

PHCOG REV.: Plant Review

Phyto-pharmacology of *Elettaria cardamomum*

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ABSTRACT

Spices are known to add taste, flavor, aroma, color to food. These spices also have been the many traditional medicines in India and elsewhere to provide treatment to various diseases. *Elettaria cardamomum* is one of the spices used in traditional medicines for several diseases. It is used in treating various gastrointestinal, cardiovascular and neuronal disorders. The inhibitory activity of cardamom extract was studied on human platelets has also been reported. This review aims to highlight the ethno botany, pharmacognostic and pharmacological uses of *Elettaria cardamomum*. This review will also highlight the patenting trends and the new compositions developed using the actives from *Elettaria cardamomum*.

INTRODUCTION

Historically known as the “Queen of all Spices”, cardamom has been used in India since ancient times. Dating back to the Vedic period (3000 BCE), there was a mention of the use of this spice in wedding ceremonies. It has been implemented as a digestive aid and as a fat reducer according to Ayurvedic (traditional Indian medicine) texts which dates back to 1400 BCE. Ancient Egyptians used cardamom as a mouth freshener.

The botanical name of the plant is *Elettaria cardamomum* and it belongs to family Scitamineaceae, Zingiberceae. The plant shows much diversity in the size and percentage of the different chemical constituents of the volatile oil in the seeds, and in the geographical area of cultivation.

As a spice, cardamom is used in Indian cuisine for curry, coffee, cakes, bread, and flavoring sweet dishes and drinks. The edible part of the plant is the fruit. The seed and the essential oil are used as a flavoring component in a variety of foods including alcoholic and non-alcoholic beverages, frozen desserts, candy, baked goods, gelatins, puddings, condiments, relishes, gravies, meat, and meat products. The extract of the seeds also finds applications in many pharmaceutical, nutraceutical as well as in cosmetic formulations which are reflected in this review.

ETHNO PHARMACOLOGY

Cardamom is traditionally used in various gastrointestinal, cardiovascular and neuronal disorders. Maharsi Carak has categorized *E. cardamom* as svasahara - anti-asthmatic, angamarda prasamana - relieves body ache and as sirovirecana - useful in cleansing nasal therapy. Cardamom is one the commonly used major constituent in many classical formulations of Ayurveda. Some important classical preparations are Eladiurna, Eladi kvatha, Eladi modak, Eladi vati, Eladyarista, Sitopaladiurna, Aravindasava, Avipattikarnaurna.

Cardamom is used in many parts of the world since ancient times. Many enthopharmacological surveys show that, it is widely used in various parts of the world’s traditional medicine system. In Ethno medical surveys in various tribes of India, it is found that cardamom is commonly used by various

tribes for various diseases like treatment of toothache, (1) to improve liver activities (2) and appetite, to cure the fever (3). It is also used as depurative (4), emmenagogue (5). Cardamom is also used for curing/treating common ailments among children (6). It is also used as antileukaemic crude drug along with many other plants by Ayurvedic Vaidyas, in Rajasthan which is a state in India (7). Cardamom is also one of the medicinal plant in 22 folk prescriptions comprising 33 medicinal plants for treating asthma by tribals and other ethnic groups in India (8). Cardamom is one of the traditional Sikh medicines used by immigrant communities such as the Sikh (Punjabi) British group of informants (9).

In vitro study of antioxidant properties of Indian traditional paan and its ingredients showed that *E. cardamomum* is one of the 22 ingredients (10). Cardamom is also one of the ingredients of Chyawanprash, an ayurvedic formulation which aims at maintaining physique, vigour and vitality, while delaying the ageing process. Cardamom is used in Chyawanprash due to its medicinal properties such as general tonic, useful in anorexia and flatulence (11).

Cardamom is also used as veterinary medicine in ethno medicine practice. In Porbandar, Gujarat, the dry seeds powder of cardamom mixed with clove powder is fed to the animal to help expel the placenta after delivery (12) and is used to treat dysentery and diarrhea in hen in Uttaranchal, India (13).

Cardamom is widely used in folklore, ethno medicine of China, Indonesia and Israel. In Fiji, an essential oil of cardamom is used to cure cold and cough (14). An entire plant of Cardamom is used for treatment of Rheumatism in Indonesia. The fruit of the cardamom is chewed for scratchy tickly cough. The fruits are also used as a remedy for stomach cramps (15). The fruit is used as Calefacient and as an Aphrodisiac in Morocco (16). The fruits of cardamom are used as an Emmenagogue in Vietnam folk medicine (17). In Thailand, dried fruit of the cardamom is used as a CNS stimulant, as a cardio tonic and as antipyretic (18).

In African folk medicine, the herb is used for bad breath (halitosis). It is used for its aphrodisiac effect, has an uplifting effect, helps to clear the mind of noise and

confusion, makes an excellent bath oil providing light, refreshing and stimulating effects. Further when the seeds are chewed they help digestion and also stimulate appetite (19).

PHYTOCHEMISTRY

The active compounds are mainly reported to be present in the fruit of *Elettaria cardamomum* which mainly comprises of the seeds and the fruit coat. The seeds contain significant amount of essential oils which are mainly volatile oils. The volatile oil and other elements of E.C seeds are mainly obtained by supercritical CO₂ extraction (SC_CO₂) (5), solvent-free microwave extraction (SFME) (20), isolation using adsorption on Amberlite XAD-2 (21), capillary gas chromatography (22), thin layer chromatography (23), chromatography on Carbowax 20M column for high boiling fractions and Carbowax 2000 for low boiling fraction (24) and enfleurage method-capillary GC-MS (25). These volatile oils mainly comprises of terpenoids belonging to the class of monoterpenes and sesquiterpenes.

The monoterpenoids are of acyclic, cyclic as well as of bicyclic in nature. The acyclic monoterpenes present in the seed of *E. cardamomum* are linalyl acetate, nerol, neryl acetate, geranyl acetate, geraniol, citronellol, linalool, cis-ocimene and methylheptenone. Figure 1 shows the acyclic monoterpenes present in *E. cardamomum*.

These monoterpenoids and the sesquiterpenoids are known to be the flavor components from the seeds of *E. cardamomum*. Further the chiral analysis of the isolates established that (R)(+)-alpha-terpinyl acetate is the major constituent of cardamom > 99% enantiomeric purity (26). The seeds also include other components such as beta-glucosidase, 3-methylpentan-2-ol, Heptanes, Heptacosane and some unidentified components.

Analysis of the lipid fractions showed that cardamom seeds contained 8.7% glycolipid (GL) and 1.9% phospholipid (PL); cardamom pods had 29.3% GL. In cardamom seeds the PL fraction consisted of cardiolipin (CL), phosphatidylethanolamine (PE), phosphatidyl-N,N-dimethylethanolamine (PE-diME), phosphatidylserine (PS), phosphatidylinositol (PI) and lysophosphatidylcholine (LPC). The sterol components in cardamom seeds were 7-ergosterol and campesterol (27). The mixed fatty acids (83%) of the crude fixed oil contained caprylic and caproic 0.3, palmitic 8.4, stearic 18.3, oleic 62.6 and linoleic acids 10.5%. (28).

The seeds also contain elements such as Mg, Al, Si, P, S, Cl, K, Ca, Ti, Mn, Fe, Cu, and Zn, with varying concentrations (29). The occurrence of a trypsin-like protease in fresh cardamom seeds is also reported as shown by the benzoyl-Arg-p-nitroanilide (BAPNA)-hydrolyzing ability of the seed enzyme under alkaline conditions (30).

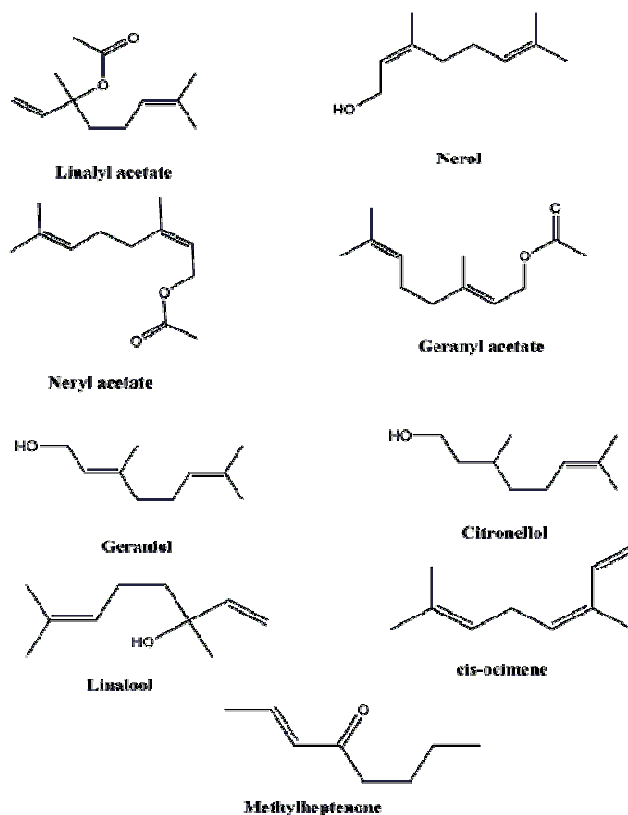
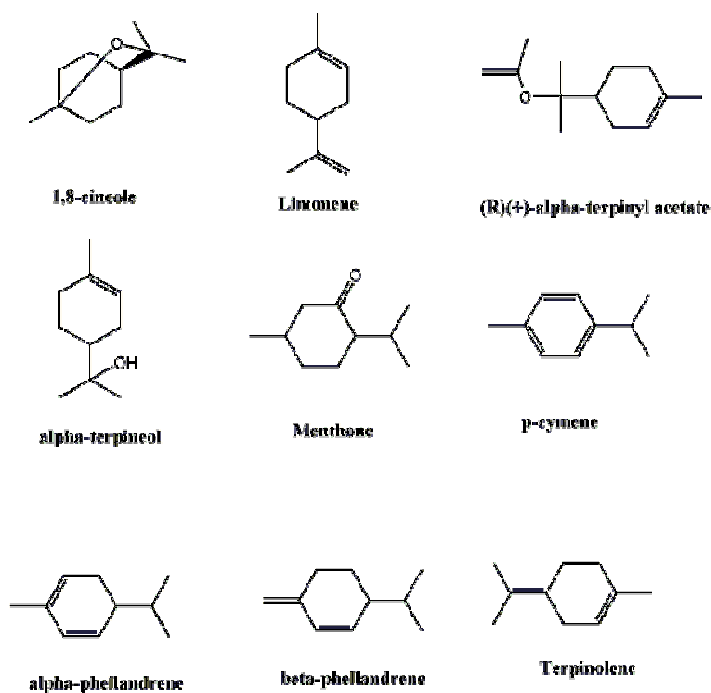
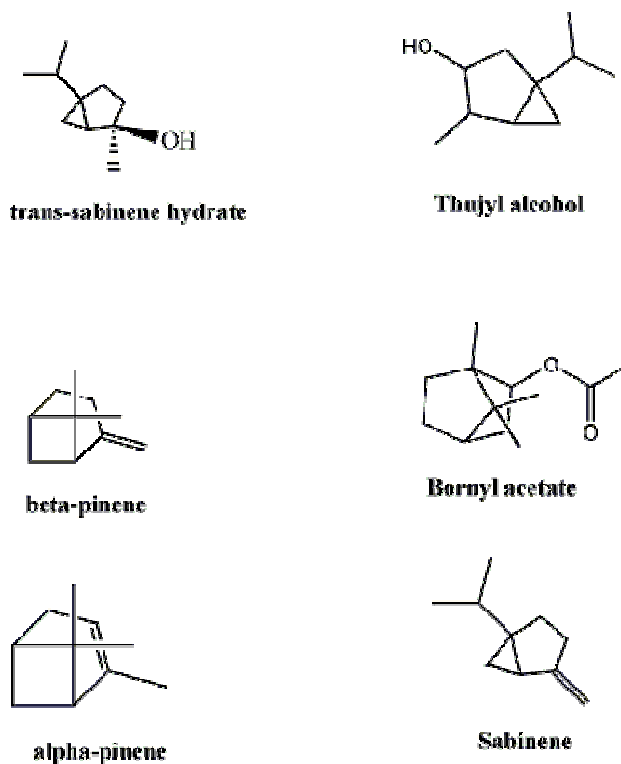


Figure 1: Acyclic Monoterpenes from *E. cardamomum*



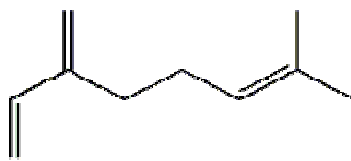
The cyclic monoterpenes present in the seed includes 1,8-cineole, limonene, R)(+)-alpha-terpinyl acetate, alpha-terpineol, menthone, p-cymene, alpha-phellandrene, beta-phellandrene and terpinolene. Figure 2 shows the cyclic monoterpenes present in *E.cardomomum*.

Figure 2: Cyclic Monoterpenes from *E.cardomomum*



The bicyclic monoterpenes includes trans-sabinene hydrate, thujyl alcohol, alpha-pinene, beta-pinene, bornyl acetate and Sabinene. Figure 3 shows the bicyclic monoterpenes present in *E.cardomomum*.

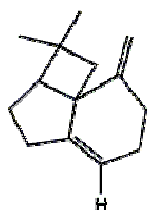
Figure 3: Bicyclic Monoterpenes from *E.cardomomum*



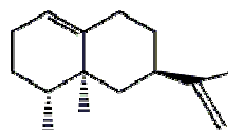
Myrcene

The diterpenoids include only myrcene which is an acyclic diterpene. Figure 4 shows the diterpenoid present in *E.cardomomum*.

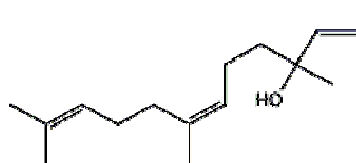
Figure 4 : Diterpenoid from *E.cardomomum*.



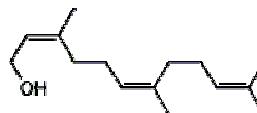
t-caryophyllene



Valencene



Nerolidol



Farnesol

The sesquiterpenoids present in the seeds of *E.cardomomum* include t-caryophyllene, valencene, Nerolidol, farnesol. Figure 5 gives the sesquiterpenoids present in *E.cardomomum*.

Figure 5 : Sesquiterpenoids from *E.cardomomum*

PHARMACOLOGY

The seed extract which mainly contains the essential oils have potential applications as antimicrobial, antibacterial, antioxidant and are also reported to act as efficient skin penetration enhancers for certain drugs. Cardamom is officially listed in the Pharmacopoeia of India. It is also officially listed in the British and U.S. pharmacopoeias and used as an aromatic stimulant, carminative and flavoring agent.

Skin permeation enhancing activity

The essential oils from the seeds of E.C have reported to have good skin permeation activity for certain drugs. The oils from *E.cardomomum* interact with the lipids of the horny layer of the skin resulting in the destruction of the structural order of the skin and thus increase the diffusion capacity of the actives by lipid intercellular pathway. The in vitro study on the permeation of the estradiol (ES) through hairless mouse skin revealed that the complex terpenes are responsible for the transdermal penetration enhancers for moderately

lipophilic drugs like estradiol (31). The in vivo and in vitro studies on the permeation of indomethacin showed that its permeation was significantly enhanced after pretreatment with cardamom oil. This increase in the permeation was mainly due to the presence of cyclic monoterpenes from *E.cardomomum* (32).

Anti-carcinogenetic activity

The oils from *E.cardomomum* exhibited in vitro anti-carcinogenic activity by inhibiting the formation of DNA adducts by aflatoxin B1 in a microsomal enzyme-mediated reaction.(33) This enzymatic modulation may be due to the chemical constituents of the oils which forms the basis for their potential anti-carcinogenic roles. An aqueous extract from *E.cardomomum* also showed protecting effect on platelets from aggregation and lipid peroxidation (34). An aqueous suspension of cardamom has protective effects on experimentally induced colon carcinogenesis (35).

Anti-ulcerogenic activity

The petroleum ether soluble extract from *E.cardomomum* seeds was screened for aspirin-induced anti-ulcerogenic activity in rats. The petroleum ether soluble extract inhibited lesions by nearly 100 percent at 12.5mg/kg (36).

Anti-microbial activity

The extracts from *E.cardomomum* exhibited antimicrobial activity against oral microbes. The essential oils from *E.cardomomum* showed marked inhibitory effects to select pathogenic and spoilage microorganisms. The alcoholic extracts of the plants were found to possess anti-bacterial activity against human pathogenic strain of *Salmonella typhi* (37). *E.cardomomum* is one of the ingredients of the herbal syrup which is found to have antimicrobial action against *E.coli*, *B.proteus*, *Klebsiella* and *Pseudomonas*.

Miscellaneous

The extracts of the seeds of *E.cardomomum* are reported as one of the ingredients in many polyherbal formulations which find applications in treating various diseases. The extract is used as one of the ingredients of the polyherbal formulation for treating dementia of Alzheimer's disease (38). The extract is also used in one of the herbal combination useful in the treatment of anxiety, tension and insomnia (39). An in vivo study of an ayurvedic formulation containing cardamom as one of the ingredients shows that the formulation has CNS-depressant and anti-convulsant activity in mice (40). A multi-ingredient herbal formulation having *E.cardomomum* as one of the ingredients is found to be useful in the treatment of sore throat (41). Cardamom is one of the ingredients of the Tibetan herbal formulation which was found to inhibit cell proliferation accompanied by the accumulation of CEM-C7H2 cells in subG1 phase, fragmentation of poly (ADP-ribose) polymerase (PARP) and nuclear body formation (42).

The volatile oils from *E.cardomomum* are also reported to reduce oedema by increasing the permeation of ion-paired DS across viable skin (43). Eugenol significantly inhibited ($P < 0.001$) tobacco-induced mutagenicity at concentrations of 0.5 and 1 mg/plate. Eugenol and the plant extracts also inhibited the nitrosation of methyl urea in a dose-dependent manner (44). The antispasmodic activity was studied on a rabbit intestine preparation using acetylcholine as agonist. The results from this study showed that cardamom oil exerts its antispasmodic action through muscarinic receptor blockage (45). The extract from the seeds of cardamom also exhibited diuretic properties. (46)

PATENTS ON *E.CARDOMOMUM*

In order to get an overview of the patents filed and granted which specifically claimed *E.cardomomum*, a search was carried out on Derwent Innovation Index (DII) and PAMEP databases. The DII is a patent search as well as analyzing tool which comprehensively covers more than 40 patent offices worldwide. PAMEP (Patents on Aromatic Medicinal and Economic Plants) is a database of patents granted by the various patent offices from all over the world developed by the Department of Biotechnology, India in association with URDIP, India.

The search retrieved about 52 relevant results which claimed *E.cardomomum* for various applications. The set of 52 patent documents were further classified based on the technological

categories to which the invention belongs. These 10 categories include

- Aromatherapy method
- Process
- Health care drinks
- Oral care compositions
- Pesticidal compositions
- Nutraceutical compositions
- Personal care products
- Use of *E.cardomomum* extract as a flavoring agent
- Pharmaceutical (herbal) compositions

The analysis as given in Figure 6 shows that most of the patents filed were on pharmaceutical (herbal) compositions which used the extract of *E.cardomomum* as one of the ingredients in these herbal compositions.

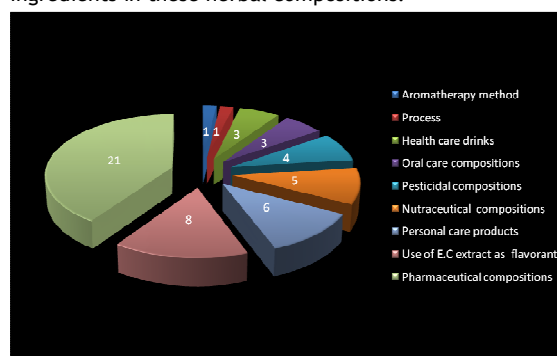


Figure 6: Distribution of the patent documents containing *E.Cardomomum*.

A list of patent numbers and the title containing *E.cardomomum* as part of the claim section of the patent are provided in the Table1.

There are about 21 patent documents disclosing the use of this natural product for the use in compositions for relieving cough, to treat erectile dysfunction, as an antidote to slow and systemic poisoning effects of tobacco, for the treatment of nausea, in pharmaceuticals, essential oil compositions for prophylaxis or treatment of inflammatory diseases by aroma therapy etc. The extract of *E.cardomomum* also finds applications in some of the herbal based cosmetic applications which include skin whitening compositions, anti-dandruff compositions, hair glowing compositions and hair growth compositions. Further the extract from *E.cardomomum* not only finds application as a flavoring agent in foodstuffs but also offer excellent benefits to oral care compositions, nutraceutical compositions, health care drinks and pesticidal compositions.

CONCLUSION

Elettaria cardamomum has been used in India since ancient times as a spice in the Indian cuisine for curry, coffee, cakes, bread, and flavoring sweet dishes and drinks. The plant is mainly cultivated in Indian and Guatemala.

Studies have revealed its use as an effective skin penetration enhancer for certain actives, as an anti-carcinogenetic agent, anti-ulcerogenic agent and anti-microbial and anti-convulsant agent. The extract also finds wide application as an

Table 1: Patent documents related to *E.Cardomomum*

Patent Number	Publication Date	Title
US2008026082	31-Jan-2008	Phytoceutical composition useful to treat erectile dysfunction comprises plants, extracts or active ingredients derived from e.g. Ajuga, Eleutherococcus, Lepidium, Panax, Astragalus, Elettaria, Tribulus, Ginkgo, Serenoa and vitamin E
CN101088394	19-Dec-2007	Preparation of bitter vegetable brine, e.g. for relieving cough, involves cutting and drying bitter vegetable, heating edible oil with scallion pieces, placing in bottle and mixing to vegetable brine, and adding condiments, e.g. pepper
IN200601797	11-May-2007	Herbofizz
US2007087053	19-Apr-2007	Multi-component composition for the treatment of dry mouth, comprises first part that releases sialogogic compound in combination with effervescent organic acid-based buffering system, and second part that releases demulcent compound
IN200700053	2-Feb-2007	Phyto composition for treatment of oral sub mucous fibrosis (OSMF)
IN200402504	17-Nov-2006	Anticigarette herbal formulation as antidote to tobacco
WO2006097447	21-Sep-2006	Use of nicotine-free herbal cigarettes for use in combination with pharmacological nicotine-withdrawal therapy or pharmacological nicotine-substitution therapy
US2006147561	6-Jul-2006	Preparation of herbal nutraceutical product as food supplement for diabetics comprises mixing powdered microwave-roasted seeds from legumes, cereal and pseudocereals and powder or extract of herbs/medicinal plants
IN200400672	02 Jun 2006	Novel refreshing drink
WO2006061848	15-Jun-2006	Composition useful as antidote to slow and systemic poisoning effects of tobacco, comprising dried plant powder/extracts obtained from e.g. Sesbania grandiflora and Catharanthus roseus
US2006110471	25-May-2006	Composition, useful for the treatment of nausea and for providing a calming and soothing feeling, comprises essential oils comprising ginger, spearmint, lavender and peppermint
US2005207982	22-Sep-2005	Aromatherapy delivery system for person or animal e.g. dog, comprises double-layered pouch of vapor-permeable material with sealable opening for inserting aromatherapy sachet materials and opposed securing straps
KR2004099574	02-Dec-2004	Composition of pesticide from plant extracts and compounds to control fowl red mites effectively
US2004219235	04-Nov- 2004	Herbal formulation, useful as a food supplement, comprises legume seed powder, herbs/medicinal plants extract, sugar/jaggery, milk powder, Piper longum and Myristica fragrans fruit powder, Elettaria cardamomum seed powder and coca powder
KR2004064485	19-Jul-2004	Acetylcholinesterase inhibiting crude drug composition
KR2004037396	7-May-2004	Pharmaceutical essential oil composition for prophylaxis or treatment of inflammatory diseases by aroma-therapy and process for preparation
KR2004028481	3-Apr-2004	Composition for controlling Pediculus humanus capitis comprising a plant extract
WO2004056212	8-Jul-2004	Herbal soft drink useful for protecting of liver disorders, comprises extracts of Phyllanthus, Glycyrrhiza glabra, Boerhaavia diffusa, Vitis vinifera, Tinospora cordifolia, Withania somnifera, Elettaria cardamomum and Cinnamomum species
US2004071757	15-Apr-2004	Preventing respiratory infection, e.g. influenza in mammal by contacting live respiratory pathogen at risk of entering respiratory tract with essential oil, such that respiratory pathogen is inactivated upon contact with essential oil
WO2003099110	04-Dec- 2003	Composition useful for treating microbial infection e.g. dental caries and periodontal disease comprises mixture of natural herbs e.g. Phellodendron amurense and medicinal rhubarb root
US2003185913	2-Oct-2003	Herbal health protective, promotive, and disease preventive nutraceutical herbal formulation comprises seed product, and herbs/medicinal plant product(s)
JP2003073224	12-Mar-2003	Melanogenesis inhibitor for use as skin whitening agent, comprises solvent extract of plants e.g. Croton eluteria belonging to Euphorbiaceae, cardamom belonging to Zingiberaceae and/or Anethum graveolens or caraway belonging to Umbelliferae
KR2002025152	3-Apr-2002	Composition containing extract derived from natural products having growth-inhibition activity against dandruff causing microorganism
KR2002089081	29-Nov- 2002	Composition for controlling helicobacter pylori and production thereof
WO2003017784	06-Mar- 2003	Formulation for general health care of e.g. expectant mothers, comprising seeds/seed products of legumes, cereals and pseudocereals and extract of plants of genera Centella, Chlorophytum, Boerhaavia and Sida
WO2003015522	27-Feb-2003	Plant oil and chemical compound having acaricidal activity

JP2001031528	6-Feb-2001	Hair glowing composition containing extract of plant such as <i>Orithosiphon aristatus</i> Bold
CN1249949	12-Apr-2000	Oral Chinese medicine liquid for treating chronic superficial gastritis and its preparation
CN1232685	27-Oct-1999	Composition for the treatment of breast cancer
JP11116492	27-Apr-1999	Melanin formation inhibitor and its use
DE19611078	19-Sep-1996	Use of wormwood, cardamom, rose flowers and/or mastix resin - for treating non-specific intestinal inflammation, especially Crohn's disease.
JP7039312	10-Feb-1995	Chewing gum deodorizing bad breath - has mixture(s) of essential oils, oleoranges and thyme extract
DE3820218	28-Dec-1989	Medicinal plant combinations for depressive syndrome treatment - containing wormwood, cardamom seed and further components
WO8909047	05 Oct 1989	Hair lotion of alcoholic cardamom extract and water - to reinforce and invigorate hair, arrest hair loss and stimulate new hair growth
JP61291515	22 Dec 1986	Cosmetic material containing at least one vegetable extract(s) - used to prevent hot feeling after sunburn, rough skin, etc.
JP58201720	24-Nov-1983	Crude drug-derived cholagogues - having long-lasting activity
JP75009862	16-Apr-1975	Date Palm extract with improved flavor - by mixing dried powder with flavourant and extracting with solvent
CN1054176	4-Sep-1991	Flavoring and preparing process thereof
WO2005070440	4-Aug-2005	Herbal formula for the treatment of allergic asthma (chronic bronchial asthma)
US6881425	19-Apr-2005	Custom made herbal health promotive formulation for females/expectant mothers
US20060153958	13-Jul-2006	Relating to flavor compositions
EP1534252	1-Jun-2005	Breath freshening and oral cleansing product using cardamom oil
IN156003	20-Apr-1985	A process and device for curing green cardamom
IN195060	25-Dec-2004	A process for preparation of the novel herbal medicinal composition useful in treatment of HIV/AIDS
IN194192	2-Oct-2004	Process for producing liquors having aromatic principles resembling musk with a characteristic taste and mouth-feeling
US20060165746	27-Jul-2006	Formulations containing microencapsulated essential oils
WO2006097074	21-Sep-2006	Medicament consisting of plant extracts as a lipase inhibitor
WO2005099473	27-Oct-2005	Cooling composition
WO2005087018	22-Sep-2005	A process for the preparation of a high protein nutritious baked snack food
US20060153959	2-Sep-2004	Flavour compositions
US20060135664	22-Jun-06	Methods and compositions of matter for treatment of cellulose
US20060134341	22-Jun-06	Protection of construction materials from pests

ingredient in formulations for treating dementia of Alzheimer's disease, anxiety, tension, insomnia and sore throat. Patenting trend reveals that the seed extract finds applications in some of the herbal based cosmetic formulations which include skin whitening compositions, anti-dandruff compositions, hair glowing compositions and hair growth compositions. The discovery of the plant bioactives responsible for these applications would lead to newly derived targets finding more applications in cosmetic products.

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