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Gut modulatory, blood pressure lowering, diuretic and sedative activities of cardamom

Anwarul Hassan Gilani [a,*], Qaiser Jabeen [a,b], Arif-ullah Khan [a], Abdul Jabbar Shah [a]

[a] *Natural Product Research Division, Department of Biological and Biomedical Sciences, Aga Khan University, Karachi 74800, Pakistan*
[b] *Department of Pharmacy and Alternative Medicine, Islamia University, Bahawalpur, Pakistan*

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Abstract

Ethnopharmacological relevance: Cardamom (*Elettaria cardamomum*) is traditionally used in various gastrointestinal, cardiovascular and neuronal disorders.
Aim of the study: To rationalize cardamom use in constipation, colic, diarrhea, hypertension and as diuretic.
Materials and methods: Cardamom crude extract (Ec.Cr) was studied using *in vitro* and *in vivo* techniques.
Results: Ec.Cr caused atropine-sensitive stimulatory effect in isolated guinea-pig ileum at 3–10 mg/ml. In rabbit jejunum preparations, Ec.Cr relaxed spontaneous and K^+ (80 mM)-induced contractions as well as shifted Ca^{++} curves to right, like verapamil. Ec.Cr (3–100 mg/kg) induced fall in the arterial blood pressure (BP) of anaesthetized rats, partially blocked in atropinized animals. In endothelium-intact rat aorta, Ec.Cr relaxed phenylephrine (1 μM)-induced contractions, partially antagonized by atropine and also inhibited K^+ (80 mM) contractions. In guinea-pig atria, Ec.Cr exhibited a cardio-depressant effect. Ec.Cr (1–10 mg/kg) produced diuresis in rats, accompanied by a saluretic effect. It enhanced pentobarbital-induced sleeping time in mice. Bio-assay directed fractionation revealed the separation of spasmogenic and spasmolytic components in the aqueous and organic fractions respectively.
Conclusion: These results indicate that cardamom exhibits gut excitatory and inhibitory effects mediated through cholinergic and Ca^{++} antagonist mechanisms respectively and lowers BP via combination of both pathways. The diuretic and sedative effects may offer added value in its use in hypertension and epilepsy.

Keywords: *Elettaria cardamomum*; Cardamom; Gastrointestinal motility; Hypotensive; Diuretic; Sedative

1. Introduction

Elettaria cardamomum Maton (cardamom, family; Scitaminaceae) locally known as "elaichi" is a perennial herb, indigenous to India, Pakistan, Burma and Sri Lanka (Nadkarni, 1976). In addition to its wide use for culinary purpose, cardamom has folkloric repute as carminative, stomachic, diuretic, abortificient, antibacterial, antiviral, antifungal and is considered useful in treatment of constipation, colic, diarrhea, dyspepsia, vomiting, headache, epilepsy and cardiovascular diseases (Khan and Rahman, 1992; Duke et al., 2002).

Phytochemical studies revealed the presence of multiple chemicals, such as α-terpineol, myrcene, heptane, subinene, limonene, cineol, α-phellandrene, menthone, α-pinene, β-pinene (Shaban et al., 1987), linalol, nerolidol (Okugawa et al., 1988), β-sitostenone, γ-sitosterol, phytol, eugenyl acetate (Gopalakrishnan et al., 1990), bisabolene, borneol, citronellol, p-cymene, geraniol, geranyl acetate, stigmasterol and terpinene (Duke, 1992).

Cardamom in combination with some other plants was found to reverse the liver damage induced by CCl_4 (Shirwaikar et al., 1992). The aqueous and methanolic extracts of eight Zingiberaceae herbs including cardamom were examined in rabbits for their effect on gastric secretion and the oral administration of either extract caused a significant decrease in gastric secretion and pepsin output (Sakai et al., 1989). In another study, cardamom was found to increase the gastric acid secre-

* Corresponding author. Tel.: +92 21 4864571; fax: +92 21 493 4294, 493 2095.
E-mail address: anwar.gilani@aku.edu (A.H. Gilani).

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tion (Vasudevan et al., 2000). Clinical studies with herbal eye drop preparation containing cardamom was found useful in cases of cataract refractive errors and some infective conditions of the eye (Ghosh et al., 1985; Mukherji and Sahai, 1985; Mitra et al., 1986). Two commonly used Ayurvedic medicines consisting of *Myristica fragrans*, *Syzygium aromaticum* and cardamom exhibited antifertility activity (Sethi et al., 1987). Its volatile oil was found to exhibit analgesic, antiinflammatory, antimicrobial and antispasmodic properties (Al-Zuhair et al., 1996; Elgayyar et al., 2001; Daswani and Bohra, 2003).

In this study, we report that cardamom exhibits combination of spasmogenic, spasmolytic, blood pressure (BP)-lowering, vasodilator, cardio-suppressant, diuretic and sedative activities. The activity-directed fractionation of the crude extract resulted in the separation of gut excitatory and relaxant components in the aqueous and organic fractions respectively.

2. Materials and methods

2.1. Plant material, preparation of crude extract and fractions

Dried fruits of *Elettaria cardamomum* were purchased from a local market in Karachi and the sample voucher (EC-SE-07-04-54) was submitted to the Department of Biological and Biomedical Sciences herbarium, Aga Khan University, Karachi. After cleaning of adulterant material, the fruits were ground with an electric grinder into a coarse powder. Extraction and fractionation was carried out as described previously (Williamson et al., 1998). About 986 g of ground material was soaked in aqueous-methanol (70%) at room temperature (23–25 °C) for 3 days with occasional shaking. It was filtered through a muslin cloth and then through a Whatman qualitative grade 1 filter paper. This procedure was repeated twice and the combined filtrates were evaporated on rotary evaporator under reduced pressure (−760 mmHg) to a thick, semi-solid pasty mass of dark brown color; i.e. the crude extract (Ec.Cr), yielding approximately 10.81%. Ec.Cr was completely solubilized both in the distilled water and saline for use in *in vitro* and *in vivo* experiments.

Activity-guided fractionation was carried out, using solvents of increasing polarity. Ec.Cr was dissolved in 300 ml of distilled water. Petroleum spirit was added to it and shaken vigorously in a separating funnel. The petroleum spirit layer (upper) was collected thrice and evaporated on rotary evaporator to give the petroleum spirit fraction (Ec.Pt). The lower layer was taken in a separating funnel, chloroform was added. The chloroform layer (lower) was collected thrice and evaporated on rotary evaporator to obtain the chloroform fraction (Ec.Cl). The other layer (upper) was again taken into a separating funnel, ethyl acetate was added into it, separated and was also evaporated in rotary evaporator to give the ethyl acetate fraction (Ec.EtAc). The remaining lower layer was collected and evaporated to yield the aqueous fraction (Ec.Aq).

2.2. Phytochemical screening

Preliminary screening of the plant extract for various phytochemical classes was carried out following the reported methods (Harborne, 1984; Akinyemi et al., 2005). Alkaloids were tested by using Dragendorff's reagent. Appearance of yellow color with $AlCl_3$ reagent and green or black with aqueous $FeCl_3$ detects flavonoids and tannins respectively. Plant material treated with petroleum ether and subsequently extracted with $CHCl_3$ was noted for green to pink or pink to purple color after reaction with acetic anhydride and HCl in succession to detect sterols and terpenes respectively. Saponins were detected on the basis of froth upon vigorous shaking. The observation of yellow florescence under UV light on filter paper impregnated with the vapors from boiling extract indicates the presence of coumarins. Benzene extract prepared from acidified plant material was treated with NH_4OH for anthraquinones based on the appearance of pink, violet or red color.

2.3. Drugs and animals

Acetylcholine chloride (ACh), atropine sulphate, furosemide, histamine, pentobarbital sodium, phenylephrine hydrochloride (PE), potassium chloride and verapamil hydrochloride were purchased from Sigma Chemicals Company, St. Louis, MO, USA. Diazepam, pentothal sodium and heparin injections were obtained from F. Hoffmann-La Roche, Basel, Switzerland, Abbot Laboratories, Karachi, Pakistan and Rotex Medica, Trittau, Germany respectively. Chemicals used for making physiological salt solutions were: potassium chloride (Sigma Chemicals Co.), calcium chloride, glucose, magnesium chloride, magnesium sulfate, potassium dihydorgen phosphate, sodium bicarbonate, sodium dihydorgen phosphate (Merck, Darmstadt, Germany) and sodium chloride from BDH Laboratory supplies, Poole, England. All chemicals used were of the analytical grade available. Stock solutions of the drugs were made in distill H_2O/saline and the subsequent dilutions were prepared fresh on the day of experiment.

Animals used in this study such as adult rabbits (1–1.5 kg), guinea-pigs (450–500 g), Sprague–Dawley rats (200–220 g) and Swiss albino mice (20–25 g) of either sex and local breed were housed at the Animal House of the Aga Khan University, maintained at 23–25 °C. Food was withdrawn from rabbits and guinea-pigs 24 h prior to the experiment and rats were deprived of water during the collection of urine. Guinea-pigs were sacrificed by cervical dislocation and rabbits by blow on back of the head. Experiments performed complied with the rulings of the Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council (NRC, 1996) and approved by the Ethical Committee of the Aga Khan University.

2.4. Isolated tissue experiments

2.4.1. Guinea-pig ileum

The guinea-pig abdomen was cut, ileum was dissected out and kept in Tyrode's solution (Gilani and Aftab, 1992). Segments, each of about 2 cm length, were mounted individually in a 10 ml