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## Natural and herbal medicine for breast cancer using *Elettaria cardamomum* (L.) Maton

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### Abstract

Breast cancer is one of the most common invasive cancers in women and also afflicts a small percentage of men. Numerous treatment methods have been developed for breast cancer, including radiation therapy, chemotherapy, palliative care, surgery, targeted cancer therapy, etc. However, these methods are often accompanied by toxic side effects impacting the patient's normal cells and overall health condition. Herbs and spices offer an alternative solution for breast cancer treatment, with bioactive components such as alkaloids, flavonoids, anthocyanin, phenylpropanoids, and terpenes that can inhibit biological processes associated with breast cancer cell growth. Spices such as *Zingiber officinale* (Ginger), *Crocus sativus* (Saffron), *Cinnamomum cassia* (Cinnamomum), *Elettaria cardamom* (Cardamom), *Piper nigrum* (Black pepper), *Nigella sativa* (Black cumin), *Allium cepa* (Onion), *Mentha* (Mint leaves) and others are used in traditional Ayurvedic treatments to prevent/inhibit cancer cell growth. Spices are a common element of the human diet that can be consumed at safe doses with few side effects. As with many spices, cardamom has been demonstrated to have antioxidant properties and shows chemopreventive activity in the prevention and inhibition of breast cancer growth. It contains the compounds DCM (diindolylmethane) and IC3 (indole-3-carbinol). It is also commonly used spice and has cancer chemopreventive potential. Cardamom DCM and IC3 compounds can kill breast cancer cells and inhibit proliferation. These compounds also provide additional anti-cancer benefits by promoting host immune responses. Various studies have suggested that daily consumption of cardamom can help prevent breast cancer. This review provides a broad outline on cardamom including its history, biochemical properties and medical uses in humans. We also highlight the ability of cardamom to inhibit breast cancer cells *in vitro* and review its use in animal experiments and human clinical trials. This paper gives an overview of the prevention of breast cancer using cardamom and provides a list of clinical trials using cardamom to help both allopathic physicians and researchers for further study.

**Keywords:** *Elettaria Cardamom*, antioxidant properties, chemopreventive, ayurvedic treatment

### 1. Introduction

Breast cancer is the most prevalent cancer affecting women in 140 of 180 countries worldwide [1]. The incidence of breast cancer is increasing in the developing world due to increases in urbanization, limited resource settings with weak health systems, and the adoption of Western lifestyles. According to the American Cancer Society, 252,710 women and 2,470 men are diagnosed with breast cancer in U.S each year [2]. The estimated number of new cases of invasive breast cancer each year is approximately 4,292,000 in China, equivalent to an average of nearly 12,000 new cancer diagnoses every day [3]. Breast cancer is the second-leading cause of death in women in developed and developing regions. The majority of women are diagnosed in its late stages. Breast cancer occurs when cells in the breast begin to grow and divide at abnormal levels. In normal cells, injury results in cell death, whereas cancer cells will continue to proliferate due to DNA mutations. The breast is composed of specialized tissue types including lobules (milk-producing glands), ducts and stroma as well as fat tissue [5, 6]. The most obvious symptom of breast cancer is the presence of a mass or lymph in the breast. Less common symptoms include other persistent changes to the breast such as swelling, tenderness, thickening, distortion, redness, nipple abnormalities, skin irritation and scarring. Breast cancer is classified into four different stages based on the rate of cancer growth, number of affected lymph nodes, invasiveness, and metastasis. In the first stage of breast cancer, the tumor is less than 2 cm and it is confined as a mass in the breast. During the second stage of breast cancer, the tumor would be somewhere between 2 cm and 5 cm and have spread to nearby lymph nodes. In stage 3 of breast cancer, the mass can be any size and it also has to have spread to at least 10 axillary or internal mammary lymph nodes. In the fourth and last stage of breast cancer, the cancer has spread to other organ systems. Treatment usually involves either breast-conserving surgery (surgical removal of the tumor and surrounding tissue, sometimes referred to as a lumpectomy) or mastectomy (surgical removal of the breast)

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depending on tumor characteristics (size, extend of spread and hormone receptor status) and patient preference. However, these treatment modalities carry harmful side effects that include swelling (oedema) of the breast, chest pain, armpit hair loss, anemia, memory loss, vaginal dryness or discharge, diarrhea, etc. [11]. Herbal treatments represent an excellent alternative solution to avoid and treat various side effects associated with these cytotoxic therapies. These herbal remedies include several spices such as black cumin seed, bay leaf, cardamom, poppy seeds, clove and others. Cardamom is the most powerful of these, with anti-oxidant, anti-proliferation, cytotoxic and anti-inflammatory properties that can inhibit cancer cell growth and promote cancer cell death. Cardamom has many anti-cancer activities resulting from its ability to promote effective immune responses. The immunomodulatory effects of cardamom oil along with its anti-microbial and anti-inflammatory properties make it an effective spice remedy for breast cancer treatment [12].

## 2. About Cardamom

### 2.1 Description

Cardamom is also known as the “Queen of Spices” and is the third most-expensive spice behind vanilla and saffron. Commonly known as true or green cardamom, *Elettaria cardamomum* is the dried fruit of a herbaceous perennial plant in the *Zingiberaceae* family [13]. There are two types of cardamom including *Elettaria* and *Amomum*; both have three-sided fruits (pods) with a rough, thin and delicate outer layer. Inside the cardamom, small deep-brown aromatic seeds are arranged in vertical order. *Amomum* pods are larger and dark brown, whereas *Elettaria* pods are small and light green. Cardamom is one of the oldest utilized spices, in use since 4000 BC; it was declared in a list of spices liable to duty in 176-180 AD. Cardamom originates from the evergreen forests of South India and is also grown in Vietnam, Sri Lanka, Cambodia, Guatemala, Papua New Guinea, etc. Nowadays, cardamom is mostly produced in tropical zones (e.g., Guatemala) featuring warm temperatures and significant amounts of rainfall [16]. The major consuming countries of cardamom are Pakistan, Saudi Arabia, Denmark, Norway, Sweden, Russia, England, Japan, Iceland, United States, Germany, and others. In India, Kerala is the main producer of cardamom, responsible for 70% of total cultivation, followed by Karnataka (20%) and Tamilnadu (10%) [17]. The planting period of cardamom cultivation is from August to March, and it is collected approximately every 3<sup>rd</sup> year during the months of October and November. Cardamom grows to a height of 2 to 4m in temperatures ranging from 10 °C to 35 °C, and it is planted at a distance of 9-10 feet between plants. Cardamom is a versatile, multi-purpose spice. It was used in ancient Egypt for its medical properties and even for breast cancer prevention. The pleasant aroma profile is an integral component of cardamom essential oil, the major constituents of cardamom essential oil are 1,8-cineole,  $\alpha$ -terpinyl acetate, pinene, sabinene, myrcene, limonene, phellandrene, terpinene, terpinolene, *p*-cymene, linalyl acetate, linalool, terpinen-4-ol, citronellol, nerol, methyl eugenol, geraniol and trans-nerolidal [14]. These also have therapeutic benefits as an antispasmodic, antiseptic, diuretic, and aphrodisiac. The immunomodulatory action of cardamom oil combined with its anti-microbial and anti-inflammatory properties makes cardamom an effective herb for cancer treatment. Cardamom has been widely used in Ayurveda for its therapeutic and aromatic activities in the treatment of bronchitis, hoarse voice, impotence, vomiting, blood pressure, vomiting, dry lips, arrhythmia,

diarrhea, toothache, and gum bleeding and more [15]. Diindolylmethane and indole-3-carbinol are natural phytochemicals of cardamom that help inhibit cancer-associated processes and regulate hormone activities in breast cancer. Cardamom exhibits chemopreventive and anti-cancer qualities, which have been suggested to significantly reduce the diameter and weight of tumors and papillomas. Other significant bioactive components present in cardamom are limonene, caffeic acid and cineole, which block the activities of cyclooxygenase-2 and cytochrome P450 and downregulate several signal transduction molecules [13]. In recent years, cardamom has been increasingly used as an aromatic spice in Arab, Eastern, and Scandinavian cuisines. Cardamom use has drastically increased since the early 1800s due to its uses in combating infection, freshening breath, and as a digestive aid [18]. *Amomum* is treated as a conventional medical product in China and in Ayurvedic medicine in India, Japan, Vietnam, Pakistan and Korea. In Greece, cardamom was introduced as a digestive medical herb and has also been used in many drinks and recipes for its fragrance and flavor. Various minor problems in humans can be cured with cardamom [28].

### 3. Health Benefits To Prevent and Cure Breast Cancer

Breast cancer is the most common malignancy and second-leading cause of cancer-related death among women in developed and developing countries. This disease begins when cancer cells in the breast begin to divide and grown in an abnormal manner. Breast cancer can be invasive or non-invasive. Most invasive breast cancers initiate in the milk ducts and spread to the surrounding breast tissue. Various factors have been shown to increase or decrease the first incidence of breast cancer, and treatments vary by breast cancer type and stage along with patient health characteristics (e.g., 15-20% of breast cancer cases are now known to be positive for the HER2 oncogene). Careful observation rather than immediate treatment is appropriate for many patients. Treatment often impacts the patient's quality of life due to side effects or complications. Current research is exploring new food-based remedies to prevent cancer and improve the patient's quality of life by reducing unnecessary treatment. A recent research study revealed that cardamom may be effective for treating breast cancer in women. The risk of breast cancer can be reduced with certain precautionary measures. Several different types of breast cancer can be prevented by cardamom, including cribriform, papillary, micropapillary, metaplastic, malignant phyllodes, medullary, mucinous, and tubular. With its anti-inflammatory, proapoptotic and anti-proliferative activities, cardamom is able to reduce the risk of breast cancer [29]. Cardamom extraction significantly improves the cytotoxic anti-cancer activity of natural killer cells and represents a therapeutic tool to regulate the inflammatory response and attenuate carcinogenesis. The chemopreventive activity of cardamom (20 mg/ml) leads to the MCF cell line and the HEP-G2 cancer cell line having reduced cancerous activity [30, 31]. According to data published in the Asian Pacific Journal of Cancer Prevention, cardamom and its compounds can kill cancer cells and impair the growth of new cancer cells, and it can regulate gene expression of factors that control cancer growth. Women show higher rates of breast cancer than men, and middle-aged women have a particularly high risk of breast cancer. Like many other herbal spices, cardamom has powerful effects that show great potential in the treatment of cancer for women. Nuclear Factor Kappa B (NF- $\kappa$ B) is a protein complex that plays a critical role in cell survival, immunity and

inflammation. NF- $\kappa$ B has been shown to promote self-renewal of breast cancer cells in a model of Her2-dependent tumorigenesis. The antimicrobial properties of cardamom inhibit NF- $\kappa$ B by considering the daily diets of cardamom. This inhibition has been shown to reduce effects of carcinogenic oxidation, inflammation, radiation, viral infection, stress and chemotherapy [33]. *In vitro* investigation of the potential immunomodulatory and anti-cancer activities of cardamom showed reductions in the carcinogenic effects of azoxymethan and inhibited breast cancer cell proliferation without disturbing healthy cell proliferation [34]. A 500  $\mu$ g/mg concentration of black cardamom seed oil results in maximum inhibition of Michigan Cancer Foundation (MCF-7) cells, an Estrogen Receptor (ER)-positive cell line that increases abnormal cell growth in monolayers. Cardamom contains phytochemicals such as IC3 and DIM, which support increased production of various white blood cells including natural killer cells and also inhibit hormone-responsive cancer cells (hormone receptor-positive breast cancer) [35]. Cardamom-based therapy has very few side effects and increases levels of the tumor suppressor p53, inhibits tumor proliferation-initiating cells, decreases expression of the metastasis promoter Snail1, and inhibits the epithelial-mesenchymal transition [36]. Extensive research has explored the role of different cardamom species in inhibiting various

breast cancer cell types including ductal carcinoma and lobular carcinoma. Thus, cardamom can destroy breast cancer cells and also shows preventive effects for breast cancer in men, though this disease is less common in men than in women.

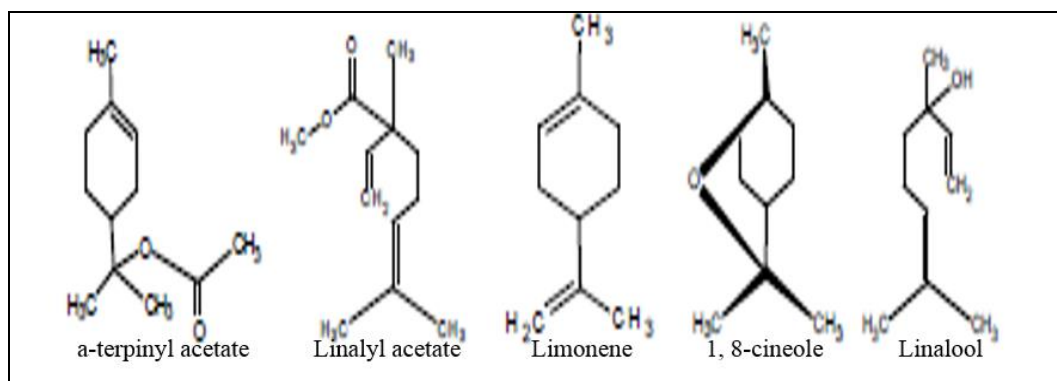
#### 4. Nutritional Profiles

Nutrient profiles are a useful method for assessing the nutritional qualities of cardamom and associated beverages. Cardamom is an excellent source of minerals, iron and vitamins, with high levels of vitamins C, B6, A, riboflavin, thiamin, niacin and pyridoxine; 100 grams of cardamom provides approximately 1,217% of the daily value of manganese, 175% of the daily value of iron and excellent levels of other minerals. Whole cardamom has a strong flavor, and its high vitamin and mineral content can cure breast cancer due to its nutritional and health benefits. It has a low amount of sodium and is free of cholesterol, with levels of potassium that aid in physiology regulation. Cardamom is widely consumed on a regular basis and provides sufficient dietary calories, dietary fiber, carbohydrates, proteins, minerals and vitamins. Below we have listed the nutrient composition of cardamom with the associated percent daily value [37, 38]

Cardamom Components	Percent Daily Value
<ul style="list-style-type: none"> <li>Basic Components</li> </ul>	<ul style="list-style-type: none"> <li>Proteins (11 g) – 19%</li> <li>Water (8.3 g)</li> <li>Ash (5.8 g) – 10.2%</li> <li>Phytosterols (46 mg)</li> </ul>
<ul style="list-style-type: none"> <li>Vitamins</li> </ul>	<ul style="list-style-type: none"> <li>FatiVitamin C (21 mg) – 35%</li> <li>Riboflavin (182mcg) – 14%</li> <li>Thiamin (198 mcg) – 16%</li> <li>Niacin (1.1 mg) – 7%</li> <li>Vitamin B6 (230 mcg) – 68%</li> <li>Vitamin A (0 IU) – 0%</li> <li>Pyridoxine (0.230 mcg) – 18%</li> </ul>
<ul style="list-style-type: none"> <li>Carbohydrates</li> </ul>	<ul style="list-style-type: none"> <li>Total Carbohydrates (68 g) – 52.5%</li> <li>Dietary Fiber (28 g) -70%</li> </ul>
<ul style="list-style-type: none"> <li>Minerals</li> </ul>	<ul style="list-style-type: none"> <li>Calcium (383 mg) – 38%</li> <li>Iron (14 mg)</li> <li>Magnesium (229 mg) – 57%</li> <li>Phosphorus (178 mg)</li> <li>Potassium (1.1 g) – 25%</li> <li>Sodium (18 mg) – 1%</li> <li>Zinc (7.5 mg) – 68%</li> <li>Copper (0.383 mcg) – 42.50%</li> <li>Manganese (28 mg)- 1217%</li> </ul>

*Elettaria cardamomum* naturally contains phenolic compounds characteristic of cardamom ( $\alpha$ -terpinyl acetate (36.8%), linalyl acetate (5.2%), limonene, 1, 8-cineole (29.2%), sabinene (3.9%) and linalool (3.1%)). Several chemical compounds in cardamom (diindolylmethane (DIM)

and indole-3-carbinol (IC3)) prevent the growth of cancer cells including breast cancer cells. Phytochemicals such as cineole and limonene have demonstrated a protective role against cancer progression [39, 40].



**Fig 2:** Cardamom (*Elettaria cardamomum*)

## 5. Clinical Trials

Limited preclinical studies on Ayurveda treatments have shown the efficacy of herbs in the treatment of breast cancer, but the effects of individual herbs and their derivatives are often not well studied or documented. Therapeutic treatments are also poorly studied in some cases due to the difficulties of conducting clinical studies with large cohorts. Due to its massive market value and demand, cardamom's use in health applications is relatively limited. Clinical trials are research studies that evaluate the effectiveness and safety of a treatment by monitoring its effects in a large group people. Since ancient times, people have known about breast cancer. In the 19<sup>th</sup> century it was uncommon because most women died too young to develop severe breast cancer. Breast cancer results from abnormal cell growth and metastasis throughout the body. Frequent and early childbearing and breast-feeding likely reduce breast cancer rates among women who survive to middle age. Mineral and herbal preparations were of particular use in reducing breast cancer mortality rates. Ayurveda methods for breast cancer prevention include particular herbs such as curcumin, ginger, and cardamom. The National Center for Complementary and Alternative Medicine has recommended determining the efficacy of herbs in future clinical studies [43]. According to Ayurveda medicine, breast cancer results from lifestyle factors such as poor hygiene, unhealthy foods, and physical trauma leading to imbalances of vata, kapha, pitta, etc. Cardamom contains limonene, eucalyptol, boneol, terpinene, and camphor, which help ease inflammation. Cardamom has excellent anti-inflammatory activities that help prevent diseases associated with inflammation. As a member of the ginger family, cardamom is beneficial for many health issues. The properties of cardamom include its anti-microbial, anti-inflammatory, anti-oxidant, diuretic & detoxification, anti-depressant, anti-carcinogenic, and anti-spasmodic effects and more. True cardamom, such as *Elettaria cardamom*, and wild cardamom, such as *Amomum Villosum*, are important herbal products with a very high value. *Amomum villosum* is a perennial herb, and 60-70% of its total yield is produced in Xishuangbana in Yunnan Province, China. Studies have shown that 10 $\mu$ L of cardamom essential oil administered for 2 weeks significantly reduces the activity of enzymes associated with xenobiotic metabolism and also inhibits the growth of cancer cells. Cardamom and black pepper given orally at concentrations of 1, 10, 50 and 100mg/mL significantly improve the cytotoxic activity of natural killer cells against Yeast Artificial Chromosome (YAC-1) lymphoma cells [13, 24]. Most of the chemopreventive and phytochemicals identified in spices have dosage levels between 50 and 60  $\mu$ g, and these treatments suppress transcription factors including NF-kB and

AP-1 as well as the enzymes COX-2 and lipoxygenase [41]. Cardamom volatile oil (2-5 mg) was administered for 4 consecutive weeks and suppressed the hepatic carcinogen metabolizing enzymes cytochrome p450, aryl hydrocarbon and glutathione S-transferase and decreased the levels of acid-soluble sulfhydryl. Cardamom oil was given to patients at 10  $\mu$ L per day for 14 days and led to the destruction of DNA adducts via aflatoxin B1 *in vitro* by a microsomal enzyme-mediated reaction [42]. Research on the treatment or prevention of breast cancer using supplements, herbs, vitamins or alternative methods should be given priority at this time. However, cardamom compounds have been studied, as briefly documented in this review, and various associated supplements have been extensively tested in humans. At this point, cardamom remedies may be suitable for use as conventional breast cancer treatments, and this herb also may be used as an alternative approach for the prevention of breast cancer. No research studies have shown the efficacy of using cardamom as a breast cancer treatment, though preliminary studies have indicated that cardamom may contain compounds with activity against cancer cells. The high consumption of cardamom in South Asia has been associated with their low breast cancer incidence. In addition, several varieties of cardamom can confer protection from cancer because they contain potassium. Cardamom oil shows effectiveness in reducing breast cancer cell growth through its anti-inflammatory and anti-cancer effects. Cardamom oil has been shown to reduce breast cancer tumor size by 33% and tumor cell proliferation by 38%. When combined with other herbs such as cinnamon and ginger, cardamom makes a delicious spice that also serves to fight breast cancer.

## 6. Discussion

Cardamom is an important spice that has been traditionally used in Ayurvedic medicine for treating asthma, blood pressure, dysuria, indigestion, etc. Cardamom has several medical properties such as Guna (qualities), Rooksha (dryness), Katu (digestion), and Sheeta (cold potency). A variety of nutritional essential oils in spices such as cardamom have been found effective in the chemoprevention and chemotherapy of cancer. In addition to strong effects of cardamom, it is a good source of nutrients and minerals. The health benefits of cardamom include its anti-inflammatory and antioxidant effects, among others, and it has strong body detoxification properties, something which has mankind for centuries. In Ayurveda, cardamom is known as Tridoshic and is used in balancing human health by the three doshas. Regular consumption of cardamom compounds such as IC3 and DIM can prevent various forms of breast cancer. The essential components of cardamom are manganese, iron, and

potassium, which are found at especially high levels in cardamom. Cardamom regulates multiple cancer-related processes such as cell cycle, hormonal regulation, differentiation, apoptosis, inflammatory responses, DNA repair, and carcinogen metabolism to prevent breast cancer. These cancer-related processes are critical in the initiation and development of cancer in humans. Currently, cardamom aqueous extracts at 1, 10, 50 and 100 mg/mL significantly enhance splenocyte proliferation in a dose-dependent manner. While cardamom has opposing effects on T helper-1 and -2 cytokines released by splenocytes, cardamom spice significantly improved the cytotoxic activity of natural killer cells against YAC-1 lymphoma cells. These results suggest that cardamom may have anticancer benefits by regulating the immune system. In addition, cardamom reduced B ( $\alpha$ ) P-induced for various health issues. Nutritionally, cardamom has excellent manganese content at 80% percent of the recommended daily value and also small amounts of fiber and iron. Cardamom also contains plenty of vitamin C, calcium, potassium, magnesium, and other nutrients. Cardamom seeds are pre-extracted seeds selected from whole green pods. Cardamom phytochemicals are well-known inhibitors of cancer. Cardamom is also able to treat/inhibit different stages of breast cancer, from Stage 0 to Stage 4. Allopathic treatments such as radiotherapy, chemotherapy, hormone therapy are used to diagnose, inhibit and prevent the spread of breast cancer cells. However these treatments are accompanied by major side effects including swelling of the breast, pain in the breast, lymphedema, and changes in breast shape, size and color, etc. Cardamom helps to inhibit/treat breast cancer because it naturally contains cancer-fighting compounds. Cardamom not only inhibits the progression of the disease and reduces tumor size, but it also prevents breast cancer when consumed at the appropriate dosage level. Cardamom has many benefits in Ayurvedic breast cancer treatment, but most people remain unaware of cardamom and its medical effects. In the future, thorough analysis and research studies should increase popular awareness of cardamom. In this paper, we present diverse information about cardamom including its history, essence and its various utilities for treating breast cancer. This review details several clinical trials on different cardamom doses in breast cancer. Previous studies have not focused extensively on these clinical trials. Because of this, the general population does not know the appropriate dosage levels of cardamom for breast cancer treatment. To solve this problem, we can extend our study of clinical trials by consulting a wide variety of researchers, doctors, and scientists.

## 7. Conclusion

Cardamom has been widely used as an herbal supplement in Chinese and Ayurvedic medicine for the treatment of various diseases such as indigestion, headache, depression, cancer and cardiovascular diseases. As such, cardamom helps prevent breast cancer in women by destroying cancerous cells. These studies clearly show that cardamom has a real potential to fight breast cancer by virtue of its antioxidant, anti-inflammatory, antibacterial, immune boosting, and anti-aging effects. The major varieties of cardamom include green cardamom (true cardamom) and black cardamom (brown cardamom). Cardamom contains the powerful antioxidant minerals manganese, copper, and vitamin-C, which prevent cancer formation and help maintain a healthy reproductive system. Cardamom is known as the Queen of Spices, and it

originated in the Asian countries of Nepal, Pakistan, Bhutan and India. Many treatments to prevent and inhibit breast cancer have major painful side effects, whereas natural remedies using spices for treating cancer are free of side effects and pain. This paper provides a detailed description of cardamom including its history, essence and its health benefits for treating breast cancer. The evidence presented in this paper suggests that cardamom spices can cure breast cancer. Cardamom has been used in several countries as a food ingredient and a medicine for different groups of people. This review has primarily concentrated on cardamom for breast cancer treatment. Cardamom spice has shown potential in the treatment of breast cancer. In the future, we can extend our study to concentrate on the effects of cardamom in combination with other spices such as black pepper and ginger. Black cardamom is a perennial herb that provides numerous health benefits, and its anti-oxidative properties help to improve human health, including benefits for the body, skin and hair. Furthermore, in forthcoming reviews we will raise awareness about Ayurvedic treatments for breast cancer because many people are unaware of the health benefits of herbs and spices. In the future, we hope that our expanded review prompts researchers and scientists to focus on cardamom for breast cancer treatment.

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