

Ocimum Basilicum as Alternative Natural Cancer Care

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Abstract

Cancer is the most dreadful disease worldwide in terms of morbidity and mortality. The exact cause of cancer development and progression is not fully known. *Ocimum Basilicum (OB)* or basil contains citric acid, essential oils, 1-8 sineol, arigin, anetol, flavonoid, boron, stigmasterol, eugenol, beta-carotene, magnesium and tryptophan. Works as an anticancer through phenolic compounds (caffeine acid, p-kumarat acid) which is an antiproliferative agent, which will increase the number of non-apoptotic cells in the synthesis phase in the cell cycle and decrease the number of non-apoptotic cells in the G2/M phase. While caffeine acid may cause an increase in FasL, which is a receptor of death (Fas). The existence of a complex between FasL and Fas can induce signaling that induces cell death. Phenolics have also been shown to decrease the Bcl2 antiapoptotic protein, so apoptosis does not work. Increased Bcl2 expression will be followed by an increase in Bax, which is produced because cancer cells may mutate in the p53 protein, triggering a dimer between the two and triggering apoptosis through Fas.

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OB extract, containing flavonoids that have an effect as a chemopreventive agent by protecting lymphocytes from cancer induction. Another compound is the essential oil (terpenoid) that can inhibit tumor by improving the performance of Human Natural Killer in immune system (immunostimulan), so as to destroy tumor cells and increase macrophage cells that act as the phagocytes of damaged cells. In this review will be discussed about the role of *OB* in the natural treatment of cancer and the working mechanisms involved in it.

Keywords: Ocimum Basilicum; Anti-cancer; anti proliferative compound; working mechanism.

1. Introduction

Cancer is a disease characterized by out-of-control cell growth leading to spread of abnormal cells to other body parts by local invasion and/or distant metastasis. It is one of the major and growing public health problem, currently accounting for over 12% deaths globally. Cancer is a major health problem that can debilitate and destroy human lives. One out of every four deaths in the U.S. is caused by cancer. Over \$124.6 billion was spent in direct medical costs for the 13.7 million cancer survivors and 1.5 million newly diagnosed cancer patients in the U.S. in 2010 [1]. The World Cancer Report showed that cancer rates would increase at an alarming rate in the global scope. In this report, cancer rates could further increase by 50% to 15% million new cases in the year 2020 [2]. Numerous natural compounds have been extensively investigated for their potential for cancer prevention over decades. Phytochemicals are compounds found in plants i.e curcumin, capsaicin, black tea and ocimum basilicum in experimental systems and clinical trials, they protect people from environmental and ingested carcinogens by arming our antioxidant enzymes, enhancing DNA repair pathways and have direct effects on the fundamental hallmarks of cancer progression and metastasis. Chemoprevention is one of the cancer prevention approaches where in natural/synthetic agents are prescribed with the aim to delay or disrupt multiple pathways and processes involved at multiple steps, i.e., initiation, promotion, and progression of cancer. Majority of human cancers are caused by environmental and life-style factors. The etiology of all cancers is associated with inherited genetic aberrations (5%-10%) and acquired genetic abnormality (90%-95%) caused by exogenous and/or endogenous environmental agents [3].

Ocimum Basilicum (OB) or basil in Indonesia is known by the name of basil, except in Sulawesi known as amping [4], grows in the tropical region and is a herb plant erect or bush, branched a lot, with height 1.3-1, 5 meters, has a distinctive fragrant sourced from citric acid, especially the flowers and leaves. Studies have shown many pharmacological effects in several diseases, with potent antioxidant, anti-aging, anticancer, antiviral, and antimicrobial properties [5]. *Ocimum* consists of several types: *Ocimum basilicum, Ocimum sanctum, Ocimum gratisimum and Ocimum americanum*. Basil includes vegetables rich in provitamin A (in 100 grams of basil leaves containing 5,000 SI of vitamin A), calcium and phosphorus, (in 100 grams of basil leaves containing 45 and 75 mg of phosphorus). Other active ingredients contain phenol, terpenoids, alkaloids, glycosides, tannins, caffeic acid, p-kumarite acid, myresin, routine, quercetin. All herbs contain volatile oils comprising: 1,8-Sineol, p-Cymene, Limonen, Linalool, Methylcaviol, Methyl cinnamate, Pinen, Safrol, alpha-Terpinent [6]. Based on the results of the research, the evaporated oil has an anti-bacterial activity that has been tested with *S. aureus, S. enteritidis* and *E. coli* and its effective antifungal activity against *C. albicans, P. notatum, and Microsporeum gyseum. Kamfor, d-limonen, myresen*, and thymol have activity as antireppelant, with ability to kill insects up to

90% at concentrations of 113-283 ppm. Basil has also been used as antiekspektoran. Fresh basil leaf and stem extract contain: *cirsilineol, circimaritin, isothymusin, apigenin, rosmarinic acid* and *eugenol*. Besides it also contains sesquiterpenes and monoterpenes such as *bornyl acetate*, α and β *pinen, kamphene, cholesterol, stigmasterol* and β -sitosterol. Eugenol contained in fresh basil leaves and extracts have antioxidant activity and work by slowly excreting the oxidation product. Its antioxidants protect cells from damage by acting as scavengers of higly reactive free radicals [7].

2. Discussion

2.1. Cancer

Cancer is the most dreadful disease worldwide in terms of morbidity and mortality. The exact cause of cancer development and progression is not fully known. There is increasingly convincing evidence to show that plant phytochemicals have significant benefits for humans. Not only do they improve our daily lives by helping our food taste, smell and look appetising, they also reduce our risk of cancer and help people living with and beyond treatments[8]. Majority of human cancers are caused by environmental and life-style factors. The etiology of all cancers is associated with inherited genetic aberrations (5%-10%) and acquired genetic abnormality (90%-95%) caused by exogenous and/or endogenous environmental agents [3].

2.2. Ocimum basilicum

Ocimum basilicum L. popularly known as Tulsi in Hindi and "Sweet Basil" in English in one of the sacred herbs for Hindus in the Indian subcontinent. And India has one of the oldest, richest, and most diverse cultural living traditions associated with the use of medicinal plants [9]. Several types of basil have become commercial commodities including *Ocimum basilicum, Ocimum sanctum, Ocimum gratisimum and Ocimum americanum*. Studies have shown many pharmacological effects in several diseases, with potent antioxidant, anti-aging, anticancer, antiviral, and antimicrobial properties [5]. Some types of *ocimum* can be seen in Figure 1 below.



ocimum Basilicum

Ocimum Gratisimum

Ocimum Sanctum

Ocimum citriodorum

Figure 1: Various Ocimum Type [10]

2.3. Ingredient substance Ocimum basilicum and its role as anti-cancer



The chemical structure of the active ingredients found in basil can be seen in Figure 2 below.

Figure 2: The chemical structure of the active ingredient found in basil [11]

Administration of basil extracts increases antioxidant enzymes such as SOD, CAT, GSH, GPx and lipid peroxide downtake [7]. *Lamiaceae* family contains *monoterpene and sesquiterpenes*. *Monoterpene* with its derivatives: *camphor, limonen, thymol, citrit, geraniol,* and *linalool*. *Phenols* and *flavonoids* consist of: *cinnamic acid, caffeic acid, sinapic acid, ferulic acid,* and *rosmarinic acid* as the main antioxidants, free radical scavengers and metal chelators. Rosmarinic acid works to inhibit the proliferation of tumor necrosis factor- α (TNF- α), and inhibit the G0-G1 and G1-S phases in cell division [12]. The role of basil as anti-cancer can be seen in the following chart below:



Figure 3: The basil mechanism (Ocimum sanctum) as anti-cancer [7]

The administration of basil leaf extract (*ocimum sanctum*) in ethanol has anti-cancer effects acting on N-methyl-N-nitroguanidine induced by gastric cancer by decreasing Bcl-2 expression regulation and increasing regulation of Bax, cytochrome C and caspase-3 expression. Basil leaves also have anti-tumor effects through the phosphorylation of phosphorylation of Akt and extracellular signal regulated kinase (ERK) and increased Bax protein proapoptosis / suppression antiapoptosis protein Bcl-2 ratios in p53 activation by regulating activation of proapoptosis pathway in animal models of lung cancer model And in A549 human cancer cells. Basil oil (Tulsi leaf) is reported to cause cytotoxic effects and apoptotic activity in COLO205 colorectal adenocarcinoma cells through proliferative barrier and suppress angiogenesis. Vicenin-2 in basil leaves is a flavonoid that has antiproliferative, anti-angiogenesis and pro apoptotic effects on prostate carcinoma cells by inhibiting EFGR (epidermal growth factor). The administration of Ocimum sanctum (200 mg/kg, once daily) egg basil in arsenicexposed mice for 4 months (100 ppm in drinking water) caused low glutathione (GSH) levels and increased reactive oxygen species (ROS) in the blood. The activity of superoxide dismutase and catalase in the organs: liver, kidney and brain decreased. After exposure to arsenic, then the rats were given basil genus extract ocimum sanctum, significantly improved levels of GSH and ROS in the blood [13]. Another basil genus Ocimum gratissimum has the effect of inhibiting the proliferation of cancer cells through several mechanism signals. In colon cancer cells (HT-29, P53 null) and prostate cancer cells (PC-3; P53 null) work to decrease cyclin D1 and induction of p21 expression in HT-29 and PC-3 cancer cells after 24 hours of extracts ocimum [14]. The administration of N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) causes gastric cancer. Gastric cells experience proliferation and angiogenesis with evasion of apoptosis, as revealed through upregulation proliferating cell nuclear antigen (PCNA), glutathione S-transferase-pi (GST-pi), Bcl-2, cytokeratin (CK) and vascular endothelial growth factor (VEGF) And Bax downregulation, cytochrome C and caspase 3 protein expression. The administration of basil leaf extract (ocimum sanctum) extracted in ethanol decreases the effect of MNNG that causes cancer in the stomach. Reduces expression of PCNA, GST-pi, Bcl-2, CK, VEGF, and Bax overexpression, cytochrome C, and caspase 3 [15]. Ocimum basillicum leaves, used as anticancer through phenolic compounds (caffeine acid, p-acid kumarat) are in large numbers. The ocimum extract contains flavonoids that have an effect as a chemopreventive agent that protects lymphocytes from cancer induction, as well as terpenoid content that can enhance macrophages in their role as phagocytes of damaged cells. The administration of this extract in ethanol has an anti-cancer effect on N-methyl-N-nitroguanidine which in gastric cancer induces me through downregulating Bcl-2 and upregulating 3 expression [14].

Based on the above explanation of basil leaves can be used as a solution of traditional cancer drugs. At this time traditional medicine is more desirable by the community, because prefer healthy with a relatively cheap and safe cost. In addition to the side effects of traditional medicine, it is believed to be smaller and even absent when compared to the use of modern chemicals or drugs.

3. Conclusion

Phytochemicals are compounds found in plants, i.e: *Ocimum basilicum*, has the effect of inhibiting the proliferation of cancer cells through several mechanism signals. Which are responsible for the colour, taste and aroma of foods. Over and above these pleasant attributes, they protect people from environmental and ingested carcinogens by arming our antioxidant enzymes, enhancing DNA repair pathways and have direct effects on the fundamental hallmarks of cancer progression and metastasis. Chemoprevention by dietary agents has evolved as an effective strategy to control the incidence of cancer. Epidemiological studies have demonstrated a positive correlation between increased consumption of vegetables, fruits, and be verages with reduced risk of cancer. The

mechanisms responsible for this chemopreventive effect still remain largely unknown but are likely related to the presence of phytochemicals associated with fruits and vegetables

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References

- [1] Haddad RI, Shin DM. Recent advances in head and neck cancer. N Engl J Med. 359:1143-54, 2008
- [2] WHO. Global Cancer Rates Could Increase by 50% to 15 Million by 2020. 2014
- [3] Stewart B, Wild CP Ed. World Cancer Report, Chapter 2, Etiology of cancer. IARC, Lyon, France. 3: 82–169, 2014
- [4] Wijayakusuma, H., Wirian, SA, Yaputra, T., Dalimartha S. Wibowo. Plant Efficacious Drugs in Indonesia, Volume IV, Pustaka Kartini, Jakarta, 1996
- [5] Sakr SA, AL-Amoudi WM. Effect of leave extract of Ocimum basilicum on deltamethrin induced nephrotoxicity and oxidative stress in albino rats. J. Appl. Pharm. Sci., v.2, n.5, 2012.
- [6] Kruger H, Wetzel SB, Zeiger B. The chemical variability of *Ocimum* species. J Herbs Spices Med Plants. 9:335–44, 2002
- [7] Singh H. Diverse role of Ocimum santum: amagic remedy of nature. Indo American Journal of pharmaceutical research, vol.3, 2013
- [8] Robert Thomas, Elizabeth Butler, Fabio Macchi and Madeine Williams. Phytochemicals in cancer prevention and management?. BJMP. 8(2):a815, 2015
- [9] Brown JP. A review of the genetic effects of naturally occurring flavonoids, anthraquinones and related compounds. *Mutation Research*. 75(3):243–277, 1980
- [10] MG Silva, FJ Matos, PR Lopes, FO Silva, MT Holanda Composition of essential oils from

three *Ocimum* species obtained by steam and microwave distillation and supercritical CO_2 extraction. ARKIVOC, 6: 66-71,2004

- [11] Jean-François Lesgards JF. Anticancer Activities of Essential Oils Constituents and Synergy with Conventional Therapies: A Review Phytother. Res, 2014
- [12] Manosroia and B Jiradej. Anti proliferative activity of essential oil extracted From Thai Medicinal plants on KB and P388 cell lines. Elzevier, Mol Cell Biol.26 (3):940-954, 2006
- [13] Banu G Sharmila, G Kumar, AG Murugesan. Effects of leaves extract of Ocimum sanctum L. on arsenic-induced toxicity in Wistar albino rats. Center for Biotechnology, Muthayammal College of Arts and Sciences, Kakkaveri, Rasipuram, 637 408 Namakkal, Tamilnadu, India, 2008. http://www.pubmedcentral.nih.gov. 2008
- [14] Webb MA. The Mecahanism By Which fractions of Ocimum Free (og) Leaf extracts thisbit the proliferation of prostate cancer (PC-3) Cells and Colon Cancer (HT-29) Cells Seventh International symposium on Recent advances in Environmental Health Research, 2010
- [15] P Manikandan.Proliferation, angiogenesis and apoptosis-associated proteins are molecular targets for chemoprevention of MNNG-induced gastric Carcinogenesis by ethanolic Ocimum sanctum leaf extract. Singapore MedJ. Jul; 48 (7): 645-51, 2007