, people with a history of atopy may be more likely to experience allergic reactions when taking royal jelly and should use these products with caution. Some reports suggest that this risk may also be higher in patients with a history of asthma [20; 21].

# CANNABIS AND CANNABINOIDS

Cannabis (*Cannabis sativa*) is one of the most popular natural medicines for patients receiving treatment for cancer. In fact, a survey conducted by the American Society of Clinical Oncology (ASCO) in 2020 found that 80% of Americans support the use of medical marijuana for patients with cancer. Approximately half of people who had cancer (or had previously had cancer) at the time of the survey stated that they wished they had more information about the benefits of cannabis for cancer-related pain, nausea, or other symptoms [22].

#### Prescription Cannabinoids

Before discussing the use of cannabis or cannabinoids purchased on the open market, patients should be made aware that some prescription cannabinoid products are approved for cancer-related purposes.

Two prescription drugs contain synthetic forms of delta-9-tetrahydrocannabinol (THC), the primary psychoactive ingredient found in cannabis. These prescription drugs—dronabinol (Marinol) and nabilone (Cesamet)—are approved by the U.S. Food and Drug Administration (FDA) for the treatment of CINV. Dronabinol is also approved for the management of weight loss and poor appetite (cachexia) in people with AIDS [23; 24].

Nabiximols is another cannabinoid drug that is often discussed. This drug is comprised of a fixed ratio of THC and cannabidiol (CBD), a nonpsychoactive cannabinoid. Unlike dronabinol and nabilone, however, this drug is not approved in the United States. Rather, it is available in Canada and some countries in Europe for treating cancer-related pain, as well as pain and muscle spasms in multiple sclerosis [25].

The approval of these products for these indications by different national regulators indicates that certain cannabinoids may offer benefit for people with cancer. However, all patients should employ caution when selecting non-prescription products found on the open market.



The American Society of Clinical Oncology (ASCO) asserts that adults with cancer who receive moderately or highly emetogenic antineoplastic agents with guideline-concordant antiemetic prophylaxis and experience refractory

nausea or vomiting may augment their antiemetic regimen with dronabinol, nabilone, or a qualitycontrolled oral 1:1 THC:CBD extract.

(https://ascopubs.org/doi/10.1200/EDBK\_431554. Last accessed February 25, 2025.)

Strength of Recommendation/Level of Evidence: WM/L (Weak recommendation based on moderatequality evidence for dronabinol and nabilone, lowquality evidence for 1:1 THC:CBD)

## Cannabinoid Comparison: Prescription versus Open-Market Products

Prescription cannabinoids are quite different from products that are purchased on the open market. Whereas prescription cannabinoids provide only a specific amount of a specific cannabinoid (often created synthetically in a lab), cannabis contains a wide range of constituents, including hydrocarbons, amino acids, sugars, fatty acids, and terpenes. Whole cannabis can also contain up to approximately 100 different cannabinoids; only a small number of these chemicals have been fully characterized or initially evaluated in laboratory or clinical research [26]. Many cannabis supplement products available on the market today are sold on the basis of their THC and CBD content. However, the other constituents present in cannabis should not be ignored. Scientists are still only beginning to learn how these many chemicals affect human physiology and how they may impact the activity of THC and CBD.

A number of cannabis and cannabinoid products available on the open market have been found to be contaminated with various unwanted substances, including pesticides, heavy metals, bacteria, and fungus. This is due in part to the fact that cannabis is a phytoremediator, or a plant that readily absorbs contaminants from the soil [27].

One of the most common sources of contamination in supplement cannabinoid products is the presence of a cannabinoid that is not listed on the label. For example, many CBD products have been found to contain large quantities of THC, despite the label claiming that the product contains pure CBD. Considering the psychoactive effects of THC, the presence of this chemical is often not desired by those who are purchasing a CBD product.

## **Potential Benefits**

Despite the widespread and longstanding popularity of cannabis and cannabinoids for use during cancer, evidence of benefit with many of these products remains relatively limited. Small studies have indicated that there may be some benefit for CINV, cancer-related pain, neuropathy, and cachexia. However, the best "strain" of cannabis, the ideal concentration of THC when used with or without CBD, and the appropriate dose and frequency of use are poorly understood [26].

CBD, when used alone, has not been found to offer particular benefit to people with cancer. Most of the available research has identified benefits with THC alone, or when THC is used in conjunction with CBD.

#### Potential Risks

THC has been associated with increased heart rate, decreased blood pressure, dizziness, and fainting. Additionally, its psychoactive nature can produce mood changes, a sense of being "high," sedation, disorientation, paranoia, and anxiety. People who use THC should be cautious about operating a vehicle or heavy machinery, as it is also known to impair and slow a person's motor function and reaction time [28].

CBD is associated with fewer adverse effects than THC. Most of the adverse effects seen with CBD, such as diarrhea and somnolence, have occurred with very high doses or when it is used in conjunction with certain medications, including antiseizure drugs. People using very high doses have also experienced decreased appetite and weight loss [29].

Many patients will choose to use cannabis and/or cannabinoids in conjunction with other treatment options, such as antiemetics and analgesics. In these cases, it is important to be aware of potential drug interactions. THC (as well as very high doses of CBD) produces CNS depressant activity, which can be compounded when used alongside other CNS depressants, such as opioids or benzodiazepines. Additionally, both THC and CBD have shown the potential to alter the activity of many enzymes in the cytochrome P450 (CYP) family, which are responsible for the metabolism of many prescription drugs. There is also some concern that different constituents in cannabis can alter platelet aggregation activity, which could increase bleeding risk [28].

## ENDOGENOUS SUBSTANCES

## Carnitine

L-carnitine is an amino acid that is sometimes used to counteract cancer-related fatigue and wasting. Some patients with cancer have been found to have low blood levels of this amino acid, which may reduce energy production and lead to fatigue. However, research shows that taking L-carnitine 2–4 grams daily for up to one month is no more effective than placebo for reducing fatigue in those with cancer [30; 31; 32]. Research on the use of L-carnitine for cancer-related cachexia, on the other hand, is more promising. Early studies have found that taking L-carnitine 4 grams daily for 12 weeks increases body mass index when compared to placebo [32]. Other research has found that when used in combination with megestrol acetate, L-carnitine improves lean body mass, fatigue, and quality of life when compared with megestrol acetate alone [33]. In the context of a benign safety profile and minimal adverse effects, L-carnitine can be considered as an adjunctive treatment for some patients with cancer-related cachexia.

Acetyl-L-carnitine, a derivative of L-carnitine, has not been studied for either cancer-related fatigue or cachexia. Instead, this ingredient has been touted for chemotherapy-induced neuropathy; however, multiple high-quality clinical studies show that taking acetyl-L-carnitine does not improve symptoms of neuropathy. Rather, these studies have indicated that some patients may have worse symptoms, with these worsened symptoms persisting for up to at least two years. In light of these findings, ASCO strongly recommends against the use of acetyl-L-carnitine for this purpose [34].

# Glutamine

This amino acid, which is naturally present in various tissues and organs in the human body, has been most extensively studied for the management of oral mucositis. Although some research has not identified any benefit, other small studies suggest that taking L-glutamine by mouth, or swishing a solution and swallowing it, may reduce the incidence, severity, and duration of oral mucositis caused by chemotherapy or radiation. The MASCC/ISOO clinical guidelines suggest the use of oral glutamine for the prevention of oral mucositis, specifically in patients with head and neck cancer who are receiving radiation therapy. No recommendation is made for patients with other forms of cancer [12].

Glutamine is also sometimes touted for the management of cachexia. Most research related to this topic has been focused on patients with AIDS-related wasting and has involved only small, preliminary studies. The benefits of glutamine in patients with cancer-related cachexia remain unclear at this time. Glutamine is considered well-tolerated when taken by mouth, although it can cause various mild-tomoderate GI adverse effects, such as belching, bloating, constipation, diarrhea, and gas. Some research in hematopoietic stem cell transplant (HSCT) has indicated that the use of intravenous glutamine (as a component of parenteral nutrition) may be associated with worsened outcomes. This association has not been identified with the use of oral glutamine, or in patients undergoing other forms of cancer treatment. However, these findings have led some experts to recommend exercising caution with the use of glutamine until more is known [12].

# Melatonin

Melatonin, an endogenous hormone produced by the brain's pineal gland, is well-known for its popular use as a sleep aid. However, it has also gained popularity for use during cancer treatment.

A range of clinical studies show that taking high-dose melatonin (10-40 mg daily) in combination with conventional chemotherapy might improve tumor regression rate in certain types of cancer. Additionally, high-dose melatonin may help to reduce a range of chemotherapy-related complications, including hematologic complications, cachexia, asthenia, and neuropathy [35; 36; 37]. While these findings appear promising, patients should discuss the use of high-dose melatonin with their oncology specialists prior to use. While low doses of melatonin are relatively benign and carry few side effects, high doses of melatonin have not been studied as extensively. Some research suggests that high doses may stimulate immune function, increase sedation, increase bleeding risk, and lower the seizure threshold.

Melatonin has also been evaluated for improving sleep quality in people with cancer. Perhaps somewhat surprisingly, however, clinical studies have found no benefit with the use of melatonin 20 mg daily for improving either sleep quality or quality of life when compared with placebo. Similarly, melatonin does not seem to be beneficial for treating cancer-related fatigue or cancer-related pain [38].

#### HERBAL SUPPLEMENTS

#### Adaptogens

Adaptogens are natural medicines that are believed to increase a person's ability to adapt to and avoid damage from harmful factors. Traditionally, they are thought to stimulate a nonspecific resistance against physical, environmental, and emotional stress. In this context, it is not difficult to see why adaptogens have become popular alternative therapies for patients being treated for cancer.

Perhaps the most popular adaptogen on the market today is ashwagandha (*Withania somnifera*). This evergreen shrub is commonly touted for a variety of uses, including anxiety, depression, and stress. While some clinical research suggests that taking ashwagandha up to 1 gram daily for two to three months can modestly improve symptoms of anxiety and chronic stress, these studies did not include patients with a cancer diagnosis [39].

Astragalus (Astragalus membranaceus) is another commonly touted adaptogen. Unlike ashwagandha, however, astragalus has been studied for a variety of chemotherapy-related adverse effects, including nausea and vomiting, fatigue, and diarrhea. Unfortunately, these studies are relatively small in size and have not always employed a placebo control group. Additionally, most of this research has evaluated intravenous astragalus, which is not available in the United States [40; 41; 42]. Research on the use of oral astragalus is far more limited and preliminary.

Various forms of ginseng are also often touted for use during cancer or chemotherapy. American ginseng (*Panax quinquefolius*) and Panax ginseng have both been studied for cancer-related fatigue. The most recent and highest quality studies have yielded conflicting evidence that suggests a lack of benefit [43; 44].



The ASCO has given a conditional recommendation for American ginseng (*Panax quinquefolius*) in the management of cancer-related fatigue during treatment at a dose of 1,000 mg twice daily (2,000 per day total) ideally dosed before noon).

(https://ascopubs.org/doi/10.1200/EDBK\_431554. Last accessed February 25, 2025.) Strength of Recommendation: Conditional

Many adaptogens have been shown to stimulate the immune system in laboratory research. This classwide effect could potentially alter the effectiveness of certain treatments and should be taken into consideration.

#### Ginger

Ginger (*Zingiber officinale*) is commonly recommended and used for the treatment of CINV. However, most clinical research, which has evaluated ginger in combination with conventional antiemetics, does not support its use for either delayed or acute CINV when compared with antiemetics alone [45; 46].

The best evidence to date indicates that ginger is unlikely to be beneficial for the management of CINV. Thus, it may be appropriate to counsel patients against the use of this product. Although it is likely safe for most adults, patients taking anticoagulants or who are at an increased risk for bleeding should use ginger with caution. Ginger may reduce platelet aggregation and increase the risk for bleeding. While this concern is based primarily on laboratory research and has not been validated in clinical research, this risk should be weighed against the apparent lack of benefit [47].

#### Turmeric

Turmeric (*Curcuma longa*) has become a prominent herbal supplement, touted for a wide range of health benefits in all patients, including those with cancer. To date, most clinical research on the use of turmeric for cancer- and chemotherapy-related complications has been inconclusive, including for

capecitabine-induced hand-foot syndrome, cancerrelated cachexia, chemotherapy-related constipation and diarrhea, and CINV.

However, a growing body of research suggests that turmeric may be beneficial for the management of oral mucositis. Studies show that using turmeric, either orally or as a mouthwash, during radiation or chemotherapy can reduce pain and the overall severity of mucositis. The doses used in these studies have ranged widely, so the best dose remains unclear at this time. However, in all studies, turmeric was administered at least three times daily [48; 49; 50; 51].

Turmeric is generally safe when taken by mouth. The most commonly reported adverse effects are constipation, dyspepsia, diarrhea, and reflux. While rare, turmeric has been associated with reports of serious liver damage. It is not entirely clear whether turmeric was the cause of liver damage in these patients; however, in most cases, the damage resolved after discontinuation of the supplement. Turmeric should be used with caution in people with existing liver dysfunction or in those taking hepatotoxic drugs [52].

The use of turmeric during cancer treatment introduces a number of other considerations related to drug interactions. For example, turmeric has antiinflammatory activity and may increase the risk of bleeding in people that are taking anticoagulants. Additionally, laboratory research suggests that turmeric may have the potential to interfere with the activity of certain chemotherapy treatments, including taxanes, alkylating agents, and antitumor antibiotics (e.g., doxorubicin, daunorubicin). While this risk remains theoretical, patients should be made aware of this possibility [53; 54].

# Miscellaneous Herbal Products

Many other herbal products have been touted for use in the management of chemotherapy- and cancerrelated complications. In some cases, these products have been found to offer no benefit, as with ginkgo for chemotherapy-related cognitive impairment [55]. In most cases, however, these products have not been adequately studied to determine their benefit or risk profiles in these patients. For example, milk thistle (*Slybum marianum*) has undergone preliminary evaluation for the prevention and treatment of chemotherapy-induced liver and kidney damage, with inconclusive and conflicting findings [56; 57; 58]. Non-psychedelic mushrooms have also recently gained popularity for a variety of health-related uses, including in the management of fatigue. Unfortunately, research on the use of these mushrooms (e.g., reishi, maitake, shiitake) remains limited.

Saffron (*Crocus sativa*), best known for its use as a vibrant red-orange spice, has shown some promise in the management of chemotherapy-induced peripheral neuropathy (CIPN). At least one study has shown that taking a specific constituent of saffron—crocin—at a dose of 15 mg twice daily for two months can improve pain scores when compared with placebo [59]. These early findings must be confirmed with further research.

## MICRONUTRIENTS

Many micronutrients, including vitamins and minerals, have been touted for use in the management of cancer-related complications. In some cases, adequate research has been conducted to evaluate these claims. In most cases, however, it remains unclear as to whether micronutrient supplements are beneficial.

The intravenous administration of certain micronutrients has been evaluated far more extensively than oral administration. Because intravenous substances can only be obtained via prescription, research on this route of administration is not discussed in this course. Instead, only the vitamins and minerals that have been adequately evaluated when taken by mouth are discussed in this section.

## Vitamin B6

Vitamin B6 is a water-soluble vitamin, also known as pyridoxine, that has been of interest for the management of capecitabine-induced hand-foot syndrome. Unfortunately, clinical research shows that taking oral vitamin B6 at a dose of 60–500 mg daily does not prevent this complication or reduce its severity when compared with control groups [60].

# Vitamin E

This fat-soluble vitamin has been considered for the management of various cancer-related concerns, although research has yielded either disappointing or inconclusive findings. Studies evaluating the use of topical or oral vitamin E for the management of oral mucositis have yielded conflicting results. Until more research is conducted, it is not clear whether vitamin E is beneficial for this purpose, or which formulation or dose may be most appropriate for use.

Vitamin E supplements have also been evaluated for CIPN, with the highest quality research showing no benefit [61]. As a result, ASCO does not recommend the use of vitamin E for the prevention or management of CIPN [62]. Similarly, research on the use of oral vitamin E for the management of breast cancer-related hot flashes found that it did not provide any benefits over placebo [63].

Many experts recommend caution with the use of vitamin E during cancer due to research indicating that vitamin E supplements may increase a person's risk for initially developing cancer, especially prostate cancer [64]. Additionally, some observational research suggests that people with head and neck cancer who take a vitamin E supplement during and after radiation therapy may have an increased risk of tumor recurrence or a second primary tumor [65]. Because there is currently no evidence of benefit with the use of vitamin E during cancer, consider steering patients away from these supplements.

# Zinc

Zinc, an essential mineral, has long been touted for the management of oral mucositis, either when taken orally or as a mouthwash. While some clinical studies have found benefit in children and adults receiving chemotherapy or radiation, other studies have not corroborated these findings. It is possible that some of these differences may be due to the form of zinc used, the severity of mucositis, and/or the source of the mucositis. For now, however, it is unclear if zinc is beneficial for this purpose. When used short-term, zinc is considered generally safe, with only limited GI adverse effects. Due to this safety profile, zinc can be considered as a shortterm adjunct treatment option for patients with oral mucositis. Doses used in studies of oral mucositis have ranged widely; those that have shown benefit utilized higher doses, providing zinc sulfate 220 mg three times daily [66; 67]. Studies of mouthwashes that have demonstrated benefit contained zinc chloride 0.2% used twice daily, and zinc sulfate 1% used three times daily [68; 69].

# OTHER MODALITIES AS COMPLEMENTARY THERAPIES

Moving beyond natural medicines, there is also growing interest in the use of many health and wellness modalities during cancer treatment. Many of these modalities are likely safe for most adults and are unlikely to interfere with the effectiveness of conventional cancer treatments.

One point of appeal for many patients relates to the fact that practitioners of alternative modalities may have more time available to spend with patients. This can provide an environment in which the patient feels heard, understood, encouraged, and/ or comforted, depending on their needs at the time. This additional level of personal attention is not always available from conventional practitioners and can be an important missing component for a patient struggling with a cancer diagnosis and its associated complications.

## EXERCISE-RELATED THERAPY

Exercise-related therapy can be a safe and beneficial option for patients who are physically able to participate in these modalities. Keep in mind, however, that any exercise should only be attempted by patients with the appropriate physical and functional status. If a patient is considering participating in yoga or qi gong but has limited mobility, balance, or perception, there are special, adapted forms of these exercise-based therapies available. Encourage them to consult with a physical therapist or seek out a recommendation for an instructor that is trained in adaptive techniques.

#### Yoga

Yoga is a health and wellness modality that has been steadily gaining in popularity as an adjunct to cancer treatment, particularly in women with breast cancer. Research in this population has found that participating in yoga can improve quality of life, pain, and well-being [70; 71; 72]. Yoga appears to improve quality of life and fatigue better than no therapy, and to a similar extent as other exercise regimens. It also seems to reduce sleep disturbance, anxiety, and depression [72].



The ASCO recommends yoga for people undergoing active treatment for cancer who are experiencing anxiety symptoms, with the highest level of evidence and strongest recommendation for persons with breast cancer.

(https://ascopubs.org/doi/10.1200/EDBK\_431554. Last accessed February 25, 2025.)

Strength of Recommendation/Level of Evidence: IM (Intermediate recommendation based on moderate-quality evidence)

When widening focus to all patients with cancer, yoga continues to demonstrate benefit. Clinical studies show that yoga can reduce cancer-related fatigue. In response to this research, the National Comprehensive Cancer Network (NCCN) guidelines list yoga as a potential nonpharmacologic option for the management of fatigue in patients with cancer [73]. The benefits of yoga for chemotherapy-related fatigue, on the other hand, may be less profound and more short-term [72].

# Qi Gong

Qi gong is a type of martial art-like exercise that is thought to integrate the mind and body and regulate the body's energy (or qi) through the use of meditation, breathing, and focus. Some forms of qi gong involve self-directed exercise with slow movements, while another form of qi gong involves external bodywork performed by a trained practitioner. Clinical research shows that qi gong can improve cancer-related fatigue when compared with no treatment, usual care, or other types of support in adults with cancer [74]. A meta-analysis of clinical studies also shows that practicing qi gong might improve quality of life and reduce chemotherapy-related side effects when compared with no treatment, but not when compared with other types of support [75].

## ACUPOINT THERAPY

Acupoint therapy derives from traditional Chinese medicine and is based on the concept that there are many pathways, or meridians, running through the body. The stimulation of acupoints on these meridians is believed to correct the flow and balance of qi through the body. A number of different modalities utilize acupoints, and many of these have been studied for the treatment of cancer-related complications. Acupoint modalities are generally considered safe when implemented appropriately by a trained practitioner.

#### Acupuncture

Acupuncture is the most well-known and wellstudied of the acupoint therapies. It involves placing needles into acupoints and leaving them in position for 10 to 30 minutes.

Although most research to date has been relatively low in quality, the available evidence suggests that acupuncture may be beneficial for cancer-related fatigue and pain. This has led the NCCN and ASCO to recommend the use of acupuncture for these purposes [73; 76; 77].

The benefits of acupuncture for CINV are less clear. A growing body of evidence suggests that it can reduce the severity of acute and delayed vomiting when compared with usual care alone. However, it does not seem to improve acute or chronic nausea when compared with usual care or sham acupuncture [78].

## Acustimulation

Another type of acupoint therapy, called acustimulation, involves the application of electrical stimulation to acupoints. An acustimulation wristband that provides electrical stimulation to a specific wrist acupoint is available via prescription in the United States. However, multiple clinical studies have found no benefit of acustimulation, when administered through wristband or when applied to the foot, for the prevention or reduction of CINV when compared with sham therapy [79; 80; 81].

## Acupressure

Acupressure utilizes the same principles as acupuncture, except with the application of pressure in place of needles. This pressure can be applied manually with the hands, thumbs, or fingers, or through the placement of a pressure-applying device over an acupoint.

Small clinical studies indicate that acupressure may be beneficial for the management of cancerrelated fatigue. It has also shown promise in the management of cancer-related pain. The NCCN and ASCO guidelines recommend acupressure as a nonpharmacologic treatment option for cancerrelated pain [76; 77].

Acupressure has also been studied extensively for CINV. Although there are mixed findings, multiple meta-analyses have found that manual acupressure can modestly reduce acute and delayed nausea, but not vomiting [82]. Acupressure wristbands have also been studied for CINV. Their benefit for this purpose remains unclear due to the mixed and conflicting findings in these studies [83; 84; 85].

# MASSAGE

Massage is another common modality that is used for the treatment of cancer-related complications. A large body of clinical research shows that massage therapy reduces pain and anxiety in patients with cancer when compared with no treatment or conventional care [86; 87; 88]. Additional clinical research shows that massage can improve sleep quality, fatigue, nausea, and mood in this population [89; 90]. Based on the available evidence, massage can be recommended as an adjunctive treatment option for patients with cancer. Patients should request that the practitioner avoid any sensitive or at-risk areas during manipulation, particularly those who have recently had surgery or radiation.

## MINDFULNESS

Mindfulness, derived from Buddhist theory, is a practice involving purposeful attention and awareness of present thoughts, emotions, and sensations, without evaluation or judgment of what is occurring. Mindfulness-based stress reduction (MBSR) is a well-studied and standardized mindfulness practice. It usually includes eight weekly 2.5-hour sessions, as well as daily home recordings of mindfulness exercises, and a half-day retreat after the sixth class. It entails didactic material, practicing mindfulness in group sessions and at home, and discussing and sharing experiences with a group.

To date, research suggests that participating in MBSR can improve cancer-related fatigue when compared with no intervention or a control group. However, most of this research suggests benefits may be short-term [91; 92; 93]. The NCCN guidelines list mindfulness as a nonpharmacologic option for patients undergoing cancer treatment or those who have completed treatment [73]. ASCO recommends this modality for patients who have finished cancer treatment [76].

The use of mindfulness for other cancer-related purposes lacks supportive evidence, and some research suggests that MBSR is not beneficial for reducing cancer-related pain [94]. Although mindfulness is a safe option for anyone who is interested in trying it, it may not be beneficial for the broad range of purposes for which it is often considered.

# CONCLUSION

Complementary therapies have become commonplace for patients undergoing cancer treatment. These options are often used with the goal of managing cancer- and chemotherapy-related complications and improving overall quality of life. While some of these therapies have strong evidence of benefit with minimal safety concerns, others may offer no benefit while introducing risk. It is important for healthcare professionals to counsel patients on the benefits and risks of these options. This is particularly true for natural medicines, which may introduce the potential for drug and condition interactions.

Patients are able to identify and utilize complementary therapies as they see fit, as these options are widely available with little to no gatekeeping. To ensure the safe use of these therapies, healthcare professionals should keep an open line of communication with their patients, encouraging regular discussion of all therapies being used, including prescription drugs, vitamins, minerals, cannabis, herbal extracts, aromatherapy, exercise-based modalities, acupoint therapies, and more.

# RESOURCES

#### National Cancer Institute

Communication in Cancer Care https://www.cancer.gov/about-cancer/coping/ adjusting-to-cancer/communication-hp-pdq

Office of Cancer Complementary and Alternative Medicine https://cam.cancer.gov/health\_information/ for\_patients.htm https://cam.cancer.gov/health\_information/ for\_health\_professionals.htm National Center for Complementary and Integrative Health https://www.nccih.nih.gov

#### American Cancer Society

Complementary and Integrative Medicine https://www.cancer.org/cancer/managing-cancer/ treatment-types/complementary-and-integrativemedicine.html

#### Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or controlbased. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

Works Cited

- 1. Latte-Naor S, Mao JJ. Putting integrative oncology into practice: concepts and approaches. J Oncol Pract. 2019;15(1):7-14.
- National Cancer Institute. PDQ Aromatherapy with Essential Oils. Available at https://www.cancer.gov/about-cancer/treatment/ cam/hp/aromatherapy-pdq. Last accessed February 17, 2025.
- Donelli D, Antonelli M, Bellinazzi C, Gensini GF, Firenzuoli F. Effects of lavender on anxiety: a systematic review and meta-analysis. Phytomedicine. 2019;65:153099.
- 4. Kang HJ, Nam ES, Lee Y, Kim M. How strong is the evidence for the anxiolytic efficacy of lavender? Systematic review and metaanalysis of randomized controlled trials. Asian Nurs Res (Korean Soc Nurs Sci). 2019;13(5):295-305.
- 5. Li D, Li Y, Bai X, Wang M, Yan J, Cao Y. The effects of aromatherapy on anxiety and depression in people with cancer: a systematic review and meta-analysis. *Front Public Health.* 2022;10:853056.
- 6. Louis M, Kowalski SD. Use of aromatherapy with hospice patients to decrease pain, anxiety, and depression and to promote an increased sense of well-being. *Am J Hosp Palliat Care*. 2002;19(6):381-386.
- Soden K, Vincent K, Craske S, Lucas C, Ashley S. A randomized controlled trial of aromatherapy massage in a hospice setting. *Palliat* Med. 2004;18(2):87-92.
- 8. Efe Ertürk N, Tașci S. The effects of peppermint oil on nausea, vomiting and retching in cancer patients undergoing chemotherapy: an open label quasi-randomized controlled pilot study. *Complement Ther Med.* 2021;56:102587.
- 9. Mapp CP, Hostetler D, Sable JF, et al. Peppermint oil: evaluating efficacy on nausea in patients receiving chemotherapy in the ambulatory setting. *Clin J Oncol Nurs.* 2020;24(2):160-164.
- 10. Liu TM, Luo YW, Tam KW, Lin CC, Huang TW. Prophylactic and therapeutic effects of honey on radiochemotherapy-induced mucositis: a meta-analysis of randomized controlled trials. *Support Care Cancer*. 2019;27(7):2361-2370.
- 11. Yang C, Gong G, Jin E, et al. Topical application of honey in the management of chemo/radiotherapy-induced oral mucositis: a systematic review and network meta-analysis. *Int J Nurs Stud.* 2019;89:80-87.
- 12. Elad S, Cheng KKF, Lalla RV, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer.* 2020;126(19):4423-4431.
- 13. Eslami H, Pouralibaba F, Falsafi P, et al. Efficacy of Hypozalix spray and propolis mouthwash for prevention of chemotherapy-induced oral mucositis in leukemic patients: a double-blind randomized clinical trial. J Dent Res Dent Clin Dent Prospects. 2016;10(4):226-233.
- 14. Kuo CC, Wang RH, Wang HH, Li CH. Meta-analysis of randomized controlled trials of the efficacy of propolis mouthwash in cancer therapy-induced oral mucositis. *Support Care Cancer*. 2018;26(12):4001-4009.
- 15. AkhavanKarbassi MH, Yazdi MF, Ahadian H, SadrAbad MJ. Randomized double-blind placebo-controlled trial of propolis for oral mucositis in patients receiving chemotherapy for head and neck cancer. *Asian Pac J Cancer Prev.* 2016;17(7):3611-3614.
- 16. Nyman GSA, Tang M, Inerot A, Osmancevic A, Malmberg P, Hagvall L. Contact allergy to beeswax and propolis among patients with cheilitis or facial dermatitis. *Contact Dermatitis*. 2019;81(2):110-116.
- 17. Araki K, Miyata Y, Ohba K, et al. Oral intake of royal jelly has protective effects against tyrosine kinase inhibitor-induced toxicity in patients with renal cell carcinoma: a randomized, double-blinded, placebo-controlled trial. *Medicines (Basel)*. 2018;6(1):2.
- Miyata Y, Araki K, Ohba K, et al. Oral intake of royal jelly improves anti-cancer effects and suppresses adverse events of molecular targeted therapy by regulating TNF-α and TGF-β in renal cell carcinoma: a preliminary study based on a randomized double-blind clinical trial. Mol Clin Oncol. 2020;13(4):29.
- 19. Mofid B, Rezaeizadeh H, Termos A, et al. Effect of processed honey and royal jelly on cancer-related fatigue: a double-blind randomized clinical trial. *Electron Physician*. 2016;8(6):2475-2482.
- 20. Li JD, Cui L, Xu YY, Guan K. A case of anaphylaxis caused by major royal jelly protein 3 of royal jelly and its cross-reactivity with honeycomb. *J Asthma Allergy*. 2021;14:1555-1557.
- Leung R, Thien FC, Baldo B, Czarny D. Royal jelly-induced asthma and anaphylaxis: clinical characteristics and immunologic correlations. J Allergy Clin Immunol. 1995;96(6 Pt 1):1004-1007.
- 22. American Society of Clinical Oncology. National Cancer Opinion Survey. Available at https://society.asco.org/sites/new-www.asco.org/files/content-files/2020-ASCO-National-Cancer-Opinions-Survey-All-Findings.pdf. Last accessed February 17, 2025.
- 23. Cesamet (nabilone) [Package Insert]. Available at https://www.accessdata.fda.gov/drugsatfda\_docs/label/2006/018677s011lbl.pdf. Last accessed February 17, 2025.
- 24. Marinol (dronabinol) [Package Insert]. Available at https://www.accessdata.fda.gov/drugsatfda\_docs/label/2017/018651s029lbl.pdf. Last accessed February 17, 2025.
- 25. Sativex (nabiximols) Australian Product Information. Available at https://pp.jazzpharma.com/pi/sativex.au.PI.pdf. Last accessed February 17, 2025.
- 26. American Cancer Society. Marijuana and Cancer. Available at https://www.cancer.org/cancer/managing-cancer/treatment-types/ complementary-and-integrative-medicine/marijuana-and-cancer.html. Last accessed February 17, 2025.
- 27. Hazekamp A. The trouble with CBD oil. Med Cannabis Cannabinoids. 2018;1(1):65-72.

- Braun IM, Bohlke K, Abrams DI, et al. Cannabis and cannabinoids in adults with cancer: ASCO guideline. JCO. 2024;42(13):1575-1593.
- Epidiolex (cannabidiol) [Package Insert]. Available at https://www.accessdata.fda.gov/drugsatfda\_docs/ label/2021/210365Orig1s011lbl.pdf. Last accessed February 17, 2025.
- 30. Cruciani RA, Dvorkin E, Homel P, et al. L-carnitine supplementation in patients with advanced cancer and carnitine deficiency: a double-blind, placebo-controlled study. *J Pain Symptom Manage*. 2009;37(4):622-631.
- Cruciani RA, Zhang JJ, Manola J, Cella D, Ansari B, Fisch MJ. L-carnitine supplementation for the management of fatigue in patients with cancer: an eastern cooperative oncology group phase III, randomized, double-blind, placebo-controlled trial. J Clin Oncol. 2012;30(31):3864-3869.
- 32. Kraft M, Kraft K, Gärtner S, et al. L-Carnitine-supplementation in advanced pancreatic cancer (CARPAN): a randomized multicentre trial. *Nutr J.* 2012;11:52.
- 33. Macciò A, Madeddu C, Gramignano G, et al. A randomized phase III clinical trial of a combined treatment for cachexia in patients with gynecological cancers: evaluating the impact on metabolic and inflammatory profiles and quality of life. Gynecol Oncol. 2012;124(3):417-425.
- 34. Loprinzi CL, Lacchetti C, Bleeker J, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: ASCO guideline update. *J Clin Oncol.* 2020;38(28):3325-3348.
- 35. Wang Y, Jin B, Ai F, et al. The efficacy and safety of melatonin in concurrent chemotherapy or radiotherapy for solid tumors: a metaanalysis of randomized controlled trials. *Cancer Chemother Pharmacol.* 2012;69(5):1213-1220.
- 36. Seely D, Wu P, Fritz H, et al. Melatonin as adjuvant cancer care with and without chemotherapy: a systematic review and meta-analysis of randomized trials. *Integr Cancer Ther.* 2012;11(4):293-303.
- 37. Mills E, Wu P, Seely D, Guyatt G. Melatonin in the treatment of cancer: a systematic review of randomized controlled trials and metaanalysis. J Pineal Res. 2005;39(4):360-366.
- 38. Fan R, Bu X, Yang S, et al. Effect of melatonin on quality of life and symptoms in patients with cancer: a systematic review and metaanalysis of randomised controlled trials. *BMJ Open*. 2022;12(9):e060912.
- 39. Akhgarjand C, Asoudeh F, Bagheri A, et al. Does ashwagandha supplementation have a beneficial effect on the management of anxiety and stress? A systematic review and meta-analysis of randomized controlled trials. *Phytother Res.* 2022;36(11):4115-4124.
- Cao A, He H, Wang Q, Li L, An Y, Zhou X. Evidence of Astragalus injection combined platinum-based chemotherapy in advanced nonsmall cell lung cancer patients: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2019;98(11):e14798.
- 41. Chen HW, Lin IH, Chen YJ, et al. A novel infusible botanically-derived drug, PG2, for cancer-related fatigue: a phase II double-blind, randomized placebo-controlled study. *Clin Invest Med.* 2012;35(1):E1-11.
- 42. Lin S, An X, Guo Y, et al. Meta-analysis of astragalus-containing traditional Chinese medicine combined with chemotherapy for colorectal cancer: efficacy and safety to tumor response. *Front Oncol.* 2019;9:749.
- 43. Guglielmo M, Di Pede P, Alfieri S, et al. A randomized, double-blind, placebo controlled, phase II study to evaluate the efficacy of ginseng in reducing fatigue in patients treated for head and neck cancer. J Cancer Res Clin Oncol. 2020;146(10):2479-2487.
- 44. Kim JW, Han SW, Cho JY, et al. Korean red ginseng for cancer-related fatigue in colorectal cancer patients with chemotherapy: a randomised phase III trial. *Eur J Cancer.* 2020;130:51-62.
- 45. Chang WP, Peng YX. Does the oral administration of ginger reduce chemotherapy-induced nausea and vomiting? A meta-analysis of 10 randomized controlled trials. *Cancer Nurs*. 2019;42(6):E14-E23.
- 46. Santos KVGD, da Silva RLM, Sarmento ACA, et al. Effect of Zingiber officinale in the management of nausea and vomiting induced by treatment with cisplatin associated with radiotherapy: a randomized controlled trial. *Integr Cancer Ther*. 2023;22:15347354231220608.
- 47. Marx W, McKavanagh D, McCarthy AL, et al. The effect of ginger (Zingiber officinale) on platelet aggregation: a systematic literature review. *PLoS One.* 2015;10(10):e0141119.
- 48. Soni TP, Gupta AK, Sharma LM, Singhal H, Sharma S, Gothwal RS. A randomized, placebo-controlled study to evaluate the effect of bio-enhanced turmeric formulation on radiation-induced oral mucositis. ORL J Otorhinolaryngol Relat Spec. 2022;84(2):103-113.
- 49. Kia SJ, Basirat M, Saedi HS, Arab SA. Effects of nanomicelle curcumin capsules on prevention and treatment of oral mucosits in patients under chemotherapy with or without head and neck radiotherapy: a randomized clinical trial. BMC Complement Med Ther. 2021;21(1):232.
- 50. Shah S, Rath H, Sharma G, Senapati SN, Mishra E. Effectiveness of curcumin mouthwash on radiation-induced oral mucositis among head and neck cancer patients: a triple-blind, pilot randomised controlled trial. *Indian J Dent Res.* 2020;31(5):718-727.
- Ramezani V, Ghadirian S, Shabani M, Boroumand MA, Daneshvar R, Saghafi F. Efficacy of curcumin for amelioration of radiotherapyinduced oral mucositis: a preliminary randomized controlled clinical trial. BMC Cancer. 2023;23(1):354.
- 52. Halegoua-DeMarzio D, Navarro V, Ahmad J, et al. Liver injury associated with turmeric-a growing problem: ten cases from the Drug-Induced Liver Injury Network [DILIN]. *Am J Med.* 2023;136(2):200-206.
- 53. Somasundaram S, Edmund NA, Moore DT, Small GW, Shi YY, Orlowski RZ. Dietary curcumin inhibits chemotherapy-induced apoptosis in models of human breast cancer. *Cancer Res.* 2002;62(13):3868-3875.

- 54. Mitchell TM. Correspondence re: Somasundaram et al., Dietary curcumin inhibits chemotherapy-induced apoptosis in models of human breast cancer. Cancer Res., 62: 3868-3875, 2002. *Cancer Res.* 2003;63(16):5165-5166; author reply 5166-5167.
- 55. Barton DL, Burger K, Novotny PJ, et al. The use of Ginkgo biloba for the prevention of chemotherapy-related cognitive dysfunction in women receiving adjuvant treatment for breast cancer, N00C9. *Support Care Cancer*. 2013;21(4):1185-1192.
- Moezian GSA, Javadinia SA, Sales SS, Fanipakdel A, Elyasi S, Karimi G. Oral silymarin formulation efficacy in management of AC-T protocol induced hepatotoxicity in breast cancer patients: a randomized, triple blind, placebo-controlled clinical trial. J Oncol Pharm Pract. 2022;28(4):827-835.
- 57. Eghbali A, Sadeghian M, Ghasemi A, Afzal RR, Eghbali A, Ghaffari K. Effect of oral silymarin on liver function in pediatric acute lymphoblastic leukemia in the maintenance phase: a double-blind randomized clinical trial. *Front Pharmacol.* 2024;15:1295816.
- Shahbazi F, Sadighi S, Dashti-Khavidaki S, et al. Effect of silymarin administration on cisplatin nephrotoxicity: report from a pilot, randomized, double-blinded, placebo-controlled clinical trial. *Phytother Res.* 2015;29(7):1046-1053.
- Bozorgi H, Ghahremanfard F, Motaghi E, Zamaemifard M, Zamani M, Izadi A. Effectiveness of crocin of saffron (Crocus sativus L.) against chemotherapy-induced peripheral neuropathy: a randomized, double-blind, placebo-controlled clinical trial. J Ethnopharmacol. 2021;281:114511.
- 60. Lian S, Zhang X, Zhang Y, Zhao Q. Pyridoxine for prevention of hand-foot syndrome caused by chemotherapy agents: a meta-analysis. *Clin Exp Dermatol.* 2021;46(4):629-635.
- 61. Kottschade LA, Sloan JA, Mazurczak MA, et al. The use of vitamin E for the prevention of chemotherapy-induced peripheral neuropathy: results of a randomized phase III clinical trial. *Support Care Cancer*. 2011;19(11):1769-1777.
- 62. Hershman DL, Lacchetti C, Dworkin RH, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014;32(18):1941-1967.
- 63. Barton DL, Loprinzi CL, Quella SK, et al. Prospective evaluation of vitamin E for hot flashes in breast cancer survivors. J Clin Oncol. 1998;16(2):495-500.
- 64. Lawson KA, Wright ME, Subar A, et al. Multivitamin use and risk of prostate cancer in the National Institutes of Health-AARP Diet and Health Study. J Natl Cancer Inst. 2007;99(10):754-764.
- 65. Bairati I, Meyer F, Jobin E, et al. Antioxidant vitamins supplementation and mortality: a randomized trial in head and neck cancer patients. *Int J Cancer*. 2006;119(9):2221-2224.
- 66. Arbabi-kalati F, Arbabi-kalati F, Deghatipour M, Ansari Moghadam A. Evaluation of the efficacy of zinc sulfate in the prevention of chemotherapy-induced mucositis: a double-blind randomized clinical trial. *Arch Iran Med.* 2012;15(7):413-417.
- 67. Rambod M, Pasyar N, Ramzi M. The effect of zinc sulfate on prevention, incidence, and severity of mucositis in leukemia patients undergoing chemotherapy. *Eur J Oncol Nurs.* 2018;33:14-21.
- 68. Oshvandi K, Vafaei SY, Kamallan SR, Khazaei S, Ranjbar H, Mohammadi F. Effectiveness of zinc chloride mouthwashes on oral mucositis and weight of patients with cancer undergoing chemotherapy. BMC Oral Health. 2021;21(1):364.
- 69. Mohammadi F, Oshvandi K, Kamallan SR, et al. Effectiveness of sodium bicarbonate and zinc chloride mouthwashes in the treatment of oral mucositis and quality of life in patients with cancer under chemotherapy. *Nurs Open.* 2022;9(3):1602-1611.
- Odynets T, Briskin Y, Todorova V. Effects of different exercise interventions on quality of life in breast cancer patients: a randomized controlled trial. Integr Cancer Ther. 2019;18:1534735419880598.
- 71. Pasyar N, Barshan Tashnizi N, Mansouri P, Tahmasebi S. Effect of yoga exercise on the quality of life and upper extremity volume among women with breast cancer related lymphedema: a pilot study. *Eur J Oncol Nurs*. 2019;42:103-109.
- 72. Yi LJ, Tian X, Jin YF, Luo MJ, Jiménez-Herrera MF. Effects of yoga on health-related quality, physical health and psychological health in women with breast cancer receiving chemotherapy: a systematic review and meta-analysis. *Ann Palliat Med.* 2021;10(2):1961-1975.
- 73. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue. Version 2.2023. Available at https://www.nccn.org/professionals/physician\_gls/pdf/fatigue.pdf. Last accessed February 17, 2025.
- 74. Kuo CC, Wang CC, Chang WL, Liao TC, Chen PE, Tung TH. Clinical effects of Baduanjin qigong exercise on cancer patients: a systematic review and meta-analysis on randomized controlled trials. *Evid Based Complement Alternat Med.* 2021;2021:6651238.
- 75. Zeng Y, Luo T, Xie H, Huang M, Cheng ASK. Health benefits of qigong or tai chi for cancer patients: a systematic review and metaanalyses. *Complement Ther Med.* 2014;22(1):173-186.
- Mao JJ, Ismaila N, Bao T, et al. Integrative medicine for pain management in oncology: Society for Integrative Oncology-ASCO guideline. J Clin Oncol. 2022;40(34):3998-4024.
- 77. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Adult Cancer Pain. Version 3.2024. Available at https://www.nccn.org/professionals/physician\_gls/pdf/pain.pdf. Last accessed February 17, 2025.
- 78. Yan Y, López-Alcalde J, Zhang L, Siebenhüner AR, Witt CM, Barth J. Acupuncture for the prevention of chemotherapy-induced nausea and vomiting in cancer patients: a systematic review and meta-analysis. *Cancer Med.* 2023;12(11):12504-12517.
- 79. Roscoe JA, Matteson SE, Morrow GR, et al. Acustimulation wrist bands are not effective for the control of chemotherapy-induced nausea in women with breast cancer. *J Pain Symptom Manage*. 2005;29(4):376-384.

- Roscoe JA, Morrow GR, Hickok JT, et al. The efficacy of acupressure and acustimulation wrist bands for the relief of chemotherapyinduced nausea and vomiting: a University of Rochester Cancer Center Community Clinical Oncology Program multicenter study. J Pain Symptom Manage. 2003;26(2):731-742.
- 81. Shen Y, Liu L, Chiang JS, et al. Randomized, placebo-controlled trial of K1 acupoint acustimulation to prevent cisplatin-induced or oxaliplatin-induced nausea. *Cancer.* 2015;121(1):84-92.
- 82. Miao J, Liu X, Wu C, Kong H, Xie W, Liu K. Effects of acupressure on chemotherapy-induced nausea and vomiting-a systematic review with meta-analyses and trial sequential analysis of randomized controlled trials. *Int J Nurs Stud.* 2017;70:27-37.
- Molassiotis A, Russell W, Hughes J, et al. The effectiveness and cost-effectiveness of acupressure for the control and management of chemotherapy-related acute and delayed nausea: Assessment of Nausea in Chemotherapy Research (ANCHoR), a randomised controlled trial. *Health Technol Assess.* 2013;17(26):1-114.
- 84. Melchart D, Ihbe-Heffinger A, Leps B, von Schilling C, Linde K. Acupuncture and acupressure for the prevention of chemotherapyinduced nausea: a randomised cross-over pilot study. *Support Care Cancer.* 2006;14(8):878-882.
- 85. Roscoe JA, Jean-Pierre P, Morrow GR, et al. Exploratory analysis of the usefulness of acupressure bands when severe chemotherapyrelated nausea is expected. *J Soc Integr Oncol*. 2006;4(1):16-20.
- 86. Lee SH, Kim JY, Yeo S, Kim SH, Lim S. Meta-analysis of massage therapy on cancer pain. Integr Cancer Ther. 2015;14(4):297-304.
- 87. Lee PLT, Tam KW, Yeh ML, Wu WW. Acupoint stimulation, massage therapy and expressive writing for breast cancer: a systematic review and meta-analysis of randomized controlled trials. *Complement Ther Med.* 2016;27:87-101.
- Zhang Y, Wang S, Ma X, et al. Massage therapy can effectively relieve cancer pain: a meta-analysis. Medicine (Baltimore). 2023;102(27):e33939.
- 89. Smith MC, Kemp J, Hemphill L, Vojir CP. Outcomes of therapeutic massage for hospitalized cancer patients. J Nurs Scholarsh. 2002;34(3):257-262.
- 90. Cassileth BR, Vickers AJ. Massage therapy for symptom control: outcome study at a major cancer center. *J Pain Symptom Manage*. 2004;28(3):244-249.
- 91. Xie C, Dong B, Wang L, et al. Mindfulness-based stress reduction can alleviate cancer- related fatigue: a meta-analysis. J Psychosom Res. 2020;130:109916.
- 92. Chayadi E, Baes N, Kiropoulos L. The effects of mindfulness-based interventions on symptoms of depression, anxiety, and cancerrelated fatigue in oncology patients: a systematic review and meta-analysis. PLoS One. 2022;17(7):e0269519.
- McCloy K, Hughes C, Dunwoody L, Marley J, Gracey J. Effects of mindfulness-based interventions on fatigue and psychological wellbeing in women with cancer: a systematic review and meta-analysis of randomised control trials. *Psychooncology*. 2022;31(11):1821-1834.
- 94. Chang YC, Yeh TL, Chang YM, Hu WY. Short-term effects of randomized mindfulness-based intervention in female breast cancer survivors: a systematic review and meta-analysis. *Cancer Nurs.* 2021;44(6):E703-E714.

#### **Evidence-based Practice Recommendations Citation**

Gowin K, Muminovic M, Zick SM, Lee RT, Lacchetti C, Mehta A. Integrative therapies in cancer care: an update on the guidelines. *Am Soc Clin Oncol Educ Book*. 2024;44(3):e431554. Available at https://ascopubs.org/doi/10.1200/EDBK\_431554. Last accessed February 25, 2025.