JOURNAL OF PALLIATIVE MEDICINE
Volume 16, Number 11, 2013

DOI: 10.1089/jpm.2013.0126

Herbal Administration and Interaction of Cancer Treatment

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Abstract

The widespread impact of cancer worldwide and noncurative treatment methods despite all developments drive patients towards investigating and using nonconventional treatment methods. Herbs, which have an important role in complementary and alternative medicine practices, may cause unfavorable results when used especially with chemotherapeutics in cancer patients due to the substances they contain and due to the properties of some, which still cannot be clarified. Further overshadowing the success of the treatments, patients do not talk about these issues with their doctors and physicians are unable to comprehend these properties of herbs. In this compilation we aimed to clarify the concepts of complementary and alternative medicine, to gather the properties of important and frequently used herbs, and to increase the awareness of physicians on this subject.

Introduction

In cancer treatment, traditional methods such as surgery, chemotherapy, and radiotherapy compose the basic treatment. Despite developments in conventional medicine, due to difficulties experienced in cancer diagnosis, relapse of many cancers surgically treated in less than five years, low effect or nonefficacy of traditional treatment methods in some cancers, low contribution to survival, and unfavorable impact of their side effects on quality of life, many cancer patients prefer using complementary and alternative medicine (CAM).[1]

Herbal drugs sold at herbalists are not subject to inspection, interact with the drugs used for the treatment of many diseases, lead to toxic reactions, and decrease the efficacy of drugs used in treatment. Perhaps most importantly, usage of these drugs is not mentioned to the physician during the assessment of clinical profiles and is not asked about by the physician.[2]

In a population-based study, the complementary methods most frequently used by surviving cancer patients have been reported as praying/psychological/spiritual practice (61.4%), relaxation (44.3%), belief/spiritual healing (42.4%), food supplements/vitamins (40.1%), meditation (15%), religious consultancy (11.3%), massage (11.2%), and support groups (9.7%).[3]

Tendencies of cancer patients towards CAM and herbal treatments require knowledge about the herbs used for this purpose and about their contents. Investigating these herbs, which may interact with conventional drugs, and knowing their possible effects on a patient's treatment, are important for treatment success. In this study the properties of the herbs frequently used, their side effects, and their interactions with chemotherapeutics are examined, and their effects on cancer treatment are indicated.

Review

Definitions

Complementary treatments are treatments performed to support scientific medicine. Without targeting cancer treatment directly, these are practices performed to increase quality of life, to decrease side effects of cancer and cancer treatments, and to provide physical and psychological support. In line with available information, usage of these methods as primary treatment (to treat cancer) is out of the question.

Alternative medicine can be defined as treatments rejecting and/or ascribing secondary importance to traditional medicine practices, being performed instead of scientific medical practices, presented to patients with the claim of success in cancer treatment, and generally accepted, and with benefits not demonstrated by high-quality scientific studies including sufficient numbers of patients. Contrary to complementary medicine practices, these practices aim to keep patients away from modern medicine.[4]

The National Center for Complementary and Alternative Medicine (NCCAM) defines CAM as health care systems, products, and practices not yet accepted as a part of conventional medicine.[5,6]

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Accepted July 12, 2013.

Table 1. Most Popular Herbs and Herbal Mixtures, and Their Intended Uses, Toxicities, and Interactions with Chemotherapeutics

Name of herb	*Intended use*	*Toxicity*	*Interaction with chemotherapeutics*
Nettle	To strengthen immune system, prostate diseases, urinary system diseases, allergy, arthritis, and antiinflammatory	Abdominal pain, diarrhea, fever, bleeding problems, gynecomastia, galactorrhea, and hypoglycemia	It may interact with cancer drugs, which metabolize where it affects cytochrome P450 enzyme system.
Garlic	Hypertension, hyperlipidemia, antineoplastic, antimicrobial	Bleeding problems	Its usage with dacarbazine should be avoided (CYP2E1 inhibition)
Green tea	In cancer prevention, prostate cancer, cardiac diseases, gastrointestinal diseases, for losing weight	Nausea, insomnia, diarrhea, confusion	While increasing the effect of drugs such as anthracycline, taxane (cytochrome P450 inhibition), it may decrease the effect of bortezomib by different interaction routes
***Ginkgo biloba* (Ginkgo tree)**	Antiemetic, antioxidant, pro-circulatory, dementia, tinnitus	Bleeding, allergy/hypersensitivity, stroke, headache	It interacts with numerous chemotherapy agents and EGFR-TKI (CYP3A4 and CYP2C19 inhibition)
Echinacea (purple cone flower)	To strengthen immune system, common cold	Hypersensitivity (including anaphylaxis)	It interacts with numerous chemotherapy agents and EGFR-TKI (CYP3A4 induction)
Soya products	Menopause symptoms, osteoporosis, cancer prevention	Meteorism, allergic reactions	It should not be used with tamoxifen in ER-positive breast cancer and in endometrial cancer
Saw palmetto (*Serenoa repens*)	Benign prostate hypertrophy	Abdominal pain, nausea, vomiting, constipation or diarrhea, bleeding problems, emboli	No significant interaction has been reported
Ginseng	Sedative, aphrodisiac, antidepressant, and diuretic	Nausea, diarrhea, euphoria, insomnia, headache, hypertension, hypotension, hypoglycemia, mastalgia, vaginal bleeding, and cerebral arteritis	It interacts with numerous chemotherapy agents and EGFR-TKI (CYP3A4 inhibition); it should not be used in ER-positive breast cancer and in endometrial cancer
St. John's wort (Tipton's weed, *Hypericum perforatum*)	Depression	Allergic dermal reactions, constipation, dry mouth, gastrointestinal disorder, dizziness, asthenia, and sleep disorder	It interacts with almost all chemotherapy agents. (CYP2B6, CYP2C9, CYP2C19, CYP2E1, CYP3A4, and P-glycoprotein induction), it decreases level of active metabolite of irinotecan and cyclophosphamide plasma concentration
Black cohosh (horseradish root)	Menopause symptoms, sedation	Dizziness, headache, nausea, vomiting	It affects CYP3A4 enzyme system. It increases the toxicity of doxorubicin and docetaxel. It increases the effect of tamoxifen.
Cranberry (blueberry, huckleberry)	Urinary tract infection	Bleeding problems	No significant interaction has been reported

(*continued*)

Table 1. (Continued)

Name of herb	*Intended use*	*Toxicity*	*Interaction with chemotherapeutics*
Valerian (*Polemonium*)	Sleep irregularities, stress	It may cause headache, restlessness, cardiac problems	It interacts with numerous chemotherapy agents (CYP2C9 inhibition, CYP2C19 induction). The ones using tamoxifen, cyclophosphamide, etoposide, and teniposide should be careful
Milk thistle (*Eryngium*)	Hepatosteatosis, cirrhosis, cancer prevention	Laxative effect and menstrual stimulation	It causes doxorubicin metabolism to decrease by interacting with cytochrome P450 system
Evening primrose (*Oenothera biennis*)	Menopausal symptoms, pain, neuropathy	Headache, nausea, and increasing risk of pregnancy complication	Since it binds to serum proteins and it may modify chemotherapy efficacy, its usage is not recommended
Kava (stonecrop)	Anxiety, insomnia, stress	Stupor, vision disorders, dizziness, yellowing at skin and nail, fatal liver toxicity	It interacts with numerous chemotherapy agents and EGFR-TKI (CYP3A4 induction)
Bilberry (blueberry)	Diabetes retinopathy	Bleeding problems	No significant interaction has been reported
Red grape seed	Allergic rhinitis, cancer prevention, hyperlipidemia	No significant toxicity has been reported.	It interacts with numerous chemotherapy agents and EGFR-TKI (CYP3A4 induction)
PC-SPES	Prostate cancer	Gynecomastia, loss of libido, gastric disorders, cramps, thrombus, diarrhea, cardiac problems, hot flush	Since it affects enzyme system in the liver, it may interact with many chemotherapeutics. It should not be used together with these
Reishi mushroom (red reishi)	Allergy, arthritis, bronchitis, gastric ulcer, diabetes, hypertension, chronic hepatitis, nephritis, insomnia, scleroderma, and cancer	Nausea, vomiting, liver toxicity, and bleeding problems	Since it affects enzyme system in the liver (CYP2E1, CYP1A2, and CYP3A inhibition), it may interact with many chemotherapeutics. It should not be used together with these
Oleander (rosebay)	Cancer treatment, cardiac failure, HIV, AIDS, rheumatoid arthritis, psoriasis	Abdominal pain, hypothermia, dizziness, respiratory paralysis, death	No significant interaction has been reported
Essiac	Cancer treatment, health maintenance, support for immunity, HIV and AIDS	No significant toxicity has been reported	It interacts with chemotherapy drugs by inhibiting CYP3A
Mistletoe (*Iscum album*)	Cancer treatment, immune stimulation, arthritis, sedation	Hepatotoxicity, anaphylactic shock	It interacts with chemotherapy drugs by CYP3A4 inhibition
Licorice	Cancer treatment, gastroprotective, antiinflammatory, antiallergic	Hypokalemia (±myopathy), hypertension, pulmonary edema, digoxin toxicity	It interacts with chemotherapy drugs by causing CYP3A induction
***Astragalus* (wild licorice)**	To strengthen immune system, diabetes, and cardiac diseases	No significant toxicity has been reported	It interacts with cyclophosphamide
Ginger	In treatment of acute and delayed nausea developing due to chemotherapy	No significant toxicity has been reported	No significant interaction has been reported
Curcuma	In colorectal cancer and leukemia	Nausea, gastric irritation, diarrhea, bleeding problems	It interacts with many drugs, mainly doxorubicin and cyclophosphamide

Integrative Medicine (IM) combines CAM treatments, demonstrating high-quality scientific evidences on efficacy and safety issues, with basic medical treatments. In the context of oncology, IM lays emphasis on integration of complementary treatments (for example, acupuncture, meditation, music therapy) with conventional treatments.[7]

Studies were identified through searches of the database PubMed between the years 1988 and 2012. The key words were "cancer" or "chemotherapy" combined with "herbal treatment" or "complementary and alternative medicine." Studies related to cancer patients and chemotherapy were included particularly. Case reports and studies that have limited numbers of patients were excluded.

Herbal Products Most Frequently Used

Nettle (Urtica diocia)

According to the results obtained from in vitro and animal experiments, although it is advocated to prevent proliferation of prostate cancer cells and to have a protective effect against the side effects of cisplatin, evidence is limited and requires extensive studies.[8–10] It may interact with cancer drugs, which metabolize where it affects the cytochrome P450 enzyme system. Additionally, it may increase the effect of diuretic and hypotensive drugs. It contains some toxic proteins that cause allergy. Abdominal pain, diarrhea, fever, gynecomastia, galactorrhea, and hypoglycemia are its known side effects. Some of its side effects may be confused with side effects of chemotherapy. In observations performed in a limited number of patients, it has been observed that it may have unfavorable effects on cells, enabling blood coagulation. How it affects chemotherapy and radiotherapy is not fully known.[11–14]

Garlic (Allium sativum)

Nowadays it is used mostly in hypertension and hyperlipidemia treatment in the belief that it has antineoplastic and antimicrobial properties.[15] Its benefit in the treatment or prevention of cancer is not known. When consumed in excessive amounts or taken in the form of intensified tablets, it may cause bleeding problems.[6] It decreases the efficacy of some antiviral and chemotherapy drugs; since it inhibits CYP2E1, its usage especially with dacarbazine should be avoided.[16–21] Although epidemiological findings demonstrate that gastric and colon cancer risk diminishes in those consuming high amounts of garlic and other *Allium* vegetables such as onion and leek, very few clinical studies support these effects.[15]

Green tea

Among all cancer patients it is used at an incidence reaching 24% to 30%. When consumed at normal amounts it is harmless. Although there are publications reporting that those consuming green tea for a long period are protected against cardiac diseases and several cancer types, mainly prostate cancer, no evidence is available demonstrating that it is efficient in cancer treatment. Phase I and II studies have found antitumor efficacy in lung and prostate cancer. Usage is most common in cancer prevention, especially for prostate cancer; cardiac diseases; gastrointestinal diseases; and for losing weight.[22–27] Polyhenols in green tea may lead to significant side effects by increasing plasma concentrations of several cancer drugs (for example, anthracycline, taxane). By inhibiting the cytochrome P450 enzyme system, they decrease the efficacy of some drugs (for example, bortezomib) by different interaction routes.[28,29] In the case of intake in tablet form at high doses, it may result in gastric disorders, diarrhea, and cramps.[18]

Ginkgo biloba (Ginkgo tree)

This product, which is used commonly worldwide, has antiemetic and antioxidant effects. Since one of its compounds, Ginkgolide-B, is a potent platelet activating factor (PAF) antagonist, it increases bleeding tendency.[15] Available antioxidant properties may decrease the effect of chemotherapy and radiotherapy. Moreover, it may lead to decrease in the efficacy of cancer drugs or increase in their side effects by affecting some enzymes in the liver (CYP3A4 and CYP2C19 inhibition). It interacts with epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKI). Especially those receiving antitumor antibiotics (adriamycine-epirubicin) should keep away.[15,17] Its most important side effects are bleeding, allergy/hypersensitivity, stroke, and headache.[15,18]

Echinacea (purple cone flower)

It has no role in cancer treatment. It decreases the efficacy of some drugs decomposing in the liver (CYP3A4 induction), and it is not recommended to be taken together with chemotherapeutics effective on EGFR-TKI. Especially those receiving erlotinib, irinotecan, topotecan, cyclophosphamide, etoposide, teniposide, paclitaxel, docetaxel, vincristine, or vinblastine should keep away. It may cause hypersensitivity (including anaphylaxis) as a side effect.[17,18]

Soy bean products (Glycine max)

Soya is used mostly for menopausal symptoms, osteoporosis, and cancer prevention, due to the estrogenic hormonal effect of soy's isoflavones. However, due to the same property, it may be harmful in patients with breast cancer and uterus cancer. As for side effects, meteorism or allergic reactions may be observed. A substance in soy, Genistein, decreases the efficacy of tamoxifen. Breast cancer patients using tamoxifen should keep away from soy bean products. Additionally, soy bean products affect the absorption and the distribution of some drugs at pharmacological doses.[16,17,30–32]

Saw palmetto (Serenoa repens)

It is used mostly for prostatic hyperplasia. It has no effect in cancer treatment. Since it contains hormonal substances, it should not be consumed by breast and uterus cancer patients.[33–36] The most frequently observed side effects are gastrointestinal complaints such as abdominal pain, nausea, vomiting, constipation, or diarrhea. It increases the risk of bleeding. It has frequently been reported that emboli have developed in the legs and lungs during usage of saw palmetto by prostate cancer patients. Its usage is contraindicated in men with prostate cancer. It has no significant interaction with cancer drugs.[15,17]

Ginseng (Panax ginseng)

In some retrospective studies, limited data are available for ginseng's reduction of cancer development risk.[17,18] Since

some ginseng preparations contain estrogenic substances, these preparations should not be used by breast and uterus cancer patients. Its effect on cancer is unknown. Ginseng products, due to their CYP3A4 inhibition and interaction with drugs targeting EGFR-TKI, should not be used together with some chemotherapeutics. Those receiving iressa and tarceva, irinotecan, topotecan, cyclophosphamide, etoposide, teniposide, taxol, docetaxel, vincristine, or vinblastine should be careful.[17,18,37–41] Its most frequently reported side effects are nervousness and excitation. Nausea, diarrhea, euphoria, insomnia, headache, hypertension, hypotension, hypoglycemia, mastalgia, vaginal bleeding, and cerebral arthritis may also be observed.[15]

St. John's wort (Tipton's weed, Hypericum perforatum)

It is used worldwide as an antidepressant in the herbal treatment field. It has been reported that hypericine in St. John's wort has a cytotoxic effect on many tumor cells following photoactivation. However, this efficacy has not been shown in randomized clinical studies.[42–47] It interacts with cancer drugs—thus patients receiving chemotherapy should certainly not use this product.[15,17] Although its side effects are rare, allergic dermal reactions, constipation, dry mouth, gastrointestinal disorder, dizziness, asthenia, and sleep disorder are the most frequently observed side effects.[15]

Black cohosh (Actea racemosa, horseradish root)

It is mostly used for menopausal complaints and sedation. It has no role in cancer treatment. As for side effects, dizziness, headache, nausea, and vomiting may be observed. It increases the toxicity of doxorubicin and docetaxel by affecting the CYP3A4 enzyme system, and it increases the effect of tamoxifen by an additive effect.[48–52]

Valerian (Valleriana officinalis)

It is used for sleep irregularities and stress. It has no role in cancer treatment. It may cause headache, restlessness, and cardiac problems. It interacts with numerous chemotherapy agents (CYP2C9 inhibition, CYP2C19 induction). Especially those using tamoxifen, cyclophosphamide, etoposide, and teniposide should not use valerian.[16,17,53–58]

Evening primrose (Oenothera biennis)

It is used mostly for menopausal symptoms, pain, and neuropathy. It has no role in cancer treatment. It may cause headache, nausea, and increasing risk of pregnancy complication. It has no significant interaction with cancer drugs; however since it binds to serum proteins, it may change drug efficacy. Thus its usage with chemotherapy is not recommended.[16,17,59–62]

Red grape seed (Vitis vinifera)

It is used mainly for allergic rhinitis, cancer prevention, and hyperlipidemia treatment. When taken at high doses it may interact with some drugs. Those receiving gefitinib and erlotinib, irinotecan, topotecan, cyclophosphamide, etoposide, teniposide, paclitaxel, docetaxel, vincristine, vinblastine, and platinum should be careful.[16,17,63–69]

PC-SPES

It is a mixture containing seven Chinese herbal extracts and one American herbal extract and is claimed to have cytotoxic and cytostatic properties and to stimulate the immune system. PC-SPES contains *Scutellaria baicalensis,* chrysanthemum (*Dendranthema morifolium*), *Ganoderma lucidum*, da qing ye (*Isatis indigotica*), dong ling cao (*Rabdosia rubescens*), saw palmetto (*Serenoa repens*), licorice (*Glycyrrhiza glabra, Glycyrrhiza uralensis*), and san qi (*Panax pseudoginseng*). It has been popular in the treatment of prostate cancer; although it is demonstrated to reduce PSA levels, it has been shown to be contaminated with substances such as warfarin, ethinyl estradiol, indometacin, and diethylstilbestrol. Sometimes though tumor reduction shows progress, PC-SPES use may lead to PSA reduction. After detection of contamination it was recalled from the market by the Food and Drug Administration (FDA). Since it affects the enzyme system in the liver, it may interact with many chemotherapeutics. It may cause gynecomastia, loss of libido, gastric disorders, cramps, thrombus, diarrhea, cardiac problems, and hot flush. PC-SPES should not be used for any purpose.[15,70,71–78]

Reishi mushroom (Ganoderma lucidum, red reishi)

It is one of the eight herbal mixtures in PC-SPES. It is used in the treatment of allergy, arthritis, bronchitis, gastric ulcer, diabetes, hypertension, chronic hepatitis, nephritis, insomnia, scleroderma, and cancer. It is believed to strengthen the body, to prolong life, and to reinforce the immune system. Although it is advocated for having anticancer efficacy by decreasing tumor cell migration, adhesion, and angiogenesis in cancers having high metastasis potential such as prostate and breast cancer, this effect has not been demonstrated by animal experiments and randomized studies. Moreover, it has been shown that the marketed products contain diethylstilbestrol. Frequently observed side effects are nausea, vomiting, liver toxicity, and increase in bleeding tendency. Since it interacts with chemotherapeutics (CYP2E1, CYP1A2, and CYP3A inhibition), it should not be used with them.[79–82]

Oleander (Nerium oleander)

Most frequently it is used for cancer treatment and in treatments of cardiac failure, HIV, AIDS, rheumatoid arthritis, and psoriasis for healing purposes. In the single Phase I study performed in humans and published, no response was observed in any of the 18 patients using the drug. Since some of its anticarcinogenic effects have been demonstrated in animal and cell experiments, it is a candidate for studies. However it should not be used in cancer treatment in its current form. Some of its adverse events are abdominal pain, hypothermia, dizziness, respiratory paralysis, and death. It has no significant interaction with cancer drugs.[82–94]

Mistletoe (Iscador, Helixor)

Mistletoe extract contains several lectins and viscotonics. Although in laboratory medium and in some animal models it is demonstrated that it has some anticancer efficacy, contrary results have been detected in randomized clinical studies.[8] It is used for cancer treatment, immune stimulation, arthritis, and sedation. In three systematic compilations, there are insufficient results for the effect of cancer treatment. Although

in many current meta-analysis it has been reported that iscador contributes to survival in cancer patients moderately, the benefit has been observed in non-randomized and biased studies. Many side effects including anaphylactic shock have been reported. In the light of evidences obtained, due to mistletoe's having no benefit it should not be used in cancer treatment. It may interact with cancer drugs (it causes CYP3A4 inhibition).[95–113]

Licorice (Glycyrrhiza glabra, Gan Cao)

It is used for its gastroprotective, antiinflammatory, and antiallergic effects. Additionally it is believed to have an anticancer effect, however there is no evidence of this. It has mineralocorticoid and glucocorticoid activity. Its side effects are hypokalemia (±myopathy), hypertension, and pulmonary edema. It interacts with many drugs and it may increase digoxin toxicity. It may interact with chemotherapy drugs by causing CYP3A induction.[114–126]

Astragalus (wild licorice)

It is used to strengthen the immune system. In a meta-analysis reviewing 34 randomized clinical studies, it has been shown that addition of astragalus to platinum-based chemotherapy ensured decrease in risk of death, increase in response rates, better performance status, and decrease in side effects. However, significant methodological limitations in the study compromise the transparency of the results on the efficacy of this herb.[8] Before being combined with chemotherapy drugs, it is indicated that its beneficial effects should be demonstrated with strictly controlled studies. It interacts with cyclophosphamide among chemotherapy drugs.[127–130]

Ginger (Zingiber officinale)

In a Phase II/III study performed with 600 participants, addition of ginger to antiemetic drugs was demonstrated to be efficient in prevention of acute and delayed nausea due to chemotherapy. Although no significant side effect is observed, acid indigestion and dermatitis may be observed.[131–132]

Curcuma (Curcuma longa, Yu Jin, Ping Xiao San; turmeric)

It is an herb recommended by traditional herbalists in early-phase colorectal cancer and in leukemia; however there is no primary evidence. In its long-term usage, nausea, gastric irritation, diarrhea, and bleeding problems may be observed. It interacts with many drugs, mainly doxorubicin and cyclophosphamide.[114,133]

We present popular herbs in Table 1.

Discussion

Since many herbal drugs are either the subject of very few investigations or not taken into any research, there is very little objective information related to the potential risks and benefits of their frequent usage.[70] The parts of the herbs used in some CAM products (such as leaf, seed, root), their harvests, intraspecies genetic differences, pesticide usage status, diversity of climate and soil where they are raised, and storage conditions are only some of the factors affecting the chemical active substance concentration.[15,134]

When patients' source of supply for CAM products is investigated, it has been observed that 29.8% of these are collected from nature directly and that they are unprocessed. Thus they are not sterile and may contain fungal spores and various bacteria. When patients receiving chemotherapy consume this type of product, the increase in their rates of infection risk are unavoidable.[135]

As also mentioned above, the interaction of these products with chemotherapy drugs leads to a decrease in the targeted effects of chemotherapy drugs or to an increase in their toxic effects, and may cause the active treatment of the disease to be interrupted or cause a false assumption as to a side effect of chemotherapy, so that the treatment is deficient due to unnecessary dose reduction. When it is taken into account that 59% of patients using CAM do not inform their doctors on this subject, it has been necessary for all physicians, mainly oncologists, to be aware of the corresponding unsolicited effects of these herbs and to question their patients fully about their histories of using CAM.[135,70]

In 23.7% of 2609 traditional Chinese medical products collected in Taiwan, at least one synthetic drug mixture—frequently, caffeine, paracetamol, indometacin, hydrochlorothiazide, and prednisolone—have been encountered. In many Chinese-origin herbal products sold outside the Asian continent, although not indicated on the label, nonsteroidal antiinflammatory drugs (NSAID) and benzodiazepines have been found. This situation causes unexpected problems, since the content of the products is not known. Although not common, heavy metal contaminations can also be encountered in herbal products. In 24 of 251 Asia-patented herbal products collected in California, lead (at least 1 ppm) has been found; in 36 of these, arsenic has been encountered; and in 35 of these, mercury content has been detected. Cases of lead, mercury, cadmium, and arsenic intoxication caused by using Chinese herbal preparations have been reported.[15,136]

Evidence obtained from randomized controlled studies that supports the existing widespread effects of herbal products, are limited. Numerous herbal products for cancer treatment and/or support treatment have been tried out with clinical studies, and except for the nausea-reducing effect of ginger, no evidence for practical application could be presented.

In a published case report it is not generally possible to detect whether the tumor regression in a patient is due to a herbal drug or not. Spontaneous remissions have been reported for various malignancies. However, when the incidental discovery history of beneficial therapeutics is taken into account, it may be thought that well-documented cases of cancer regression due to an herbal drug may compose the basis for initiation of extensive studies. However, limited data exist related to the effect of case reports and case series on the initiation of extensive pre-clinical or clinical trials, confirmed by controlled clinical studies.[70] It has been shown that herbal treatments have been unsuccessful as a result of two randomized controlled studies that aimed to show improvement in the quality of the lives of patients and decrease in side effects of chemotherapy and radiotherapy.[137,138] In a systematic compilation, no satisfactory evidence has been found to support efficacies of the herbal products used by individuals for any purpose.[139] In a study where 371 breast cancer patients were screened 10 years after the diagnosis, 217 of these used herbal products and 154 of these did not use them.

It has been determined that overall survival in the users was worse; however the study did not achieve statistical significance.[140]

In another study performed recently, it has been reported that 54.2% of the patients receiving chemotherapy use CAM and 95% of the patients using CAM prefer herbal methods. And in the evaluation of CAM usage in terms of quality of life, no effect could be demonstrated in CAM users except the loss of appetite.[135]

The efficacy of many herbs resulting in positive outcomes has not been discovered yet clearly with randomized studies. Many useful herbs have been defined by the observations of patients treated, with the preclinical methods assessed as nontraditional approaches. When reliable data suggesting that cancer patients obtain potential benefits from herbal or other nontraditional approaches are available, we recommend that investigator groups conduct extensive research. The purpose should be the development of an integrative set of information—and when doing this, caring for the quality of specific models, considering scientific inquiry rules, is a necessity.

Author Disclosure Statement

No conflicting financial interests exist.

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