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# DOES THE *'QUEEN OF SPICES'* LIVE UP TO ITS NAME? THE THERAPEUTIC POTENTIAL OF ELETTARIA CARDAMOMUM: A NARRATIVE REVIEW OF CURRENT EVIDENCE AND MOLECULAR MECHANISMS

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**ABSTRACT**

**Background:** Green cardamom is the dried fruit of the herbaceous plant *Elettaria cardamomum*, originating from India. Due to its rich heritage in Ayurvedic medicine, mostly as a respiratory and digestive aid, as well as its distinct flavour, it has been historically known as the „Queen of Spices". Despite its comprehensive pharmacological profile, green cardamom is frequently overshadowed by other functional spices, such as turmeric or cinnamon.
**Purpose:** This narrative review aims to evaluate current evidence on green cardamom's clinical therapeutic efficacy, with emphasis on metabolic, cardiovascular and gastrointestinal health, as well as potential anti-cancer and neuroprotective properties.
**Methods:** A comprehensive review of literature was performed, using databases such as PubMed and Google Scholar. Relevant articles were found, including human clinical trials, animal models, in vitro studies, meta-analyses and systematic reviews.
**Results:** Current evidence suggests that green cardamom's therapeutic effects are primarily mediated through antioxidant and anti-inflammatory pathways. In metabolic and cardiovascular contexts, cardamom consistently improves insulin resistance, endothelial function, triglyceride levels and provides cardioprotection during ischemic events. However, human clinical data regarding its effects on obesity indexes and total cholesterol remain inconsistent. Gastrointestinally, the spice acts as both a spasmogenic and spasmolytic agent and offers protection against gastric ulcers. Oncological research highlights cardamom's selective cytotoxicity, particularly against triple-negative breast cancer. In in vitro and animal models, the spice has shown promising results in management of Alzheimer's disease and anxiety. Furthermore, its essential oil exhibits broad-spectrum antimicrobial activity.

**KEYWORDS**

Green Cardamom, Elettaria cardamomum, Cardiovascular Health, Metabolic Diseases, Anti-Cancer Properties, Anti-Inflammatory Effects

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# 1. Introduction

Do you smell that? Of course you do, as one of the most recognized scents in the world belongs to that of Elettaria Cardamomum, also known under names: green cardamom, small cardamom, or true cardamom. It has for centuries been associated with hospitality and cultural rituals. Its whole seeds, as well as seed powder have various culinary uses, from providing aroma to the famous South Indian masala chai (tea) and traditional Arabic gahwa (coffee) to delivering a defining note in Scandinavian baking. That being said, viewing the Queen of Spice solely through a culinary lens overlooks its profound medicinal applications.

Cardamom originated historically from the evergreen Western Ghats in South India. They were not just mere culinary luxuries but also crucial to ancient pharmacy. Early physicians working within the Ayurvedic, Unani and ancient Greek medical systems made use of cardamom to treat various pathologies. It was traditionally used as a curative treatment method for conditions like asthma, teeth and gum infections, digestive issues and kidney disorders, as well as many others. To this day, chewing on cardamom seeds after meals to freshen ones breath and stimulate digestion, remains a wide-spread habit in many countries.

Today, we understand that these cultural habits were basically a way to incorporate plant compounds into the diets of the general population. The oils of the seeds contain compounds like 1,8-cineole and α-terpinyl acetate. Ancient healers through centuries of clinical observation concluded that it was these compounds that were responsible for cardamom's biological effects. Presently, these substances are known for their antimicrobial and anti-inflammatory effects [2].

Nowadays, Elettaria cardamomum is grown mainly in Guatemala, which is the world's largest exporter, and India (regions of Kerala, Karnataka and Tamil Nadu), which is its native home [12]. The Idukki district in Kerala is the primary hub for small cardamom, accounting for a massive share of India's cultivation, with 80

to 90 percent of the cardamom grown there being consumed domestically. Even though Indian small cardamom is renowned globally for its superior quality, because of high domestic demand India imports cheaper, lower-quality cardamom from Guatemala [1]. The purpose of this narrative review is to bridge the gap between cultural relevance and modern medicine and determine whether *Elettaria cardamomum's* recent scientific evidence aligns with its historical implementations. The focus will be mainly on evaluating cardamom's beneficial effects on cardiovascular and metabolic health, as well as gastroprotective and neuroprotective action. The review will also explore the spice's antineoplastic efficacy and touch on its main molecular mechanisms of action.

## 2. Phytochemistry - Main Chemical Compounds of E.cardamomum

The phytochemical profile of Elettaria cardamomum is a unique composition of macronutrients, minerals, and bioactive secondary metabolites. Proximate analysis reveals that dried cardamom capsules are primarily composed of carbohydrates (approximately 68.2%), followed by proteins (10.6%), fats (2.4%), and ash (5.3%) [3]. The spice is also a rich source of essential minerals, including potassium, phosphorus, magnesium, calcium, sulfur, and iron, along with trace elements like manganese, zinc, and copper [3,4]. Therapeutically, cardamom is highly valued for its non-volatile secondary metabolites, which include tannins, carotenoids (such as lutein and β-carotene), and various flavonoids, most notably quercetin, kaempferol, rutin, myricetin, and catechin [3,5].

### 2.1 Essential Oil

However, the most pharmacologically significant and aromatic constituent of cardamom is its essential oil, which yields between 0.2% and 14% depending on the plant's maturity, processing, and extraction method [3]. The essential oil is mostly composed of oxygenated monoterpenes, with 1,8-cineole (eucalyptol) and α-terpinyl acetate consistently identified as the two major compounds across various studies. Independent analyses revealed concentration of 1,8-cineole ranging between 21% and 45% of the essential oil, whereas α-terpinyl acetate, a monoterpene ester, was found to take up from 26% to 45% of the essential oil. These two predominant phytochemicals are believed to be responsible for the oil's distinct flavor and aroma [3, 5-11]. Furthermore, they have also been found to possess important medicinal activities.

#### 2.1.1 1,8-cineole

1,8-cineole is known to be an effective co-medication in respiratory diseases, such as asthma, COPD, bronchitis or sinusitis, due to its strong anti-inflammatory action, as well as spasmolytic and mucolytic effects. In addition to that, it is a histamine receptor antagonist, thereby preventing histamine-induced smooth muscle contractions [13]. Another study showed that intravenous administration of 1,8-cineole caused a dose-dependant reduction in aortic pulse pressure by vasodilation, suggesting cardiovascular benefits [14]. Moreover, 1,8-cineole has significant efficacy in human lipoprotein metabolism. It prevents low-density lipoproteins (LDL) from oxidation and protects high-density lipoproteins (HDL) from oxidative damage and proteolysis, thus increasing their antioxidant effects. In the hypercholesterolemic zebrafish model, 1,8-cineole was shown to lower serum total cholesterol and triglycerides, decrease lipid accumulation in the liver and reduce inflammatory markers such as serum amyloid A (SAA) and IL-6, solidifying its lipid-lowering and anti-inflammatory activity [15]. According to different studies, 1,8-cineole exhibited gastro-protective effects against ethanol-induced mucosal damage and prominent decline was observed in ethanol-induced gastric injury [8

When it comes to the antimicrobial activity of 1,8-cineole, it demonstrates broad-spectrum antibacterial effects against many pathogens (including Staphylococcus aureus, Escherichia coli, Klebsiella sp., Salmonella sp. and Pseudomonas aeruginosa), as well as antiviral effects [13].

#### 2.1.2 α-terpinyl acetate

The other major phytoconstituent of E. cardamomum seeds, α-terpinyl acetate, shows therapeutic potential in neurological context, particularly Alzheimer's Disease. It has been documented to prevent cholinergic deficits by inhibiting both acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) enzymes. It also inhibits the formation and aggregation of amyloid fibrils, which are responsible for the pathology of Alzheimer's disease, forming plaques in the brain, disrupting neuronal communication and causing cognitive decline. α-terpinyl acetate protects neurons from cell death induced by β-amyloid fibrils and shows anti-oxidant capacity [16].

### 2.1.3 Other bioactive substances

In addition to these primary constituents, the essential oil contains a complex mixture of other monoterpenes and sesquiterpenes in smaller but considerable quantities, including sabinene, α-terpineol, linalool, limonene, myrcene, nerol, 4-terpineol, and α-pinene [3,5,7-9,11]. Furthermore, the fixed oil of cardamom seeds is primarily composed of oleic acid (49.2%), palmitic acid (26.4%), and linoleic acid (15.2%), and it contains health-promoting tocopherols (α, γ, and δ-tocopherol) that act as effective natural antioxidants [3].

## 3. Core Molecular Mechanisms of Action

The therapeutic efficacy of Elettaria cardamomum is deeply rooted in its ability to modulate intracellular antioxidant and anti-inflammatory signaling networks [22,25].

### 3.1 Antioxidant Pathways

Cardamom's constituents act as direct scavengers of reactive oxygen species (ROS) and free radicals, demonstrating neutralizing abilities in DPPH, ABTS, and nitric oxide scavenging assays [44,49]. More importantly, cardamom actively modulates Phase II detoxification enzymes [48]. Supplementation significantly upregulates the activities of vital antioxidant and detoxifying enzymes—including Superoxide Dismutase (SOD), Catalase (CAT), Glutathione Peroxidase (GPx), and Glutathione-S-transferase (GST), while simultaneously increasing levels of reduced glutathione (GSH) [27,48,50]. The effect is restoration of oxidant/antioxidant balance and suppression of oxidative tissue damage, leading to a profound reduction in pathological markers such as lipid peroxidation (measured via malondialdehyde, MDA) and advanced protein oxidation products (APOP) [22,50].

### 3.2 Anti-Inflammatory Pathways

At the core of cardamom's anti-inflammatory mechanism is activation of Sirtuin-1 (SIRT1) and regulation of the Nuclear Factor-kappa B (NF-κB) pathway [25]. Once activated, SIRT1 effectively suppresses the primary NF-κB inflammatory signaling cascade [25,33]. By neutralizing NF-κB, cardamom inhibits systemic release of major pro-inflammatory cytokines [25]. Clinical and experimental models confirm that cardamom significantly downregulates both the gene expression and circulating serum levels of Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), Interleukin-1 beta (IL-1β), and high-sensitivity C-reactive protein (hs-CRP) [25,26,33,50].

Furthermore, cardamom extract reduces the expression and activity of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS), thereby diminishing the synthesis of pro-inflammatory mediators [46]. Another study additionally revealed that cardamom's essential oil constituents (such as eucalyptol, beta-pinene, and geraniol) can directly neutralize pro-inflammatory cytokines like TNF-α and IL-1β [45].

## 4. Therapeutic Potential in Metabolic and Cardiovascular Diseases

### 4.1 Glycemic control and Type 2 Diabetes

The therapeutic potential of Elettaria cardamomum in managing glycemic control and Type 2 Diabetes (T2DM) is primarily driven by its ability to modulate insulin sensitivity and resistance, though its direct impact on fasting blood sugar showed mixed results in human trials. In a 10-week clinical trial involving overweight or obese T2DM patients, a 3g/day supplementation of green cardamom significantly decreased serum HbA1c, fasting insulin levels, and HOMA-IR (an important marker of insulin resistance) compared to a placebo group [17]. This metabolic improvement is believed to be mediated by the activation and elevation of SIRT1, a protein that regulates glucose metabolism, protects pancreatic β-cells, and improves insulin resistance [17,25]. Despite these improvements in insulin functioning, the study noted no significant changes in fasting blood sugar (FBS) levels between the groups [17]. These findings align with an earlier 8-week trial, which also found that 3g/day of cardamom had no significant beneficial effects on FBS, insulin, or HbA1c in T2DM patients [18].

However, cardamom has demonstrated strong glycemic-related effects in other populations suffering from metabolic and insulin-resistant conditions. In overweight or obese patients with non-alcoholic fatty liver disease (NAFLD), cardamom supplementation for three months significantly reduced fasting blood insulin and HOMA-IR, while simultaneously increasing insulin sensitivity (QUICKI) and serum irisin, a myokine known to positively modulate glucose metabolism and insulin functioning [19]. Moreover, when combined with a low-calorie diet in obese women with polycystic ovary syndrome (PCOS), green cardamom significantly

decreased FBS, insulin, HbA1c, and HOMA-IR [20]. On the other hand, a 2-month trial involving overweight pre-diabetic women observed no significant differences in FBS, insulin, or HOMA-IR between the cardamom and placebo groups, demonstrating inconsistency and suggesting that the spice's clinical efficacy may depend on the specific metabolic baseline or duration of the intervention [21].

Animal models strongly support cardamom's role in combatting insulin resistance and glucose intolerance at a systemic level. In high-carbohydrate, high-fat (HCHF) diet-induced obese rats, cardamom powder supplementation successfully improved overall glucose metabolism, diminished glucose intolerance during oral glucose tolerance tests (OGTT), and prevented the increase of tissue oxidative stress that typically impairs pancreatic insulin secretion [22]. Additionally, in animal models, cardamom intake enhanced glucose tolerance during feeding periods, showing improved metabolic flexibility [23]. Another experimental model investigated cardamom's efficacy compared to the standard anti-diabetic drug, pioglitazone, to counteract dexamethasone-induced hyperglycemia and insulin resistance. The study concluded that cardamom demonstrated effects comparable to pioglitazone, especially in preventing dexamethasone-induced fasting hyperglycaemia [24].

### 4.2 Lipid metabolism and obesity

#### 4.2.1 Obesity and anthropometric measurements

The therapeutic efficacy of Elettaria cardamomum in modulating obesity and dyslipidemia is supported by strong experimental evidence, though human clinical trials reveal significant inconsistencies. In human studies, the impact on general obesity indexes is mixed; multiple trials on patients with Type 2 Diabetes (T2DM), non-alcoholic fatty liver disease (NAFLD), and pre-diabetes have reported no significant reductions in body weight or Body Mass Index (BMI) compared to placebos [18,19,21,25]. However, isolated improvements take place, depending on the specific population and intervention model: cardamom significantly decreased waist circumference in pre-diabetic women [21] and, when combined with a low-calorie diet, showed considerable reductions in BMI and overall body fat percentage in obese women with polycystic ovary syndrome (PCOS) compared to diet alone [20].

#### 4.2.2 Lipid profile

Similarly, while animal models consistently demonstrate that cardamom prevents the rise of all major lipid fractions, human data is less uniform [18,19,21]. In humans, the lowering of triglycerides (TG) and low-density lipoproteins (LDL), alongside the elevation of high-density lipoproteins (HDL), are the most consistently observed lipid benefits [18,19]. Cardamom supplementation successfully and significantly lowered triglycerides in a trial of NAFLD patients [19] and in a specific trial of T2DM patients [17]. Additionally, it significantly increased high-density lipoproteins (HDL) in NAFLD patients [19]. However, a separate trial on a different T2DM cohort found no significant differences in TG or HDL compared to a placebo [18], and a trial on pre-diabetic women found that cardamom only prevented a drop in HDL rather than actively increasing it [21].

In contrast, clinical evidence for lowering total cholesterol (TC) and LDL is much weaker. Multiple trials including patients with T2DM [17,18], NAFLD [19], and pre-diabetic cohorts [21], consistently reported no significant reductions in total cholesterol compared to a placebo. Similarly, LDL reductions were absent in T2DM and pre-diabetic trials [17,18,21], although one NAFLD trial noted a borderline significant trend ($p=0.07$) towards lowering LDL [19].

In a recent animal study, effects of cardamom's specific extracted fractions on lipid metabolism have been examined. Cardamom oil significantly reduced blood total cholesterol by 31% and low-density lipoprotein (LDL) cholesterol by 44%. Dietary whole cardamom also decreased total serum cholesterol by 17% and LDL cholesterol by 28%. Cardamom oil supplementation caused a 42% decrease in serum triglycerides, with whole cardamom and de-oiled cardamom lowering serum triglycerides by 24% [27].

#### 4.2.3 Lipid-lowering mechanisms

Despite these macroscopic inconsistencies in clinical trials, cardamom's mechanisms of action on lipid metabolism are well-documented. At the molecular level, the spice's phytochemicals modulate the expression of crucial metabolic genes. In obese women with PCOS, cardamom significantly downregulated the expression of the obesity-associated gene (FTO), the leptin receptor (LEPR), and LAMIN, while upregulating peroxisome proliferator-activated receptor gamma (PPAR-γ), a regulator of lipid storage and metabolism [20].

Additionally, cardamom was proved to influence sterol regulatory element-binding proteins (SREBP-1 and SREBP-2), thus suppressing the endogenous synthesis of cholesterol and triglycerides [21].

Recent animal models highlight cardamom's impact on fat distribution. In animal models of high-carbohydrate/high-fat (HCHF) diet-induced [22] and chemically-induced (dexamethasone) obesity [24], cardamom supplementation successfully prevented abdominal and peritoneal fat deposition, and protected against the development of hepatic steatosis. It achieves this by stimulating lipolysis in subcutaneous and visceral adipose tissues through the increased phosphorylation of hormone-sensitive lipase (HSL), leading to significantly smaller adipocyte size [23].

### 4.3 Hypertension and cardioprotection

#### 4.3.1 Blood pressure and vascular function.

Similar to its effects on lipid fractions and obesity indexes, the impact of Elettaria cardamomum on human blood pressure exhibits notable inconsistencies that seem to be dependent on intervention duration and patient baseline health. In a 12-week study involving newly diagnosed stage 1 hypertensive patients, a 3g/day dose of cardamom significantly decreased systolic, diastolic, and mean blood pressure to near-normal levels [29]. A separate 10-week trial involving patients with Type 2 Diabetes Mellitus (T2DM) also reported a significant decrease in systolic blood pressure compared to a placebo [33]. On the other hand, shorter 8-week trials found that the same 3g/day dosage failed to produce any significant reductions in systolic or diastolic blood pressure in cohorts of T2DM patients [31] and overweight pre-diabetic women [21].

Despite the mixed clinical evidence on blood pressure, cardamom consistently improves vascular and endothelial function in human trials. In T2DM patients, cardamom supplementation significantly increased serum levels of cardioprotective nitric oxide (NO) [33] and significantly decreased the circulating levels of pro-atherogenic adhesion molecules, including ICAM-1, VCAM-1, and E-selectin [11]. It also reduces systemic inflammation by lowering high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) [11,33]. These vascular improvements are attributed to cardamom's polyphenols activating Sirtuin-1 (SIRT1), which enhances endothelial NO synthase (eNOS) and inhibits the NF-κB inflammatory pathway, thereby promoting plaque stability [11,33]. Additionally, cardamom enhances plasma fibrinolytic activity and total antioxidant status in hypertensive patients, and its constituent 1,8-cineole has been shown to effectively inhibit human platelet aggregation [36].

#### 4.3.2 Vasodilation and diuresis

Experimental animal models help clarify the mechanisms driving cardamom's hypotensive potential. In anesthetized normotensive rats, intravenous administration of cardamom extract induces a dose-dependent fall in arterial blood pressure in two ways: it functions as a calcium channel blocker (restricting Ca++ influx) while simultaneously activating endothelial cholinergic (muscarinic) receptors, resulting in active vascular relaxation. Furthermore, cardamom administration caused a significant diuretic effect in experimental models, which complements its vasorelaxant and blood pressure lowering properties [32].

#### 4.3.3 Myocardial Infarction and cardioprotection

Beyond blood pressure modulation, experimental animal models demonstrate structural cardioprotection during severe ischemic events, such as myocardial infarction (MI). In isoproterenol-induced MI models, pretreatment with cardamom prevents the decline of hemodynamic indices and preserves left ventricular function by significantly improving contractility and relaxation, while preventing pathological increases in preload (left ventricular end-diastolic pressure) [35].

At the cellular level, cardamom prevents the decrease of myocardial endogenous antioxidants (such as reduced glutathione, superoxide dismutase and catalase) and inhibits lipid peroxidation (malondialdehyde formation). This mechanism preserves myocyte membrane integrity, significantly reducing the leakage of cardiac injury marker enzymes (CK-MB and LDH) into the bloodstream [35]. Histological and structural examinations confirm these biochemical findings, showing that cardamom prevents myonecrosis, edema, and inflammatory cell infiltration during both chemically-induced MI [35] and surgical coronary artery ligation models [30]. Finally, dietary cardamom has been shown to significantly lower the atherogenicity index and restore protective heart phospholipids in hypercholesterolemic animal model [27], solidifying its role as a comprehensive cardiovascular defender.

# 5. Gastroprotective and Digestive Health Benefits

## 5.1 Gastroprotective Activity and Ulcer Prevention

Cardamom exhibits strong gastroprotective properties, specifically against chemically induced gastric mucosal damage. In experimental rat models, pretreatment with cardamom's methanolic extract, essential oil, and its petroleum ether-soluble fraction significantly inhibited gastric lesions induced by ethanol and aspirin. Notably, in aspirin-induced ulcer models, the petroleum ether fraction inhibited lesions by nearly 100% at extremely low doses (≥12.5 mg/kg), demonstrating a gastroprotective efficacy greater than the standard ulcer drug ranitidine [37]. Interestingly, cardamom does not protect the stomach lining by altering gastric acid levels or mucus wall thickness, nor does it protect against ulcers induced by pylorus ligation [37]. Researchers suggest that the core of its protective mechanism is decreasing gastric motility; while simultaneously inhibiting the overproduction of pro-inflammatory chemicals, like leukotrienes [37].

## 5.2 Dual-Modulatory Effects on Gut Motility

An interesting aspect of cardamom's pharmacology is its unique, dual-modulatory effect on gastrointestinal motility, which justifies its traditional use in treating both hyperactive (diarrhea/colic) and underactive (constipation/dyspepsia) digestive disorders [32].

### 5.2.1 Spasmogenic (Excitatory) Action

The aqueous fractions of cardamom exert a stimulatory effect on the gut mediated through a cholinergic pathway. By functioning as a cholinomimetic and activating M3 muscarinic receptors, it stimulates healthy peristaltic movements, which helps in digestion and relieves constipation [32].

### 5.2.2 Spasmolytic (Relaxant) Action

Conversely, cardamom's essential oil and organic fractions demonstrate strong antispasmodic properties. At a molecular level, cardamom phytochemicals relax smooth muscle contractions by functioning as calcium channel blockers and by inhibiting phosphodiesterase (PDE) enzymes [32,38].

## 5.3 Antidiarrheal and Antimicrobial Efficacy

The spasmolytic mechanisms of cardamom translate directly into already mentioned antidiarrheal effects. In animal models of castor oil-induced diarrhea, oral administration of cardamom essential oil provided significant, dose-dependent protection against diarrheal episodes. Furthermore, cardamom essential oil eases gastrointestinal distress by neutralizing the pathogens that cause it. It exhibits notable bacteriostatic and antibacterial activity against diarrhea-causing Gram-negative bacteria, specifically Escherichia coli and Pseudomonas aeruginosa. Comparative studies note that the Indian variety of E. cardamomum (which has higher concentrations of compounds like α-terpinyl acetate and 1,8-cineole) exhibits stronger antidiarrheal and antimicrobial efficacy than the Guatemalan chemotype [38].

## 5.4 Antiemetic Potential (Nausea and Vomiting)

Beyond the lower gastrointestinal tract, cardamom demonstrates significant clinical potential as an antiemetic, particularly via inhalation aromatherapy. In a randomized, placebo-controlled clinical trial involving mothers undergoing spinal anesthesia for elective cesarean sections, inhaling cardamom essential oil significantly reduced the severity of intraoperative and postoperative nausea. Compared to a saline placebo, cardamom aromatherapy significantly decreased the overall episodes of nausea, which correspondingly reduced the participants' need for postoperative antiemetic medications like ondansetron. However, while highly effective at managing nausea the aromatherapy did not significantly reduce the incidence of actual vomiting compared to the placebo, indicating it may be best used as a complementary intervention alongside standard antiemetic care [39].

## 6. Anticancer and Chemopreventive Properties

The anticancer and chemopreventive potential of Elettaria cardamomum is very complex, producing results through direct cytotoxicity, modulation of critical molecular pathways and systemic immunomodulation.

### 6.1 Selective cytotoxicity and in vitro effects

Cardamom essential oil, its extracts and its isolated bioactive compounds (such as cardamonin) demonstrate evident, dose-dependent cytotoxicity towards specific malignant cell lines while sparing normal healthy cells. In vitro models reveal that cardamom is highly cytotoxic to Triple-Negative Breast Cancer (TNBC) cells (MDA-MB-231 and BT-549) [42,43], human embryonic kidney cells (HEK 293) [42], and human skin cancer cells (A431) [47]. What's worth noticing is that cardamonin selectively induces cell death in TNBC without affecting normal breast epithelial cells (MCF-10A) [43]. Furthermore, recent investigations highlight that aqueous extracts of cardamom pods demonstrate significant concentration-dependent growth inhibition against the human colorectal cancer cell line (HT-29), achieving nearly 72% inhibition at dose of 300 µg/mL [49].

However, cardamom's efficacy seems to be applicable only in specific cancers; it shows weak or negligible direct cytotoxicity against certain glioblastoma (U87-MG) and gastric cancer (MKN-45) cell lines [42,47].

### 6.2 In vivo chemoprevention: Skin and Forestomach Models

Cardamom acts as a powerful "blocking agent" during the initiation phases of chemically induced cancers. In animal models of 7,12-dimethylbenz[a]anthracene (DMBA)-induced skin papillomagenesis and Benzo(a)pyrene (B(a)P)-induced forestomach carcinogenesis, dietary administration of cardamom delayed tumor latency and reduced tumor incidence, multiplicity, and burden by up to 74% [41,48]. This structural protection is achieved by boosting the host's antioxidant and xenobiotic detoxification systems. As mentioned before, cardamom upregulates Phase II detoxification enzymes (Glutathione-S-transferase [GST] and Glutathione peroxidase [GPx]) which neutralize ultimate carcinogenic metabolites like BPDE into excretable forms [48].

### 6.3 Immunomodulatory Anti-Tumor Action

Beyond directly attacking cancer cells, cardamom also strengthens the body's natural immunological defenses against tumors. Cardamom aqueous extracts have been proved to stimulate the cytotoxic activity of Natural Killer (NK) cells. When treated with cardamom, the ability of NK cells to identify and destroy these tumor cells is significantly enhanced in a dose-dependent manner, highlighting a crucial immunomodulatory anti-cancer mechanism [46].

### 6.4 Advancements in Nanomedicine

To maximize bioavailability and targeting, cardamom extract has recently been utilized in the green synthesis of (3-aminopropyl) trimethoxysilane-modified iron oxide nanoparticles (EC-AMIONPs). In mice with induced Ehrlich ascites carcinoma (EAC), these nanoparticles inhibited tumor cell growth by nearly 90%. By generating localized reactive oxygen species combined with the release of cardamom's phytochemicals, the nanoparticles induced mitochondrial dysfunction and autophagy in cancer cells, at the same time successfully restoring normal hematological, hepatic, and renal architecture damaged by the tumor [44].

# 7. Neurological Health

## 7.1 Cognitive Enhancement and Alzheimer's Disease

Elettaria cardamomum demonstrates promising neuroprotective properties, particularly in slowing down cognitive decline and acting against the pathology of Alzheimer's disease (AD) [50,54]. In animal models of both scopolamine-induced amnesia and diabetes-induced AD, supplementation with cardamom extracts successfully reversed spatial learning and memory deficits, which was evidenced by significant improvements in the Morris water maze and passive avoidance tasks [50,54].

There are a couple of mechanisms behind green cardamom's cognitive preservation. Firstly, cardamom has a direct effect on two main protein aggregates, responsible for Alzheimer's disease - the spice significantly reduces accumulation of amyloid-beta (Aβ 1-42) deposits and neurofibrillary tangles of hyperphosphorylated tau protein (p-tau) in the brain [50]. In vitro assays show that the essential oil actively prevents the oligomerization of Aβ42; notably, the full natural extract acts stronger than pure 1,8-cineole in this regard, suggesting that other minor active constituents of cardamom might also add to the anti-amyloid effect [51]. Secondly, cardamom exerts cholinergic effects. Its extract acts as a acetylcholinesterase (AChE) inhibitor, inhibiting the breakdown of acetylcholine [50,54]. Furthermore, it elevates expression of critical glutamatergic receptors—specifically the AMPA GluR1 subunit and NMDA receptor subunits (NR1, NR2A, NR2B)—which are fundamental for learning and working memory [50]. Nowadays, there is increasing evidence of insulin resistance playing an important role in the pathophysiology of Alzheimer's disease, possibly due to abnormal Glycogen synthase kinase-3 beta (GSK3β) activation, causing accumulation of intra- and extracellular amyloid-beta proteins. In animal models with central insulin resistance, cardamom strongly suppressed the activity of GSK-3β, an enzyme implicated in the hyperphosphorylation of tau protein [50].

Last but not least, cardamom alleviates chronic neuroinflammation by lowering hippocampal levels of pro-inflammatory cytokines, specifically TNF-α and IL-1β [50].

## 7.2 Psychiatric Potential: Anxiety and PTSD

Beyond memory retention, cardamom methanolic extract displays anxiolytic activity. In rat models of post-traumatic stress disorder (PTSD) subjected to single prolonged stress, cardamom administration significantly improved anxiety-like behaviors, which was tested in open-field and elevated plus-maze tests [52]. This psychiatric benefit is linked to the plant's rich flavonoid content, particularly quercetin, which is presumed to exert its anxiolytic effects by modulating GABA-A receptors and corticotrophin-releasing factors [52].

# 8. Antimicrobial Action

Elettaria cardamomum exerts strong, broad-spectrum antimicrobial activity against a diverse range of human and foodborne pathogens, including Gram-positive bacteria, Gram-negative bacteria, and multiple fungal strains [6,9,49,58]. While Gram-positive bacteria are generally more sensitive to cardamom due to the lack of the complex lipopolysaccharide outer membrane that acts as a barrier in Gram-negative species [6,58], cardamom essential oils and extracts still show significant lethality against dangerous Gram-negative pathogens like Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, and Campylobacter species [6,38,49,56]. Interestingly, regional varieties differ in strength of their antimicrobial activities; for instance, Indian green cardamom essential oil demonstrates a stronger bactericidal effect against E. coli and P. aeruginosa compared to the Guatemalan chemotype [38].

The main mechanism of cardamom's direct antimicrobial action involves damage of the bacterial cell membrane. Cardamom essential oil changes membrane integrity and permeability, which causes vital intracellular constituents, such as nucleic acids, proteins, and electrolytes, to leak out [56].

Beyond directly killing pathogens, cardamom is highly effective at preventing and eradicating microbial biofilms—dense, extracellular matrix networks, produced by bacteria, that provide protection from antibiotics and host immune defenses [55,57]. Against methicillin-resistant Staphylococcus aureus (MRSA), cardamom essential oil disrupts mature biofilms by neutralizing bacterial metabolic activity and inhibiting initial cell adhesion. It achieves that by suppressing the synthesis of the polysaccharide intercellular adhesin (PIA) and reducing the formation of extracellular polymeric substances [57].

Furthermore, cardamom functions as a powerful anti-quorum sensing (QS) agent, meaning it disrupts the cell-to-cell communication systems that bacteria need to coordinate infections [9]. Even at low concentrations, cardamom inhibits biofilm formation in E. coli O157:H7 and Salmonella Typhimurium by up

to 85% and 100%, respectively [55]. It also heavily suppresses QS-controlled virulence factors in Pseudomonas aeruginosa, significantly decreasing the production of tissue-damaging elastase and protease enzymes [9].

Recent advancements have successfully integrated cardamom's phytochemicals into nanomedicine to fight against multidrug resistance. By using cardamom extract as a stabilizing agent in the green synthesis of (3-aminopropyl) trimethoxysilane-modified iron oxide nanoparticles (EC-AMIONPs), researchers have created bio-functionalized nanoparticles that show improved, broad-spectrum antibacterial and anti-biofilm effects against multidrug-resistant pathogens compared to the extract alone [44].

## 9. Safety and Toxicity

Cardamom's growing worldwide consumption raises questions about its safety. Under normal dietary conditions and intended use as a flavoring agent, cardamom oil is extensively evaluated and considered to be of no safety or toxicological concern [28]. Animal studies confirm its exceptionally low acute toxicity, with oral administration of the essential oil and methanolic extract showing no mortality in mice at doses up to 2000 mg/kg [5,47]. However, high experimental doses of cardamom have been shown to induce significant neurotoxicity; administration of the extract at high concentrations (e.g., 800 mg/kg or 1.5 g/kg) or the essential oil at a dose of 0.75 mL/kg, act as strong skeletal muscle relaxants and anesthetics that cause significant motor impairment and movement toxicity in physical endurance tests [5,52]. Furthermore, in vitro assessments of oral cells show that while cardamom's hydroalcoholic extract is safe for human gingival fibroblasts at low concentrations, the essential oil exhibits significant dose-dependent cytotoxicity against these cells [58].

A major potential health risk associated with cardamom consumption comes not from the plant's endogenous compounds, but from environmental heavy metal contamination [4]. Global market evaluations have identified elevated levels of toxic elements in commercial cardamom depending on its agricultural origin. For example, green cardamom from Bahrain was found to contain the highest cadmium content (0.9 μg/g) among 17 locally tested spices [53]. Similarly, cardamom cultivated in urban agricultural fields in Bangladesh accumulated copper and lead at concentrations exceeding their maximum allowable food safety limits [4]. This implies that excessive consumption of contaminated cardamom seeds could result in exceeding the reference limit of those toxic elements, as well as the target carcinogenic risk thresholds for both adults and children [4], highlighting the need for moderation in the spice's dietary intake as well as careful assessment of the quality of products that enter the market.

## 10. Discussion

The collective findings of this review show that Elettaria cardamomum possesses a unique phytochemical composition. It is a source of bioactive phytochemicals, such as 1,8-cineole, α-terpinyl acetate and cardamonin [3,43], as well as phenolic compounds and flavonoids, that may contribute to the beneficial effects in addressing cardiovascular, metabolic, inflammatory and infectious diseases. Although the molecular mechanisms of its components—especially their ability to modulate antioxidant and anti-inflammatory pathways, primarily through SIRT1 activation and NF-κB suppression [25,33]—present a strong foundation for therapeutic use, the existing clinical studies remain heterogeneous and in some areas, inconclusive.

In metabolic and cardiovascular health, clinical evidence is highly mixed and often inconsistent. While some interventions in patients with Type 2 Diabetes (T2DM), polycystic ovary syndrome (PCOS), and non-alcoholic fatty liver disease (NAFLD) report significant reductions in hemoglobin A1c (HbA1c), fasting insulin, HOMA-IR, and triglycerides (TG) [17,19,20], other trials show no significant differences compared to placebos for fasting blood sugar (FBS), total cholesterol (TC), or low-density lipoproteins (LDL) [17,18,21]. In contrast, experimental animal models consistently demonstrate that cardamom lowers all major lipid fractions, improves glucose tolerance, prevents hepatic steatosis and provides structural cardioprotection during ischemic events [22,27,35].

Regarding blood pressure, there are some inconsistencies in that field too. While 10-week and 12-week clinical trials showed significant decreases in systolic, diastolic, and mean blood pressure [29,33], shorter 8-week interventions often failed to produce a significant hypotensive effects [31], suggesting a future need for longer interventions to be able to draw solid conclusions. Despite that, human trials reliably show that cardamom improves endothelial function by significantly increasing cardioprotective nitric oxide (NO) and decreasing pro-atherogenic adhesion molecules like ICAM-1, VCAM-1, and E-selectin [11,33]. Beyond

metabolic parameters, cardamom demonstrates profound therapeutic potential in other emerging areas, though this is currently limited entirely to pre-clinical evidence:

Oncology: Experimental models confirm strong in vitro cytotoxicity and apoptosis induction—particularly against triple-negative breast, colorectal, and kidney cancers - alongside significant reductions in tumor incidence and burden [42,45,49]. *In vivo* animal models demonstrated how dietary cardamom reduced chemically induced skin and forestomach tumor incidence and multiplicity by up to 74% [41,48]. Furthermore, cardamom-modified iron oxide nanoparticles have been shown to inhibit tumor growth by nearly 90% in animal models [44].

Neurology: Animal models consistently highlight cardamom's efficacy against Alzheimer's disease pathology by inhibiting cholinesterase enzymes and reducing amyloid-beta and tau protein accumulations, while additionally providing notable anxiolytic benefits for psychiatric conditions like PTSD [51,52,54].

Microbiology: Cardamom essential oil consistently acts as a strong, broad-spectrum antimicrobial agent capable of destroying mature pathogen biofilms and inhibiting bacterial quorum sensing to suppress virulence [6,44,46].

Furthermore, despite the spice being generally safe at dietary levels, the potential for heavy metal contamination in commercial cardamom highlights a need for frequent quality controls of dietary products and food safety regulations [53].

## 11. Conclusions

Elettaria cardamomum, widely known as the queen of spices, is a rich source of bioactive phytochemicals—most notably 1,8-cineole and α-terpinyl acetate—that have been proven to provide health-promoting effects, mainly through antioxidant and anti-inflammatory mechanisms. In experimental models, cardamom consistently demonstrates cardioprotective, neuroprotective, gastroprotective, chemopreventive, and broad-spectrum antimicrobial properties, including anti-biofilm and anti-quorum sensing activities. However, human clinical trials present a much more complex picture; while improvements in endothelial function, glucose tolerance and specific lipid fractions like triglycerides are somewhat reliable, the clinical evidence regarding general obesity indexes, total cholesterol, and blood pressure reduction remains rather inconclusive.

There are some limitations to the existing research on green cardamom’s therapeutic efficacy. The reviewed clinical studies differed in intervention periods, study designs and dosages of cardamom.

Those issues emphasize the need for larger clinical trials that would be unified in terms of dosages, duration, and population choice, which would help resolve the contradictory metabolic and cardiovascular outcomes and draw more trustworthy and solid conclusions.

While the experimental efficacy of cardamom in oncological, neurological, and antimicrobial areas is overwhelmingly positive, the complete lack of human clinical evidence in these fields calls for large-scale, standardized, double-blind, placebo-controlled human trials that are required to translate these extensive pre-clinical successes into reliable, evidence-based medical treatments. Finally, exploring advanced delivery systems—such as nano-encapsulation, nanostructured lipid carriers, and nanoliposomes—might be a crucial future direction to maximize the stability, targeted release, and overall clinical efficacy of cardamom's bioactive compounds in clinical settings.

Addressing the existing research gaps will definitively establish cardamom's clinical efficacy and optimal therapeutic application in modern medicine, thereby once and for all solidifying Elettaria cardamomum’s right to the name - „Queen of Spices”.

**Conflict Of Interest:** No conflicts of interest to declare.

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