Journal of Diseases and Medicinal Plants
2015; 1(1): 19-23
Published online April 28, 2015 (http://www.sciencepublishinggroup.com/j/jdmp)
doi: 10.11648/j.jdmp.20150101.13

Medicinal Plants in Breast Cancer Therapy

Tagne Simo Richard[1], Armel Herve Nwabo Kamdje[1], Farah Mukhtar[2]

[1]Department of Biomedical Sciences, University of Ngaoundere, Ngaoundere, Cameroon
[2]Department of International Center for Chemical and Biological Sciences, University of Karachi, Karachi, Pakistan

Email address:
rstagne@gmail.com (R. Tagne Simo), armel.nwabo@gmail.com (A. H. Nwabo Kamdje), kamdjewa@yahoo.fr (A. H. Nwabo Kamdje)

To cite this article:
Tagne Simo Richard, Armel Herve Nwabo Kamdje, Farah Mukhtar. Medicinal Plants in Breast Cancer Therapy. *Journal of Diseases and Medicinal Plants*. Vol. 1, No. 1, 2015, pp. 19-23. doi: 10.11648/j.jdmp.20150101.13

Abstract: Various active compounds (or their semi-synthetic derivatives) derived from medicinal plants have been assessed for their efficacy and tolerability in the treatment of breast cancer. Some of these plant species, including Taxus baccata (paclitaxel, docetaxel), Podophyllum peltatum (etoposide), Camptotheca acuminata (camptothecin) and Vinca rosea (vinblastine, vinorelbine) have well recognized antitumour activity in breast cancer, and have been evaluated in clinical trials. For example, results from recent Phase II/III trials have established docetaxel as the most active single agent in the treatment (first or second-line) of advanced metastatic breast cancer. The treatment of breast cancer, the most common malignancy among women worldwide, remains puzzling partly due to the resistance to therapeutics, which associates with the heterogeneity of case clinical presentations, and limits in the current understanding of the pathogenesis of solid cancers. Oxidative stress is closely related to various diseases, including cancer. The human body is exposed to free radicals, which cause oxidative stress. Oxidative stress may lead to gene mutations leading to carcinogenesis. Antioxidants are protector of the body, preventing oxidative stress, by stabilizing free radicals. Plants are good and cheap sources for the prevention and treatment of oxidative stress and cancer. Major drawbacks to Antioxidant from plants -based therapy and use in breast cancer are herein briefly discussed.

Keywords: Medicinal Plants, Natural products, Breast Cancer, Therapy, Anticancer, Free radicals, Antioxidant, Oxidative Stress, Carcinogenesis

1. Introduction

The term cancer is used in the medical sciences for the unregulated cell growth. Cancer cells grow in uncontrollable manner, and result in malignant tumors which attack on the nearby parts of the body. Various active compounds (or their semi-synthetic derivatives) derived from medicinal plants have been assessed for their efficacy and tolerability in the treatment of breast cancer. Some of these plant species, including Taxus baccata (paclitaxel, docetaxel), Podophyllum peltatum (etoposide), Camptotheca acuminata (camptothecin) and Vinca rosea (vinblastine, vinorelbine) have well recognized antitumour activity in breast cancer, and have been evaluated in clinical trials. For example, results from recent Phase II/III trials have established docetaxel as the most active single agent in the treatment (first or second-line) of advanced metastatic breast cancer. For other plant species such as Panax ginseng and Allium sativum, antitumour activity has been evaluated in experimental studies using cultured cells and animal models, but the therapeutic potential in patients remains to be determined. Antitumour activity derived from medicinal plants may produce results via a number of mechanisms, including effects on cytoskeletal proteins which play a key role in mitosis (paclitaxel), inhibition of activity of topoisomerase enzymes I (camptothecin) or II (etoposide), stimulation of the immune system (Viscum album), or antiprotease-antioxidant activity. Medicinal plant-derived antineoplastic agents may be used in single agent or in combinational therapies, and have been used in first-line or second-line (including anthracycline-refractory patients) treatment of localized or metastatic breast cancer. Adverse effects resulting from the use of these agents include neutropenia and peripheral neuropathies. The cancerous cell, when spread to other parts of the body through lymphatic or blood stream, is called metastasis. All the tumors are not cancerous in nature; some of them are benign, which do not invade the nearby tissue, and do not spread to other parts of the body. More than 200 types of cancer have been identified that harm the human body. Various factors have been identified that increase the risk of cancer, such as smoking, exposure to radiation, obesity, lack of physical activity, environmental pollutants and oxidative

stress. Cancer caused mutation, which some time results in other diseases. The hereditary role in cancer was identified to be from 5-10%. Cancer can be diagnosed by using the biochemical screening tests and medical imaging. The chemotherapy, radiation therapy and surgery are normal procedures adopted for the treatment of cancer. These procedures either have less or more side effect, while the usage of medicinal plants in the treatment of cancer is safer than usual procedures.

2. Medicinal Plants Oxidative Stress Antioxidant and Cancer

Various active compounds (or their semi-synthetic derivatives) derived from medicinal plants have been assessed for their efficacy and tolerability in the treatment of breast cancer. Active oxygen may cause cancer through two possible mechanisms: gene mutations and the effects on signal transduction and transcription factors. Oxidative stress causes damages to DNA, phospholipids, proteins and carbohydrates on the cell membrane. Oxidation and injury to DNA induce genetic mutation. The presence of free radicals may enhance the mutation of some genes. An antioxidant is "any substance that delays, prevents or removes oxidative damage to a target molecule" [1]. Antioxidants can act by diverse mechanisms in the oxidative sequence. The human body complex antioxidant defense system consists of the dietary intake of antioxidants, as well as the endogenous production of antioxidative compounds, such as glutathione, etc. [2]. Antioxidants can be classified into a number of different groups as enzymatic and non enzymatic strategies. The enzymatic antioxidant involve superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase, while non enzymatic antioxidants include the vitamins A, C, and E, glutathione, and lipoic acid, mixed carotenoids, several bioflavonoids, antioxidant minerals (copper, zinc, manganese, and selenium), etc. Antioxidants may work either alone, or in association with each other against different types of free radicals. Vitamin E inhibits the propagation of lipid peroxidation; the combination of vitamin C and vitamin E suppress the formation of hydroperoxide; metal complexing antioxidant such as penicillamine inhibit free redical formation in lipid peroxidation [3]. Human body is constantly generating free radicals, which causes oxidative stress. Factors such as drugs, pollution, immune responses to viruses, deficiency of natural antioxidants, ultraviolet rays and tobacco destroy the body potential of stabilizing free radicals. In addition to those exogenous sources, endogenous sources of oxidative stress include mitochondria, or microsomes and peroxisomes, and enzyme NADPH. The body has the power to neutralize them, but if there is an imbalance between the free radicals and the ability of the body to neutralize it, it causes oxidative stress. Oxidative stress may cause various problems and diseases such as diabetes, Alzheimer's disease, Parkinson's disease, aging and cancer. Oxidative stress causes Lipid peroxidation in cell membranes, determined as free radicals, reacting with polyunsaturated fatty acids. Cell membranes contain polyunsaturated fatty acids (PUFAs) and lowdensity lipoproteins (LDL). They are sensitive to free radicals [4]. The interaction of ROS and lipids consists of three different steps: initiation, propagation and termination. The molecular oxygen reacts with carbon-centered free radicals, and thus, lipid hydroperoxides (LOOH) are formed. LOOH alter the membrane structure and function. Free redicals cause proteins oxidation. There are various markers of protein oxidation, which include protein carbonyl derivates, oxidized amino acid side chains and formation of advanced glycation end products. In the oxidation process, Protein carbonyl derivates are formed early, and are generated as the peptide main chain as some amino acid side chains that are cleaved (arginine, lysine, or threonine), are oxidized [5-7]. The carbonyl groups are relatively stable [7], and may result in loss of protein function, as well as increased degradation of soluble proteins [5]. Protein oxidation has also been shown to be a chain reaction and may be inhibited by chain-breaking antioxidants [8]. Oxidation of proteins may develop some problem, but protein damage can be repaired, and is a non-lethal event for the cell [9]. DNA is especially sensitive to damage due to its potential to create cumulative mutations, which may disrupt cellular homeostasis [10]. DNA may be damaged by ROS and cause permanent structural changes in, as base-pair mutations, deletions, insertions, rearrangements and sequence amplification [11]. Continuous oxidative damage to DNA may lead to alterations in signaling cascades or gene expression, and may cause replication errors and genomic instability [10]. In recent years, oxidative stress and the mechanisms by which cancer is caused has been extensively studied. Cancer development is a multistage process which involves mutations in critical genes required for maintenance of the cellular homeostasis [10]. Oxidative stress causes initiation, promotion and progression of carcinogenesis [12]. ROS play an important role in the development of cancer. Oxidative damage to DNA or of antioxidant defense systems leads to mutation, activated transcription factors, modification of gene expression and chromosomal aberrations, processes which have been described as the agents of progressions of cancer. Inflammation also causes DNA mutaion [13]. 25% of all cancers in the world is due to chronic inflammation due to infection or injury [14]. Various chemicals such as chlorinated compounds, metal ions, aromatic hydrocarbons and some peroxisome proliferators have been shown to induce oxidative stress, which damages the DNA. They may, therefore, partly account for the development, especially of workrelated cancers. Many cancers are associated with increased production of ROS [12]. Natural products, especially plants, have been used for the treatment of various diseases from ancient times. People of Egypt, China, India and Greece have been using terrestrial plants as medicines, and a large number of modern drugs have been developed from them. Medicinal plants have been used in the treatment of many diseases, such as diabetes, obesity and cancer, etc.

There are many evidences that the generation of free radicals inside the body cause damages to DNA and lead to the development of cancer, etc., and if these free redicals are neutralized by the antioxidants from different medicinal plants, then it prevents cancer. Several studies have shown that plant derived antioxidant scavenge free radicals and modulate oxidative stress. Free radicals are the cause of many diseases such as cancer, atherosclerosis, diabetes, neurodegenerative disorders and aging; different experimental and clinical studies have proved that higher intake of antioxidant rich food is associated with decreased risk of cardiovascular diseases and cancer. The free radical neutralizing property of several plants have been screened by various researchers. Plants have been used in the treatment of cancer. The National Cancer Institute collected about 35,000 plant samples from 20 different countries, and has screened around 114,000 extracts for anticancer activity. 60% of the commercialy available anticancer drugs are from natural sources. Treatment by herbal medicines may have some advantages over treatment by single purified chemicals [15]; as hebal medicine are the mixtures of more therapeutic or preventive components, and so might have more activity than single products alone. The antioxidant and anti-tumor effects of extracts from various herbs and medicinal plants have been proved experimentally and clinically. Several in vitro or in vivo studies have proved the anticancer potential of the extracts from several medicinal plants [16-18]. Experimental studies of aqueous extracts from willow (Salix sp.) leaves show prevention of proliferation of cancer cells [18]. Ganoderma lucidum methanolic extracts induced apoptosis in human breast cancer cells Hu *et al*. [17] and Kao *et al*. [19] studied that an aqueous extract of Bu-Zhong-Yi-Qi-Tang (a mixture of ten herbs), had the ability to induce apoptosis in hepatoma cells. Most of the plants contain phenolic and flavonoid compounds, which have antioxidant activities, and thus, prevent oxidative stress and cancer [20]. The effect of an aqueous extract of Paeoniae lactiflora were studied on HepG2 and Hep3B hepatoma cells, which showed apoptosis. Yano *et al*. [21] stated that aqueous extract of Sho-Saiko-To caused inhibition of the proliferation of KIM-1 human hepatoma cells. It was stated by Bonham *et al*. [16] that PE-SPES (mixture of eight herbs) had been used as a clinical treatment of prostate cancer. Chemical and diferent studies of various extracts from the herbs were found to to be useful in preventing radiation damages and purify blood quality [22,23]. The seeds of Luffa aegyptiaca has the ability to destroy the human metastatic melanoma [24].

3. Medicinal Plants in Clinical Use

The anticancer agents, vinblastine and vincristine from the Madagascar periwinkle, Catharanthus roseus G. Don. (Apocynaceae), introduced a new era of the use of plant material as a medication for treatment. They were the first agents to advance into clinical use for the treatment of cancer. Vinblastine and vincristine are used in combination with other cancer drugs, for the treatment of various kinds of cancers, including leukemias, lymphomas, advanced testicular cancer, breast and lung cancers The isolation of paclitaxel (Taxol®, 3) from the bark of the Pacific Yew, Taxus brevifolia Nutt. (Taxaceae), is another good step in the discovery of natural product drug. Various parts of Taxus brevifolia and other Taxus species (e.g., Taxus Canadensis Marshall, Taxus baccata L.) have been used by several native American tribes for the treatment of various diseases, while Taxus baccata was reported to use in India as a medicine for the treatment of cancer. The paclitaxel was clinically introduced to the US market in the early 1990s. Paclitaxel is active against a number of cancer types, for example: ovarian cancer, advanced breast cancer, small and non-small cell lung cancer. Camptothecin was isolated from the Chinese ornamental tree, Camptotheca acuminate Decne (Nyssaceae), the clinical trials in the 1970s dropped it because of severe bladder toxicity. Derivatives of camptothecin, Topotecan and irinotecan, are used for the treatment of ovarian and small cell lung cancers, and colon cancers, respectively.

4. Medicinal Plants in Breast Cancer Therapy

Among Complementary and alternative medicines, herbal medicine is the most commonly used group of treatment. Herbal treatment is the oldest used system of medicine in the world with more than 2000 years history [25]. Other names used for herbal therapy are phytomedicine, phyto-therapy or botanical medicine. It is a medicine made exclusively from plants such as roots, bark, flowers, seeds, fruits, leaves, or branches and is used in all societies and common to numerous cultures including Asia, Africa, Europe and America. There are various types of herbal medicine that spring from different cultures around the world however they vary in the way they are prepared and in their treatment approaches [26]. Certain herbs defend the body from malignancy by augmenting detoxification or cleaning role of the body. Some biological response modifiers, derivatives of herbs, are recognized to hinder the growth of cancer by modifying the activity of precise hormones and enzymes, while other herbs diminish lethal side effects and complications of chemotherapy and radiotherapy [27]. Moreover, phytoconstituents resulting from the herbs such as Vinca rosea, Taxus species, Allium sativum, Aloe vera, Angelica sinensis, Astragals membranaceus, Glycine max, Glycyrrhiza glabra, Hordeum vulgare, Hydrocotyle asiatica, Medicago sativa, Morinda citrifolia, Panax pseudoginseng, Saussurea lappa, Taxus wallichiana, Tinospora cordifolia, Viscum album, Withania somnifera, Zingiber officinale etc. have been used in numerous preparations to improve function of the body's immune cells that stimulates production of cytokines including interleukin, interferon, tumor necrosis factor as well as colony stimulating factor. These preparations assist the body to battle cancer more efficiently and also decrease the harmful side effects of chemotherapy and radiotherapy [27]. Herbal formulae have been prescribed

to adults, children, and elderly, as well as pregnant and lactating mothers. Compared to Eastern part of the world where herbal treatments play a central role, they are not as popular in the United States. Such treatments form a complete medical system that is integrated in modern hospitals and clinics throughout most of Asia. Literature documents the current popularity of natural alternatives to conventional medical treatments, especially among patients with chronic life-threatening diseases such as cancer [28]. Most cancer patients combine herbal remedies with conventional therapy in the hope of boosting the effect of conventional medicine [25,29]. A study of women being treated for early stage breast cancer showed that 10.6% had been using one or more herbal remedies at the time of diagnosis, while an additional 28.1%began using herbal remedies after surgery [11]. Similarly a multinational survey found that 35.9% of cancer patients were either past or present users of complementary and alternative medicine. Herbal medicines were by far the most commonly used group of treatments, escalating in use from 5.3% before the diagnosis of cancer to 13.9% after the diagnosis of cancer [26]. Generally, herbal products are utilized for two reasons, first, to lessen symptoms of disease and second to prevent sickness. Examples include palliative use of St. John's Wort (Hypericum perforatum) for relief of acute depression, the use of Ginkgo biloba for enhancement in perception/understanding and the use of Echinacea for improving cold symptoms [30]. In the second circumstance, herbal supplements are taken especially in the anticipation of averting disease or modifying the effects of threat for certain illnesses. Such as intake of green tea and other ?avonoid rich botanicals to yield benefit of the natural antioxidants in them and the consumption of garlic because of the high organo-sulfur compounds that have been experimentally proven to prevent cancer in animals [30]. In the domain of cancer prevention, herbs may performance through numerous mechanisms to shield the body. Initiation of phase I and phase II metabolic enzymes by herbal supplements is quite typical and maybe liable for some of this action [30]. These phase I and II enzymes provide major protection against carcinogenesis, mutagenesis, and other forms of toxicity mediated by carcinogens through initiation of their metabolism, particularly phase 2 enzymes such as glutathione S-transferases (GSTs), UDP-glucuronosyl transferases, and quinone reductases [31]. Taking example of garlic, its intake and supplement use is prevalent in both, Eastern and Western cultures [32]. Garlic along with numerous other organo-sulfur compounds derived from garlic demonstrate robust chemo-preventive action against experimentally induced cancers of the mammary gland as well as esophagus, stomach, colon, liver and lungs [30]. Initiation of phase I and phase II enzymes, nonetheless, can result in a likely significant side effect of herbal products. Such as St. John's Wort that is extensively utilized, has been shown to encourage the CYP3A family of activation enzymes, through which half of current medications are also metabolized, hence offering the likelihood of herb-drug interactions [30].

5. Conclusion

Free radicals are the cause of oxidative stress, which may causes injury to cells, gene mutation, and may lead to cancer. Oxidative stress causes cancer, by the interaction with intracellular signal transduction and transcription factors, directly or indirectly. Medicinal plants are main sources in healing of the cancer around the world. This property of the plants is because of the presence of potent anti cancer substances. Medical plants treatment of cancer is prevalent, especially in our country where resources are limited. Several medicinal plants have been known to cure and control cancer. Most of the medications used word wise contains herbal product, with no side effects.

References

[1] Halliwell B, Gutteridge J (2007) Free radicals in biology and medicine. (4th Edn), Oxford University Press, Oxford, USA.

[2] Clarkson PM, Thompson HS (2000) Antioxidants: what role do they play in physical activity and health Am J Clin Nutr 72: 637S-646S.

[3] Feher J, Csomos G, Vereckei A (1987) Free radical reactions in medicine. Springer-Verlag, Berlin-Heidelberg, USA 40-43.

[4] de Zwart LL, Meerman JH, Commandeur JN, Vermeulen NP (1999) Biomarkers of free radical damage applications in experimental animals and in humans. Free Radic Biol Med 26: 202-226.

[5] Berlett BS, Stadtman ER (1997) Protein oxidation in aging, disease, and oxidative stress. J Biol Chem 272: 20313-20316.

[6] Dean RT, Fu S, Stocker R, Davies MJ (1997) Biochemistry and pathology of radical-mediated protein oxidation. Biochem J 324 : 1-18.

[7] Morabito MA, Sheng M, Tsai LH (2004) Cyclin-dependent kinase 5 phosphorylates the N-terminal domain of the postsynaptic density protein PSD-95 in neurons. J Neurosci 24: 865-876.

[8] Benderitter M, Maupoil V, Vergely C, Dalloz F, Briot F, et al. (1998) Studies by electron paramagnetic resonance of the importance of iron in the hydroxyl scavenging properties of ascorbic acid in plasma: effects of iron chelators. Fundam Clin Pharmacol 12: 510-516.

[9] Valko M, Leibfritz D, Moncol J, Cronin MT, Mazur M, et al. (2007) Free radicals and antioxidants in normal physiological functions and human disease. Int J Biochem Cell Biol 7 : 44-84.

[10] Powell JM, McCrory DF, Jackson-Smith DB, Saam H (2005) Manure collection and distribution on Wisconsin dairy farms. J Environ Qual 34: 2036-2044.

[11] Cerutti PA (1994) Oxy-radicals and cancer. Lancet 344: 862-863.

[12] Cook PLM, Wenzhöfer F, Rysgaard S, Galaktionov OS, Meysman FJR, et al. (2006)Quantification of denitrification in permeable sediments: Insights from a two dimensional simulation analysis and experimental data. Limnol Oceanogr Methods 4: 294-307.

[13] Cook A, Blaustein M, Spinazzola J, van der Kolk B (2003) Complex trauma in children and adolescents. National Child Traumatic Stress Network, Complex Trauma Taskforce.

[14] Coussens LM, Werb Z (2002) Inflammation and cancer. Nature 420: 860-867.

[15] [15]. Vickers A (2002) Botanical medicines for the treatment of cancer: rationale, overview of current data, and methodological considerations for phase I and II trials. Cancer Invest 20: 1069-1079.

[16] Bonham M, Arnold H, Montgomery B, Nelson PS (2002) Molecular effects of the herbal compound PC-SPES: identification of activity pathways in prostate carcinoma. Cancer Res 62: 3920-3924.

[17] Hu H, Ahn NS, Yang X, Lee YS, Kang KS (2002) Ganoderma lucidum extract induces cell cycle arrest and apoptosis in MCF-7 human breast cancer cell. Int J Cancer 102: 250-253.

[18] El-Shemy HA, Aboul-Enein AM, Aboul-Enein MI, Issa SI, Fujita K (2003) The effect of willow leaf extracts on human leukemic cells in vitro. J Biochem Mol Biol 36: 387-389.

[19] Kao ST, Yeh CC, Hsieh CC, Yang MD, Lee MR, et al. (2001)The Chinese medicine Bu-Zhong-Yi-Qi-Tang inhibited proliferation of hepatoma cell lines by inducing apoptosis via G0/G1 arrest. Life Sci 69: 1485-1496.

[20] Meyers KJ, Watkins CB, Pritts MP, Liu RH (2003) Antioxidant and antiproliferative activities of strawberries. J Agric Food Chem 51: 6887-6892.

[21] Yano H, Mizoguchi A, Fukuda K, Haramaki M, Ogasawara S, et al. (1994) The herbal medicine sho-saiko-to inhibits proliferation of cancer cell lines by inducing apoptosis and arrest at the G0/G1 phase. Cancer Res 54: 448-454.

[22] Wang X, Wei L, Ouyang JP, Muller S, Gentils M, et al. (2001) Effects of an angelica extract on human erythrocyte aggregation, deformation and osmotic fragility. Clin Hemorheol Microcirc 24: 201-205.

[23] Xie F, Li X, Sun K, Chu Y, Cao H, et al. (2001) An experimental study on drugs for improving blood circulation and removing blood stasis in treating mild chronic hepatic damage. J Tradit Chin Med 21: 225-231.

[24] Poma A, Miranda M, Spanò L (1998) Differential response of human melanoma and Ehrlich ascites cells in vitro to the ribosome-inactivating protein luffin. Melanoma Res 8: 465-467.

[25] Ma H, Carpenter CL, Sullivan-Halley J, Bernstein L (2011) The roles of herbal remedies in survival and quality of life among long-term breast cancer survivors-results of a prospective study. BMC Cancer 11: 222.

[26] Olaku O, White JD (2010) Herbal therapy use by cancer patients: A literature review on case reports. Eur J Cancer [Article in Press].

[27] Sakarkar DM, Deshmukh VN (2011) Ethnopharmacological Review of Traditional Medicinal Plants for Anticancer Activity. International Journal of PharmTech Research 3: 298-308.

[28] Boon H, Stewart M, Kennard MA, Gray R, Sawka C, et al. (2000) Use of complementary/alternative medicine by breast cancer survivors in Ontario: prevalence and perceptions. J Clin Oncol 18: 2515-2521.

[29] Burstein HJ, Gelber S, Guadagnoli E, Weeks JC (1999) Use of alternative medicine by women with early-stage breast cancer. N Engl J Med 340: 1733-1739.

[30] Michael JW, Cynthia W, Destiny MH, Mary EZ (2001) Herbals, Cancer Prevention and Health. American Society for Nutritional Sciences, Journal of Nutrition 131: 3034?3036.

[31] Kwak MK, Egner PA, Dolan PM, Ramos GM, Groopman JD, et al. (2001) Role of phase 2 enzyme induction in chemoprotection by dithiolethiones. Mutat Res 480-481: 305-315.

[32] Fleischauer AT, Arab L (2001) Garlic and cancer: a critical review of the epidemiologic literature. J Nutr 131: 1032S-40S.