Botany, traditional uses, phytochemistry and biological activities of cardamom [Elettaria cardamomum (L.) Maton] – A critical review

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ABSTRACT

Ethnopharmacological relevance: Small cardamom [Elettaria cardamomum (L.) Maton, (Family: Zingiberaceae)] capsules (fruits) have been used for traditional medicine applications including for the control of asthma, teeth and gum infections, cataracts, nausea, diarrhea, as well as cardiac, digestive and kidney disorders. The versatile use of cardamom capsules has several other beneficial health effects that are relevant in light of traditional and modern pharmaceutical perspectives.

Aim of the study: This review aims to provide a critical and comprehensive evaluation of the traditional and current medical uses of E. cardamomum, and compare these applications with modern research studies. This critical review also discusses the botanical distribution, phytochemical constituents and biological activities of cardamom capsule extracts and essential oil.

Materials and methods: An online survey was conducted of the traditional uses, phytochemical composition, and pharmacological applications of cardamom essential oil (CEO) and extracts. Pertinent data were obtained from several electronic scientific databases (Science Direct, Elsevier, Web of Science, PubMed, Springer, ACS publications, Taylor and Francis, Wiley On-line Library and Google Scholar), and additional information was obtained from textbooks and local prints and scripts.

Results: Cardamom fruits (capsules) are used widely as a spice and flavoring ingredient in foods, and are often recognized for their beneficial health properties. They are also used in fragrances. Phytochemical analyses have described important chemical constituents of cardamom including carbohydrates, proteins, minerals, lipids, essential oils, flavonoids, terpenoids and carotenoids. CEO has several biological roles including antioxidant, antidiabetic, antibacterial, anticancer, gastro-protective and insecticidal activities.

Conclusion: The widespread availability and recommendation of synthetic compounds for addressing human health have several side effects besides higher costs. Hence, examining natural bioactive compounds is imperative. This review investigates and presents the pertinent information on cardamom and its traditional uses, as well as potential pharmacological properties of CEO and extracts. Additional research studies are needed to understand the mechanism of action of bioactive constituents.

1. Introduction

Elettaria cardamomum (L.) Maton is commonly known as small cardamom, green cardamom, or true cardamom and is grown in India, Guatemala, Sri Lanka, Nepal, Indonesia, Costa Rica, Mexico and Tanzania (Garg et al., 2016). In India, cardamom is cultivated in altitudes ranging from 900 to 1400 m above msl (mean sea level) covering three southern Indian states (Kerala, Karnataka and Tamil Nadu). In Kerala, it is cultivated mainly in the Indian Cardamom Hills covering an area of 1050 square kilometers designated as Cardamom Hill Reserves, (Madhusoodanan et al., 2002). The botanical name of cardamom, Elettaria cardamomum, originated from the Tamil word “Elettari” which refers to the seeds of cardamom (Mahindru, 1982).

In general, the cardamoms are the capsules of dried fruits in different genera of the Zingiberaceae family, primarily Elettaria, Amomum and Aframomum. Among them, Elettaria cardamomum (L.) Maton is most important and is grown predominantly in southern India (Govindarajan et al., 1982). The false cardamom, large cardamom, or black cardamom from the allied genus Amomum is native to Nepal, Sikkim, Bengal and southeast Asian countries. African cardamom, which is botanically known as Aframomum danielli (Hook.f.) K. Schum., is native to south east Africa especially in Tanzania, Cameroon, Madagascar and Guinea.
Small cardamom is extensively cultivated in Nepal and Sikkim and to a limited extent with the large cardamom (Amomum subulatum Roxb.). However, interna-
tively cultivated in Nepal and Sikkim and to a limited extent with
the large cardamom (Govindarajan et al., 1982; Adegoke et al., 1998). Small cardamom is
considered because of high prices. Worldwide, card-
amom is recognized as the “queen of spices” for its pleasant aroma and taste, and is the third most expensive spice after saffron and vanilla.

For centuries, cardamom capsules have been used for culinary and
traditional medicine applications including controlling asthma, teeth
and gum infections, digestive and kidney disorders (Hamzaa et al.,
2012; Saeed et al., 2014), cataracts, nausea, diarrhea and cardiac dis-
orders (Gilani et al., 2008; Khan et al., 2011). The essential oil and
other bioactive metabolites accumulated in cardamom capsules con-
tribute to their characteristic aroma and utility as a functional food,
pharmaceutical, and nutraceutical (Hamzaa et al., 2012). The essential
oil (EO) content of cardamom capsules varies from 6 to 14% depending
upon the type and processing methods (Menon, 2000). EO of cardamom
capsules possess predominantly monoterpenic constituents, such as 1,8-
cineole, α-pinene, α-terpineol, linalool, linalyl acetate and nerolidol
and the ester constituent α-terpinyl acetate (Kaskoos et al., 2006;
Yashin et al., 2017; Ashokkumar et al., 2019b), all of which have
therapeutic benefits including antioxidant, anticancer, antidiabetic,
anti-inflammatory, antifungal, antiviral and gastroprotective activities
(Nirmala, 2000; Marongiu et al., 2004; Hamzaa et al., 2012; Winarsi
e et al., 2014). Recent reports claimed that flavonoids, terpenoids, an-
thocyanins, alkaloids and other phenolic constituents from cardamom
were being used for controlling cardiovascular, pulmonary, kidney and
lung associated disorders (Vaidya and Rathod, 2014). The aim of this
review is to highlight the main phytochemicals and beneficial effects of
cardamom essential oil (CEO) and extracts on human health.

2. Botany

Small cardamom (Elettaria cardamomum L. Maton), belongs to the
Zingiberaceae family. The basic chromosome number x = 12 and
2n = 48 indicates its balanced tetraploid nature (Madhusoodanan
et al., 2002). The habitat and field view of the cardamom plant is shown in
Fig. 1. Cardamom is an herbaceous perennial plant that grows 2–5 m
in height, with underground rhizomes and is propagated by vegetative
division of rhizomes. The aerial stem is formed by encircling the leaf
sheaths. The leaves are 30–35 cm long and 7–10 cm wide, lanceolate
with acuminate tip and dark green in colour. Tillers emerge from the
axils of underground stems. Most of the vegetative buds are produced
during monsoon periods (Murugan et al., 2016). Inflorescences arise
from the rhizomes as a panicle possessing a long cane-like peduncle
having nodes and internodes. Normally, 2–4 panicles emerge from the
swollen base of tillers and certain cultivars have panicles with multiple
branches. Flowers of most cardamom types and varieties are white with
the central lip streaked with pink (Telja et al., 2006). The flowers are
bisexual, irregular and cross-pollination is most common. The labellum
is oval and indistinctly 3 lobed. The calyx is tubular, split about ¼ of its
length on one side and shortly 3 toothed. The corolla is unequally three
lobed with the larger one at the posterior side. The fertile stamen is
united without connective appendages, but prolonged into a short crest.
The crest is positioned above or below the stigma. Anthers are two
lobed, adnate to the filament and dehisce vertically. The size of pollen
gains varies from 75 to 120 μm in diameter. The stigma is funnel
shaped with cilia around a small cavity. The ovary is inferior, trilocular
with axial placental and ovules are numerous in each carpel. An-
thesis typically starts at 3.30 am and continues until 7.30 am, the
maximum pollen bursting occurs between 5.30 am and 6.30 am
(Prameshwar and Venugopal, 1974).

Capsules (fruits) mature completely in about 120 days from flow-
ering. The fruits are ellipsoidal or almost spherical, non-deshiscent,
fluffy and leathery when dry. The fruit colour is green and turns golden
yellow on ripening and is 1–2 cm in length. Depending upon the gen-
otype, each capsule contains 12 to 32 seeds and the ripe seeds are black
and covered with a white mucilaginous coat (Murugan et al., 2016).
Cardamom is highly cross-pollinated and depends on honeybees for
pollination. Cardamom is classified into three types based on the nature
of the panicles namely, Malabar (prostrate panicle), Mysore (erect pan-
icle) and Vazhukka (semi-erect panicle), shown in Fig. 2. The three
cardamom types are briefly described below.

(a) Malabar: This type is well suited for lower elevation of 600–1000 m
above msl (mean sea level) and plants reach 2–3 m height on matura-
ty. Panicles are absolutely prostrate (Fig. 2). This type is rela-
tively less susceptible to thrips and shoot borer infestation. It can
bloom even under low rainfall conditions in Kerala and Tamil Nadu.
Cured capsules are generally round and approximately 18 mm in
length.

(b) Mysore: This type is adapted to elevation ranging from 900 to
1200 m above msl. Plants are robust and attain 3–4 m height on matura-
ty. Panicles are completely erect (Fig. 2). It is best adapted to
regions in Kerala and Karnataka with well distributed rainfall.
Cured capsules are three cornered and ribbed and tend to be slightly
longer than Malabar type, being about 21 mm length.

(c) Vazhukka: This type is a natural hybrid between Malabar and
Mysore types and exhibits intermediate characteristics of both. It is
well adapted to elevations ranging from 900 – 1200 m above msl.
Plants are robust and panicles are semi-erect (Fig. 2). Capsules are
bold, globose or ovoid shape.

A typical photograph of the various botanical features of these three
types including flower types, androecium, gynoecium, panicles, ma-
tured and cured capsules and seeds are presented in Fig. 3.

Fig. 1. Field view and habitat of Elettaria cardamomum (L.) Maton.
3. Traditional uses and ethnopharmacology

Small cardamom capsules have been used since the 4th century BC by Indian Ayurveda doctors and ancient Greek and Roman doctors for treating various health problems such as bronchitis, asthma and constipation (Al-Zuhair et al., 1996; Bisht et al., 2011), cold, cough, diuretic, carminative, teeth and gum infections, urinary and kidney disorders, congestion of lungs, pulmonary tuberculosis, and irritation of eyelids (Jafri et al., 2003; Hamzaa et al., 2012; Saeed et al., 2014), and cataracts, nausea, diarrhea and cardiac disorders (Gilani et al., 2008; Khan et al., 2011). In Chinese traditional medicine, cardamom was used to treat constipation, stomach ache, bladder infections and dysentery in children (Kapoor, 1990; Duke et al., 2003). Cardamom has also been widely used to treat food poisoning in Ayurvedic medicine. Currently, cardamom oils are used in manufacturing of some plant-based hand creams and soaps (Ajmera et al., 2018). Powdered cardamom capsules mixed with pulverized cloves, ginger and caraway have been used for digestive ailments (Govil, 1998). Cardamom powder drink is also an antidote for snake and scorpion venom. The consumption of cardamom capsules reduces inflammation and headaches (Govil, 1998).

Cardamom capsule powder is used for bronchial asthma patients with excess saliva and mucus in the respiratory tract, and as an excellent cough suppressant. Cardamom tablets can be used for controlling cold and related symptoms (Nair and Unnikrishnan, 1997). In Indian traditional medicine, cardamom capsules are considered as excellent digestive and balancing Kapha, mainly in stomach and lungs. Also, it is useful for pacifying Vata dhosa (https://www.mapi.com/ ayurvedic-recipes/spices/cardamom.html). The cardamom seeds are chewed to avoid bad breath, vomiting and indigestion. Cardamom capsules reduce the caffeine constituent in coffee and the combination of cardamom and coffee is called ‘gavah’ which is popular in Arabian culture to relieve headaches and stress. Adding two drops of cardamom
cardamom can be used to maintain healthy skin (http://ayurvedicoils.com/tag/ ayurvedic-health-benefits-of-cardamom-essential-oil). In Tibetan traditional medicine, cardamom capsules are combined with cinnamon and long pepper to treat obesity, glycemic imbalance, liver, kidney and heart diseases (https://www.sowawellness.com/2017/10/07/ cardamom/). Some people believe that drinking macerated seeds in hot water at night has aphrodisiac potential (http://www. agricultureinindia.net/cultivation/cardamom/cardamom-cultivation- varieties-and-uses-spices-agriculture/15625). In Kerala and Tamil Nadu, crushed cardamom capsules are boiled with tea and water to impart a pleasant aroma to tea, which is popularly called “Blakkai tea” and which has been used to relieve tiredness due to over work and depression. Cardamom capsules contain significant concentration of β-carotene (0.5μg g⁻¹), (Ashokkumar et al., 2019a). In traditional medicine, consumption of cardamom daily with a tablespoon of honey improves the eyesight (Singh and Singh, 1996). However, some people believe that excessive uses of cardamom capsules could cause impotency in humans (Nair, 2011).

In Ayurveda, cardamom capsules have been used in many important preparations in the form of powders, oils and decoctions, as well as medicinal fermented beverages like as Arishta and Aasava (Sahadevan, 1965). The cardamom preparation, ‘Eladigana’ is commonly used to cure arthritis, congestion and itching. Intake of cardamom increases urine production. A mixture of medicines known as Aryan kashayam (six grains including cardamom) is used for curing skin diseases in children (Nair, 2011). Huang et al. (1999) examined the effect of cardamom extract on the transdermal-dermal delivery of indometacin and observed that cardamom oil has enhanced the permeation of indometacin significantly in in vitro (rabbit, rat and human) and in vivo (rabbit) situations.

4. Chemical composition

4.1. Proximate and mineral composition

The proximate composition of cured cardamom capsules includes carbohydrate 68.2%, protein 10.6 %, fat 2.4 % and ash 5.3 % (Sontakke et al., 2018). One hundred g of cured capsules contained calcium (93 mg), magnesium (182 mg), potassium (124 mg), phosphorus (183 mg), sulphur (100 mg) and iron (13 mg) (Sontakke et al., 2018; Ereifej et al., 2015; Murugan et al., 2012). These are essential mineral elements for normal day-to-day physiological activities of humans. Cardamom capsules and leaves contain significant levels of manganese, zinc and copper (Table 1). Ashokkumar et al. (2019a) reported nutritionally important metabolites of cardamom capsules that include flavonoids (catechin, myricitin, quercitin and kaempferol) and carotenoids (lutein and β-carotene) (Table 1).

4.2. Cardamom essential oil (CEO) and its composition

The yield of the EO from cardamom varied between 0.2% and 8.7%, on a dry basis, depending on the variety, plant parts and extraction methods used (Table 2). The EO estimation by various methods is summarized in Table 2. The profiling of EO of cardamom seeds sampled from southern India predominantly exhibited 1, 8-cineole (28.94%), α-terpinyl acetate (26.7%), α-terpineol (14.6%), sabine (13.5%), nerol (5.0%) and α-pinene (2.4%), (Ashokkumar et al., 2019b). Sharma et al. (2011) indicated that seeds of cardamom collected across the cardamom growing region of India chiefly contained α-terpinyl acetate, 1, 8-cineole and α-terpineol. The EO of cardamom seeds from Guatemala, which is the global leader in cardamom production, possessed α-terpinyl acetate, 1, 8-cineole, sabine, linalyl acetate and linalool as key constituents (Singh et al., 2008). The characteristic aroma of cardamom capsules and seeds is principally developed by a combination of two major constituents namely 1, 8- cineole and α-terpinyl acetate (Olivero-

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Proximate and mineral composition of dry matter basis of cardamom (Elettaria cardamomum).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximate composition (%)</td>
<td>Capsules</td>
</tr>
<tr>
<td>Carbohydrates (%)</td>
<td>68.2</td>
</tr>
<tr>
<td>Protein (%)</td>
<td>10.6</td>
</tr>
<tr>
<td>Fat (%)</td>
<td>2.4</td>
</tr>
<tr>
<td>Ash (%)</td>
<td>5.3</td>
</tr>
<tr>
<td>Acid insoluble ash (%)</td>
<td>1.76</td>
</tr>
<tr>
<td>Crude fibre (%)</td>
<td>16.3</td>
</tr>
<tr>
<td>Phenols (%)</td>
<td>3.26</td>
</tr>
<tr>
<td>Minerals (mg/100g)</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>92.7</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>188.5</td>
</tr>
<tr>
<td>Sodium</td>
<td>17.0</td>
</tr>
<tr>
<td>Potassium</td>
<td>124.2</td>
</tr>
<tr>
<td>Iron</td>
<td>12.8</td>
</tr>
<tr>
<td>Copper</td>
<td>0.5</td>
</tr>
<tr>
<td>Magnesium</td>
<td>181.5</td>
</tr>
<tr>
<td>Manganese</td>
<td>41.7</td>
</tr>
<tr>
<td>Zinc</td>
<td>3.6</td>
</tr>
<tr>
<td>Sulphur</td>
<td>100.8</td>
</tr>
<tr>
<td>Metabolites (µg/g)</td>
<td></td>
</tr>
<tr>
<td>Flavonoids</td>
<td></td>
</tr>
<tr>
<td>Catechin</td>
<td>281.8</td>
</tr>
<tr>
<td>Myricetin</td>
<td>18.6</td>
</tr>
<tr>
<td>Quercetin</td>
<td>4.9</td>
</tr>
<tr>
<td>Kaempferol</td>
<td>8.7</td>
</tr>
<tr>
<td>Total flavonoids</td>
<td>314.0</td>
</tr>
<tr>
<td>Carotenoids</td>
<td></td>
</tr>
<tr>
<td>Lutein</td>
<td>2.4</td>
</tr>
<tr>
<td>β-carotene</td>
<td>0.5</td>
</tr>
</tbody>
</table>

4.3. Cardamom fixed oil and its composition

The composition of oil from cold pressed cardamom seeds predominantly consisted of oleic acid (49.2 g/100 g of oil), palmitic acid (26.4 g/100 g of oil) and linoleic acid (15.2 g/100 g of oil); these along with other minor fatty acids are shown in Table 4 (modified from Parry et al., 2006). Among the fatty acids, cardamom oil contains 30.8, 51.3 and 17.9 g/100 g of oil of total saturated fatty acids, total mono unsaturated fatty acid and total unsaturated fatty acid, respectively. The fatty acids and their breakdown products have a major role in several...
pathogen defense strategies in plants (Kachroo and Kachroo, 2009). Cardamom oil also contains several forms of tocopherols namely, α-tocopherol (10.4 mg/kg of oil), γ-tocopherol (4.3 mg/kg of oil) and δ-tocopherol (1.6 mg/kg of oil) (Parry et al., 2006). Tocopherols which have vitamin E activity are also commonly found in oils of sunflower, olive, maize and soybean. Tocopherol is an effective antioxidant (Robertsii et al., 2007), and diets containing vitamin E are linked with lower risk of several types of human cancers such as kidney cancer (Shen et al., 2015), lung cancer (Zhu et al., 2017) and bladder cancer (Wang et al., 2014). Additionally, diets rich in tocopherol resulted in a 23% reduction in age related cataracts (Zhang et al., 2015). Therefore, cardamom may play a key role in disease prevention and health promotion.

5. Biological effects of CEO and extracts

The CEO and cardamom extracts have various biological effects including antioxidant, antibacterial, anticancer, insecticidal and other miscellaneous activities that are summarized in Table 5.
Table 5
The activities of cardamom extracts and essential oil components.

<table>
<thead>
<tr>
<th>Pharmacological activities</th>
<th>Study extract/ CEO</th>
<th>In vitro/ In vivo</th>
<th>Target/Model</th>
<th>Control(s)</th>
<th>IC 50/Dosage</th>
<th>Results /Remarks</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibacterial activity</strong></td>
<td>CEO</td>
<td>In vitro</td>
<td>S. aureus</td>
<td>Positive: Amoxicillin and ciprofloxacin</td>
<td>MIC: 6.25 mg/ml MBC: 12.5 mg/ml</td>
<td>Moderate antibacterial activity @ 6.25 mg/ml</td>
<td>Grădinaru et al. (2014)</td>
</tr>
<tr>
<td></td>
<td>1,8-cineole</td>
<td>In vitro</td>
<td>S. aureus</td>
<td>Positive: Amoxicillin and ciprofloxacin</td>
<td>MIC: 1.25–2.5 mg/ml MBC: 2.5 mg/ml</td>
<td>Noteworthy antibacterial activity @ 2.5 mg/ml</td>
<td>Kaushik et al. (2010)</td>
</tr>
<tr>
<td></td>
<td>Aqueous cardamom capsule extract</td>
<td>In vitro</td>
<td>E. coli, S. typhi and S. aureus</td>
<td>Positive: Tetracycline Negative: Distilled water</td>
<td>MIC: 0.5–4.1 mg/ml MBC: 6.25–12.5 mg/ml</td>
<td>Inhibition zone ranged from 12.3 to 20.6 mm with best inhibitory effect against S. aureus</td>
<td>Grădinaru et al. (2014)</td>
</tr>
<tr>
<td><strong>Antifungal activity</strong></td>
<td>CEO</td>
<td>In vitro</td>
<td>Candida spp. and S. cerevisiae</td>
<td>Positive: Amphotericin B Negative: Distilled water</td>
<td>MIC: 0.048–0.097 mg/ml MFC: 6.25–12.5 mg/ml</td>
<td>Inhibition zone ranged from 13.3 to 21.7 mm with best inhibitory effect @ 0.048 mg/ml against Candida parapsilosis</td>
<td>Noumi et al. (2018)</td>
</tr>
<tr>
<td><strong>Cardioprotective activity</strong></td>
<td>Aqueous cardamom capsule extract</td>
<td>In vivo</td>
<td>Wistar male albino rats induced by Isoproterenol</td>
<td>Positive: Isoproterenol (ISO) Negative: Normal Saline</td>
<td>100 mg and 200 mg/kg/ oral for 30 days</td>
<td>Treatment with cardamom extracts (100 &amp; 200 mg/kg) resulted in significant decline of arterial pressure indices, systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP) and myocardial enzymes than control</td>
<td>Goyal et al. (2015)</td>
</tr>
<tr>
<td><strong>Antidiabetic and hypcholesterolemic activity</strong></td>
<td>Ethanol leaf extract</td>
<td>In vivo</td>
<td>Alloxan (120 mg/kg) induced Sprague Dawley diabetic rats</td>
<td>Negative: Normal Saline</td>
<td>Not reported</td>
<td>Oral administration of ethanolic leaf extract for 14 days, decreased blood glucose level from 201.7 to 102.8 mg/dl. However, dose and positive control was not reported, it reducing the reliability of results</td>
<td>Winarsi et al. (2014)</td>
</tr>
<tr>
<td><strong>Antidiabetic activity</strong></td>
<td>Capsule/tablet</td>
<td>In vivo</td>
<td>Eighty overweight or obese patients with type 2 diabetes</td>
<td>Positive: Iritis, and Sirtuin1 (SIRT1) Negative: Distilled water</td>
<td>1 g /3 times/day for 10 weeks</td>
<td>The results of this trial provides clinical evidence on the effectiveness and safety of cardamom supplementation in patients with Type 2 diabetes</td>
<td>Aghasi et al. (2018)</td>
</tr>
<tr>
<td><strong>Anti-obesity and nonalcoholic fatty liver disease (NFLD)</strong></td>
<td>Capsule/tablet</td>
<td>In vivo</td>
<td>Overweight or obese patients with nonalcoholic fatty liver disease (NFLD)</td>
<td>Negative: Placebo</td>
<td>3 g /d for 8 weeks</td>
<td>No significant decrease in systolic and diastolic blood pressure, glycemic indices, and serum lipids values in cardamom and placebo groups. This study also reported that 3 g/day of cardamom would be a large but not unreasonable amount to consume as a part of the diet.</td>
<td>Fatemeh et al. (2017)</td>
</tr>
<tr>
<td><strong>Antidiarrheal activity</strong></td>
<td>Hot water capsule extract</td>
<td>In vivo</td>
<td>Wistar male albino rats induced by magnesium sulphate 4g/kg for 5h</td>
<td>Positive: Magnesium sulphate</td>
<td>10 ml/kg body weight</td>
<td>Cardamom extract showed significant antidiarrhoeal activity against magnesium sulphate in the induced animal model. However, in this study dosage was at an unreasonable high level, and dosage details were not clearly reported, thus reducing the reproducibility of the results</td>
<td>Rahman et al. (2008)</td>
</tr>
<tr>
<td><strong>Antihyperphrogenic activity</strong></td>
<td>CEO</td>
<td>In vivo</td>
<td>Ethanol induced gastric ulcer in rats</td>
<td>Negative: Distilled water</td>
<td>50 mg/kg body weight</td>
<td>Both doses had noteworthy reduction in serum creatinine and urea and LDH activity when compared to corresponding values in the control</td>
<td>Jamal et al. (2006)</td>
</tr>
<tr>
<td><strong>Anticancer activity</strong></td>
<td>CEO</td>
<td>In vivo</td>
<td>Diethylnitrosamine (DENA) induced oxidative stress in rat</td>
<td>Negative: Distilled water</td>
<td>100 and 200 mg/kg/day for 26 weeks</td>
<td>Both doses had noteworthy reduction in serum creatinine and urea and LDH activity when compared to corresponding values in the control</td>
<td>Elguindy et al. (2018)</td>
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</tbody>
</table>

(continued on next page)
5.1. Antioxidant activity

Oxidative stress is a chief factor for induction of several chronic and degenerative diseases such as diabetes, cancer, immune dysfunction and Parkinson’s (Haliwell, 2000; Metodiewa and Koska, 2000). Antioxidants are natural or synthetic compounds that can be used for prevention of free radical formation through scavenging and suppression of chronic and degenerative diseases (Haliwell, 2000). Currently, there is an increasing interest towards natural antioxidants from herbal sources (Larson, 1988; Velioglu et al., 1998). Cardamom capsules and seeds are rich sources of antioxidant substances that neutralize free radicals by preventing oxidation of other components. Nair et al. (1998) reported that cardamom capsules have a moderate level of natural antioxidant properties owing to the presence of phenol compounds such as quercetin, kaempferol and luteolin. Natural antioxidants are thought to be safer than synthetic forms (Saeed et al., 2014). Like phytonutrients and vitamins, EO of cardamom acts as an antioxidant and helps scavenging free radicals, thus reducing cellular ageing (Nanasombat and Wimuttigosol, 2011; Saeed et al., 2014). However, some of the studies of antioxidant activity based on chemical tests including DPHH assays no longer have pharmacological relevance. Their potential under in vitro and in vivo conditions need to be studied for these effects to be considered clinically relevant (Harnly, 2017).

5.2. Anticancer activity

The essential oil of cardamom capsules in in vitro studies showed anticarcinogenic effects by inhibiting damage to adult DNA by aflatoxin B1 in a microsomal enzyme intermediated reaction (Hashim et al., 1994). This might be due to bioactive components present in the essential oil that have potential anticancer roles. Cardamom oil increased the glutathione transferase and acid-soluble sulfhydryl activities and arbitrates the oxidation and detoxification of xenobiotics (Banerjee et al., 1994). Bhattacharjee et al. (2007) reported that the constituents of phytochemicals of CEOs such as 1,8-cineole and limonene demonstrated a protective role against cancer development. Further they said aqueous cardamom extract could improve the activity of the detoxifying enzyme glutathione S-transferase and reduce lipid peroxidation. Elguindy et al. (2016) stated that oral administration of CEO at doses of 100 and 200 mg/kg/day for 26 weeks significantly decreased serum creatinine and urea, and LDH activity in diethylnitrosamine (DENA) induced oxidative stress in rats. Only a few studies have investigated the anticancer potential of cardamom extracts and CEO, and these were conducted in animal models, not in humans. Hence, future investigations should be focused on the bioactivity of CEO in various clinical studies with humans.

5.3. Cytotoxic activity

Cardamom capsule extracts considerably enhanced the cytotoxic effects of natural killer cells and indicated their anticancer potential (Majdalawieh and Carr, 2010). According to Raksamiharja et al. (2012), CEO enhanced the amount of lymphocyte, CD4+ and CD8+ in doxorubicin treated rats in a dose dependent manner. Additionally, Elguindy et al. (2016) reported that cardamom essential oil or geraniol (200 mg/kg) decreased the level of TNF, IL-1 and NF-κB in diethylnitrosamine induced rats. These researchers also showed that CEO was an immune stimulant agent for chemotherapy. Even though the safety of cardamom extracts and CEO was indicated, the use of cell lines based only on in vitro assays limits the pharmacological relevance of this outcome.

5.4. Antimicrobial and antibacterial activity

The EO of cardamom has robust antibacterial effects against various food-borne microorganisms (Kubo et al., 1991). Growth of M. aeruginosa...
morgani was moderately inhibited by the application of cardamom oil (Shakila et al., 1996). CEO (10 mg/ml) showed antibacterial activity against S. aureus, E. coli, S. typhi, Streptococcus mutans and C. albicans (Abdullah et al., 2018), Bacillus subtilis and Listeria monocytogenes (Bano et al., 2016). Hence, CEO could play a vital role in developing safe and novel antibiotics in modern medicine. According to Mejd et al. (2015), CEO has potential broad-spectrum antibacterial and antifungal activities that could be used to prevent damage from food-borne pathogens and food spoilage organisms. The majority of studies focusing on the antibacterial activity of cardamom extracts and CEO have been conducted using the disc diffusion method (Grđinaru et al., 2014; Kaushik et al., 2010), however given its inherent limitations, the method needs to be supplemented by the more relevant MIC assay (Van Vuuren, 2008).

5.5. Insecticidal activity

The development of bioactive constituents that are less persistent will be beneficial to both farmers and the environment. Exploitation of natural products such as EOs are being considered as substitutes to chemical pesticides due to their low toxicity effect on non-target organisms and their lower persistence in the environment. Therefore, EO of cardamom could be used as a stored grain protectant by killing or disturbing various life stages of insect pests (including Sitophilus zeamais and Tribolium castaneum) attacking wheat, through direct interaction and fumigant action (Huang et al., 2000). Chegini and Abbaspour (2017) investigated insecticidal activity of CEO against various stages (egg, 2nd larval instars and adults) of tomato leaf minor (Tuta absoluta) and noticed that CEO has LC_{50} (lethal concentration, 50%) values for eggs, larvae and adult insects of 351.19, 7.88 and 1.55 μL L^{-1}, respectively and observed that CEO has high potential for controlling T. absoluta, particularly under protected situations. Thus far, only one study has investigated the insecticidal activity of CEO, so additional research is required in this promising application.

5.6. Miscellaneous activity

Recently, CEO has been extracted and commercially used in the food industry as a flavoring agent in bread, cakes, curry powder and pickles. Capsules and volatile oils of cardamom are being used as flavoring constituents in various types of foods, including alcoholic and non-alcoholic beverages, frozen desserts, candies, puddings, baked goods, condiments, gravies and meat products. Cardamom oil is also mixed with massage oil, perfumes and lotions, because of its soothing properties (Madhusoodanan et al., 2002).

Three CEO components (α- pinene, β- pinene and α- terpineol) had synergistic effects with 1, 8-cineole and enhanced the penetration of indometacin. Hence, addition of CEO in ointments and lotions increased the absorption of medicines through the skin. Al-Zuhair et al. (1996) observed that CEO has antispasmodic action through receptor blockage, in addition to diuretic properties. Lahhou et al. (2002) assessed the cardiovascular activity of CEO 1,8-cineole in animal experiments and observed intravenous bolus injections of 0.3–10 mg/kg (1,8-cineole) stimulated dose dependent decline in aortic pulse pressure. Elkomy et al. (2015) proposed that the administration of gentamicin along with powdered cardamom at 100 mg/kg and 20 mg/kg had noteworthy protection of rat kidneys.

6. Conclusion

In the present review, we summarize the knowledge on botany, ethnobotanical and traditional uses, phytochemistry and pharmacological activities of E. cardamomum, which has been widely used to treat several illnesses in ancient and modern India. According to the classical Indian medical treatises, E. cardamomum has been traditionally used to treat teeth and gum infections, asthma, nausea, diarrhea, digestive, kidney disorders and others. Over a very long history, E. cardamomum has been demonstrated to be reliable, and now it is important to understand whether modern pharmacological studies on E. cardamomum are available to assess the traditional uses. We demonstrate that some of the modern in vitro and in vivo pharmacological studies have confirmed the traditional use of E. cardamomum.

Based on the currently available information, more than 100 secondary metabolites have been isolated from E. cardamomum, and of these 1, 8-cineole is an most important active compound, which showed antitumor, anti-inflammatory and cardiovascular activities. Furthermore, cardamom extracts and CEO has been extensively explored for their beneficial constituents (Table 5). However, gaps exist in the scientific studies on E. cardamomum, and we have provided recommendations of several topics that should have priority for detailed investigations.

Firstly, based on the currently available phytochemistry reports, the investigations on the structural characterization of metabolites in E. cardamomum capsules are very limited. Thus, in-depth investigations of structural identification and purification of the bioactive metabolites from cardamom is essential.

Secondly, the essential oil of cardamom loses its flavor rapidly upon storing under normal ambience/environment. The change in the aroma or flavor can also cause changes in the constituents of its phytochemicals. Yet very little research has been conducted on maintaining the shelf-life quality of CEO.

Thirdly, insufficient pharmacological studies have been conducted on cardamom. Some biological activity studies were performed using very high dosage concentrations, some were lacking in comparison with standard positive and negative controls, and others lacked determination of MIC values, possibly leading to false positive results.

Fourthly, previous pharmacological investigations were mostly focused on the CEO and organic fractions of crude extracts with little attention on the aqueous extracts; we need to give attention to its traditional usage. Likewise, comprehensive placebo-controlled and double-blind clinical trials are required to evaluate efficacy and safety.

Fifthly, although E. cardamomum possesses various potential therapeutical effects on antioxidant, anti-inflammatory, antidiarrheal, anticancer, cytotoxic and cardio-protective activities, these studies were performed only in animal and cell models and clinical investigations in humans have rarely been implemented. Hence, future investigation should be focused on the bioactivity of CEO in various clinical studies with humans. Such research will benefit future pharmaceutical applications of CEO.

Overall, E. cardamomum appears to be both a nutraceutical and a functional food, with regular consumption of cardamom capsules having potential to protect humans from various chronic diseases. The presence of biologically active molecules such as 1, 8-cineole, α-terpinyl acetate, α-terpineol and sabinene as major components in cardamom oil can serve as a new potential natural source, which can be used in the food, aroma, cosmetics and pharmaceutical domains. In the future, studies are needed on the bioavailability and pharmacokinetics of E. cardamomum to search for the metabolites responsible for its activities. Thus far, the available pharmacological studies are insufficient to assess the ethnobotanical uses. Further research should be conducted to expand the medical application of E. cardamomum.

Author contributions

K.A and M.M conceptualized the manuscript. K.A. wrote the manuscript, M.M. and M.K.D. collected and reviewed the literature on the chemical composition and biological activities. T.W. contributed to the manuscript editing. All authors approved the final version.

Conflicts of interest

The authors have no conflict of interest.
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