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Coriander fruit exhibits gut modulatory, blood pressure lowering and diuretic activities

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ABSTRACT

Aim of the study: Coriander (Coriandrum sativum) is traditionally used for various gastrointestinal and cardiovascular disorders and this study was designed to rationalize its use in dyspepsia, abdominal colic, diarrhea, hypertension and as diuretic.

Materials and methods: Coriander crude extract (Cs.Cr) was evaluated through in vitro and in vivo techniques.

Results: Cs.Cr caused atropine sensitive stimulatory effect in isolated guinea-pig ileum (0.1–10 mg/ml). In rabbit jejunum preparations, Cs.Cr evoked a similar contractile response but in the presence of atropine, it exhibited relaxation against both spontaneous and high K+ (80 mM)-induced contractions as well as shifted the Ca2+ concentration–response curves to right, similar to that caused by verapamil. Cs.Cr (1–30 mg/ml) caused fall in arterial blood pressure of anesthetized animals, partially blocked by atropine. Cs.Cr produced vasodilatation against phenylephrine and K+ (80 mM)-induced contractions in rabbit aorta and cardio-depressant effect in guinea-pig atria. Cs.Cr produced diuresis in rats at 1–10 mg/kg. Bio-assay-directed fractionation revealed the separation of spasmogenic and spasmolytic components in the aqueous and organic fractions respectively.

Conclusions: These results indicate that coriander fruit exhibits gut stimulatory, inhibitory and hypotensive effects mediating possibly through cholinergic, Ca2+ antagonist and the combination of these mechanisms respectively. Diuretic activity adds value to its use in hypertension.

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1. Introduction

Coriandrum sativum (coriander; family, Umbelliferae) is a well-known herb, native to Europe and Western Asia and cultivated throughout the world including Pakistan (Azhar and Mazhar, 2003). In addition to its culinary value, coriander is known for its wide range of healing properties. It is generally used in gastrointestinal complaints such as anorexia, dyspepsia, flatulence, diarrhea, griping pain and vomiting (Usmanghani et al., 1997). Coriander fruit is also reputed as refrigerant, tonic, diuretic and aphrodisiac, while, the oil is considered useful in flatulent colic, rheumatism, neuralgia, etc. (Nadkarni, 1976). Coriander is also used as antiedemic, anti-inflammatory, anti-septic, emmenagogue, anti diabetic, anti hypertensive, lipolytic and myorelaxant, and possess nerve-soothing property (Duke et al., 2002).

The plant has been widely studied for its chemical constituents. The fruit of coriander contains anethol, borneol, bornyl acetate, camphor, camphene, carvone, cineole, cymene, coriandrin, dihydrocoriandrin (Ceska et al., 1988), coriandrones A, coriandrones B (Baba et al., 1991), coriandrone C-E (Taniguchi et al., 1996), p-hydroxybenzoic acid, limonene, linoleic acid, myrcene, myristic acid, myristicin, oleic acid, palmitic acid, α-phellandrene, β-phellandrene, α-terpinene, γ-terpinene, terpineol, umbelliferone, etc. (Duke, 1992), α-pinene, β-pinene, quercetin, rutin, sitosterol and stigmasterol (Zlatanov and Ivanov, 1995).

Different studies have proven its efficacy as antidiabetic (Swanson-Flatt et al., 1990), hypolipidemic, antioxidant (Chithra and Leelamma, 1997, 1999) and larvicidal (Consoli et al., 1988). The essential oil from the seeds has been found to possess antimicrobial (Baratta et al., 1998) and antifungal activities (Garg and Siddiqui, 1992). Coriander has been shown to stimulate gastric acid secretion by a cholinergic mechanism (Vasudevan et al., 2000), lower blood pressure (BP) in laboratory animals (Medhin et al., 1986) and cause diuresis (Aissaoui et al., 2008).

Despite the popular medicinal use of coriander, no data are available with respect to its usefulness in gastrointestinal motility disorders and as a botanical diuretic. Mechanisms underlying its hypotension effect are yet to explored. This study on coriander...
fruit extract and resultant fractions was undertaken to investigate the activities and mechanisms mediating its medicinal use in dyspepsia, vomiting, diarrhea, abdominal colic and hypertension.

2. Methods and materials

2.1. Drugs and animals

Acetylcholine chloride (ACh), atropine sulphate, furosemide, norepinephrine bitartrate (NE) and phenylephrine hydrochloride (PE) were obtained from the Sigma Chemical Company, St. Louis, MO, USA. Pentothal sodium and heparin injections were from F. Hoffmann-La Roche, Basel, Abbott Laboratories, Karachi, Pakistan and Rotex Medica, Tittau, Germany respectively. Stock solutions of all the chemicals were prepared in distilled water and the dilutions were made fresh on the day of the experiment.

Balb-C mice (20–25 g), Sprague-Dawley rats (180–200 g) and guinea-pigs (500–600 g) of either sex used in the study were housed in the animal house of Aga Khan University under a controlled environment (23–25 °C). Animals were given tap water ad libitum and a standard diet consisting of (g/kg): flour 380, fibroin 380, molasses 12, sodium chloride 5.8, nutritive L 2.5, potassium metabisulphate 1.2, vegetable oil 38, fish meal 170 and powdered milk 150. For in vitro studies, animals were fasted 24 h before the experiment and were sacrificed by cervical dislocation. All procedures and experimental protocols were approved by the Ethical Committee for Research on Animals (ECRA) at Aga Khan University.

2.2. Plant material, extraction and fractionation

Dried fruits of coriander were purchased from a local market in Karachi, Pakistan. A sample of the coriander fruit was submitted to the herbarium of Natural Products Research Unit at the Department of Biological and Biomedical Sciences, the Aga Khan University, with a voucher no. CS-SE-08-03-52. The ground fruit (1.9 kg) was collected and the remaining aqueous layer were later evaporated to obtain the chloroform (Cs.Cl), ethyl acetate (Cs.EtAc) and aqueous fractions (Cs.Aq) with respective yields of 2.08, 0.43 and 80.84%. The organic fractions were solubilized in 10% di-methyl sulfoxide (DMSO). The aqueous layer was re-extracted with chloroform (upper) was collected. The procedure was repeated thrice and the petroleum spirit layer (lower) was collected. Petroleum spirit was added to it and the mixture was shaken vigorously. The mixture was allowed to separate into two layers and the petroleum spirit layer (upper) was collected. The procedure was repeated thrice and the combined filtrates were evaporated on rotary evaporator under reduced pressure to a thick, semi-solid crude extract. The aqueous layer was re-extracted with chloroform and ethyl acetate in the similar manner. The organic layers so collected and the remaining aqueous layer were later evaporated to obtain the chloroform (Cs.Cl), ethyl acetate (Cs.EtAc) and aqueous fractions (Cs.Aq) with respective yields of 2.08, 0.43 and 80.84%. The organic fractions were solubilized in 10% di-methyl sulfoxide for the experiments.

2.3. Isolated tissue experiments

Isolated tissue experiments were performed following the methods previously employed in our laboratory (Gilani et al., 2005a).

2.3.1. Guinea-pig ileum

Segments of 2 cm length were mounted in 10 ml tissue baths containing Tyrode’s solution, aerated with carbogen and maintained at 37 °C. Isotonic responses were recorded on Harvard student oscillographs. A preload of 1 g was applied to each tissue and kept constant throughout the experiment. Under these conditions, ileum behaves as a quiescent preparation (Gilani and Aftab, 1992). Following an equilibration period of 30 min, isotonic contractions to ACh (0.3 μM) were repeated to stabilize the preparation. Stimulant effect of the extract was determined on the resting baseline of the tissue and was assessed as percent of the maximum effect produced by the control drug, ACh (1 μM).

2.3.2. Rabbit jejunum

To test spasmogenic and spasmolytic activities of the plant material, rabbit jejunal preparations of 2 cm length were mounted in 10 ml tissue baths containing Tyrode’s solution maintained at 37 °C and aerated with 5% carbon dioxide in oxygen (carbogen). The composition of Tyrode’s, in mM, was: KCl 2.7, NaCl 136.9, MgCl2 1.1, NaHCO3 11.9, NaH2PO4 0.4, glucose 5.6 and CaCl2 1.8 (pH 7.4). A preload of 1 g was applied, the tissues kept undisturbed for an equilibration period of 30 min, after which, control responses of ACh (0.3 μM) were obtained and the tissue presumed stable only after the reproducibility of the said responses. Spasmogenic effects of the test material were compared with ACh evoked maximum contractile responses.

2.3.3. Determination of Ca2+ antagonist effect

To assess the presence of calcium channel blocking (CCB) effect as possible mechanism of spasmylytic activity, high K+ (80 mM) was used to depolarize the preparations as described by Farre et al. (1991). Test materials were then added in a cumulative fashion to obtain concentration-dependent inhibitory responses (Van-Rossum, 1963). To confirm the Ca2+ antagonist action of the test substance, the tissue was allowed to stabilize in normal Tyrode’s solution, which was then replaced with Ca2+-free Tyrode’s solution containing EGTA (0.1 mM) for 30 min in order to remove Ca2+ from the tissues. This solution was further replaced with K+-rich and Ca2+-free Tyrode’s solution, having the following composition (mM): KCl 50, NaCl 91.04, MgCl2 1.05, NaHCO3 11.90, NaH2PO4 0.42, glucose 5.55 and EGTA 0.1. Following an incubation period of 30 min, the concentration–response curves (CRCs) of Ca2+ were constructed in the absence and the presence of different concentrations of the test materials.

2.3.4. Guinea-pig atria

Cardiac inhibitory effect of the plant material was studied on spontaneously contracting paired atria from guinea-pigs, mounted separately in 20 ml tissue baths containing Kreb’s solution at 32 °C (unsteady recording at >32 °C) and aerated with carbogen gas. The tissues were allowed to beat spontaneously under a resting tension of 1 g. An equilibrium period of 30 min was given before the application of any drug. Control responses of ACh (0.1–0.3 μM) and isoprenaline (0.1 μM) were obtained at least in duplicate. Tension changes in the tissue were recorded via a Grass force-displacement transducer (model FT-03) using Grass model 7 Polygraph.

2.3.5. Rabbit aorta

To study the effect on vascular resistance, the thoracic aorta ring preparations from rabbit were used. Aortic rings 2–3 mm wide were individually mounted in 20 ml tissue baths containing Kreb’s solution, at 37 °C and aerated with carbogen gas. A resting tension of 2 g was applied to each tissue and an equilibrium period of 1 h was allowed before studying the effect of test materials. The changes in isometric tensions of the rings were measured via a force-displacement transducer (FT-03) using a Grass model
7 Polygraph. PE (1 μM) and K+ (80 mM) were used to induce sustained contractions and the vasodilator effect of the extract was assessed by adding in a cumulative fashion.

2.4. In vivo experiments

2.4.1. Measurement of BP

These experiments were performed on adult rats of either sex as described previously (Ghayur and Gilani, 2005). The animals were anesthetized with intraperitoneal injection of sodium thiopental (Pentothal, 70–90 mg/kg body wt.) and the BP was recorded on Grass model 7 Polygraph through carotid artery cannulation. After a 20 min period of equilibrium, the rats were injected intravenously with 0.1 ml saline (NaCl 0.9%) or with the same volume containing the test substance through jugular vein cannulation. Arterial BP was allowed to return to the resting level between injections. Control responses of standards as ACh (1 μg/kg) and NE (1 μg/kg) were obtained before testing the extract. Changes in BP were recognized as the difference between the steady state values before and the lowest readings after injection. Mean arterial blood pressure (MABP) was calculated as the diastolic BP plus one-third pulse width.

2.4.2. Diuretic effect

Diuretic activity of the plant extracts was studied on Wistar rats of either sex (200–250 g) as described previously (Consolini et al., 1999). Negative and positive control groups comprising of five animals each, received saline and standard diuretic drug: furosemide (10 mg/kg, i.p.), while rest of the groups, with similar number of animals, were given different doses of the plant extracts dissolved in saline (50 ml/kg, i.p.). Subsequently, the animals were placed individually in metabolic cages. The urine was collected in graduated cylinder during 6 h at 1 h intervals. Total urine excreted out was collected and volume was calculated. The pH of the pooled urine from each animal was measured using pH meter.

2.4.3. Acute toxicity

Acute toxicity test of Cs.Cr was done in mice of 18–25 g body wt, kept separately and given food and drinking water ad libitum. Animals were divided in groups of five mice each (Gilani, 1991). The control group of mice was given saline (10 ml/kg) p.o. while other groups received increasing doses of the extract up to 10 g/kg. Observations were made closely for 2 h, then at 30 min intervals for 6 h, and then mortality was noted at 24 h.

2.5. Data analysis

The data are expressed as mean ± standard error of mean (S.E.M., n = number of experiments) and the median effective concentrations (EC50 values) with 95% confidence intervals (CI). Statistical analyses were performed with GraphPad program (GraphPAD, San Diego, CA, USA). For comparison between the groups, either one-way analysis of variance (ANOVA) followed by post hoc Dunnett’s test or Student’s t-test was used (Dawson-Saunders and Trapp, 1990). p < 0.05 was considered statistically different. CRCs were analyzed by non-linear regression (GraphPAD program).

3. Results

3.1. Effect on ileum

The crude plant extract caused a dose-dependent (1.0–10.0 mg/ml) spasmogenic effect in guinea-pig ileum (Fig. 1). The maximum contractile effect was 72.3 ± 5.78% (mean ± S.E.M., n = 5) of ACh maximal response and was completely blocked when tested in the presence of atropine (1 μM). Pretreatment with atropine (1 μM) completely blocked the contractile responses of Cs.Cr similar to that of ACh but did not affect histamine responses (data not shown).

3.2. Effect on jejunum

In the spontaneously contracting rabbit jejunum preparations, Cs.Cr produced contractions at the concentration range of 0.3–10 mg/ml (Fig. 2), followed by relaxation at the higher dose. The contractile effect was abolished in the presence of atropine (0.03 μM), similar to that of ACh, and the relaxant effect became more prominent with EC50 values of 2.24 mg/ml (1.18–4.25, 95% CI). Cs.Cr also relaxed high K+ (80 mM)-induced contraction (Fig. 3A) with EC50 value of 1.677 mg/ml (1.11–2.54), similar to verapamil (Fig. 3B) and shifted the Ca2+ concentration–response curves in a
3.3. Effect on BP

Intravenous administration of the aqueous-methanolic extract of coriander (Cs.Cr) produced a dose-dependent (1-30 mg/kg) fall in both systolic and diastolic blood pressure in normotensive rats under anesthesia (Fig. 5), with a maximum effect of 40.84 ± 6.34% (n = 5). Pretreatment of the animals with atropine (1 mg/kg) caused a partial blockade of the BP lowering effect.

3.4. Effect on atria

Cs.Cr caused concentration-dependent (0.3–5.0 mg/ml) inhibitory effect when tested on isolated paired atria (Fig. 6). Maximum inhibitory effect on atrial force of contractions was 53.82 ± 7.55% (n = 5) of the baseline value. Pretreatment of the tissues with atropine (1.0 µM) abolished inhibitory effect of ACh (0.3 µM) but partly diminished the effect of Cs.Cr. Reduction in atrial rate of contraction was also observed in an initial experiment by increasing the speed of recording chart paper (data not shown) but only ionotropic effect was studied in subsequent experiments as the existing experimental setup did not allow simultaneous recordings of heart rate.

3.5. Effect on aorta

When tested against PE (1 µM) and high K+ (80 mM)-induced contractions, Cs.Cr produced concentration-dependent vasodilator
Fig. 6. Tracing showing the concentration-dependent inhibitory effect of Cs.Cr on atrial force of contraction in the absence and the present of atropine (n=5).

Fig. 7. Concentration–response curves showing vasodilator effect of (A) Cs.Cr and (B) verapamil on K⁺ (80 mM)- and phenylephrine (PE, 1 μM)-induced contractions. The symbols represent mean ± S.E.M. (n=5).

effect (Fig. 7A) with respective EC₅₀ values of 0.42 (0.36–0.49) and 2.53 mg/ml (2.02–3.17), qualitatively similar to that of verapamil with 1.53 (0.87–2.69) and 0.89 μM (0.53–1.48) respectively (Fig. 7B).

3.6. Diuretic effect

Urine output/100 g body wt./6 h in saline treated group was 4.39 ± 0.08 ml while furosemide (10 mg/kg) increased it to 8.29 ± 0.17 ml (p < 0.0001). In groups treated with Cs.Cr, a mild increase in the urine output was observed at the dose of 30 mg/kg (5.1 ± 0.60 ml), while a significant diuretic effect (p < 0.01) was caused by the dose of 100 mg/kg (6.47 ± 0.44 ml). An increase in the urine volume was evident within 1 h of administration of furosemide, while the onset of diuretic effect was 3–4 h with Cs.Cr. The pH remained unchanged (pH 6.2–6.6) for all the urine samples.

3.7. Effect of fractions

The aqueous fraction (Cs.Aq) was devoid of any effect on spontaneously contracting rabbit jejunum but produced a dose-dependent (1–10 mg/ml) spasmodic effect in guinea-pig ileum (a quiescent preparation) comparable to the maximum response of ACh (Fig. 1). Pretreatment of the tissue with atropine (1 μM), inhibited the stimulant effect of Cs.Aq similar to ACh but did not alter the tissue response to histamine (data not shown).

Intraperitoneal administration of Cs.Aq caused dose-dependent diuretic effect in rats (Fig. 8B). Total urinary output/100 g body wt. within 6 h of administration of 30 and 100 mg/kg of Cs.Aq was 5.73 ± 0.34 ml (p < 0.01 vs. saline) and 6.52 ± 0.33 ml (p < 0.001 vs. saline).

None of the organic fractions (Cs.Pet, Cs.Cl and Cs.EtAc) exhibited contractile effect in gut preparations but caused dose-dependent relaxation of spontaneous contractions in rabbit jejunum (Fig. 9A) with respective EC₅₀ values of 1.74 mg/ml (1.29–2.33), 0.44 mg/ml (0.31–0.63) and 0.24 mg/ml (0.19–0.31) and K⁺ (80 mM)-induced contractions at 1.57 mg/ml (1.04–2.36), 2.15 mg/ml (1.28–3.58) and 0.86 mg/ml (0.55–134) respectively (Fig. 9B). Diuretic effect was not caused by any of the organic fractions.

3.8. Acute toxicity

Cs.Cr showed no acute toxicity when given orally up to a dose of 10 g/kg. All animals showed no convulsions or writhing, and reflexes like rightening reflex and corneal reflex remained present.

4. Discussion

In view of its well-known use as carminative, the crude extract of coriander (Cs.Cr) was studied on gut preparations for the possible stimulatory effect. When tested on guinea-pig ileum, Cs.Cr caused a dose-dependent excitatory effect, like that caused by ACh and histamine. Pretreatment of the tissue with atropine, a muscarinic receptor antagonist (Arunlakhshana and Schild, 1959) blocked the stimulatory effect of Cs.Cr, similar to that of ACh but did not alter the histamine responses, indicating that coriander causes gut stimulation via cholinergic pathway. ACh is a neurotransmitter released by the parasympathetic nervous system, mediates its action in gut by activation of M₃ muscarinic receptor subtypes and hence plays an important physiological role to regulate the peristaltic movements of gut (Brown and Taylor, 1996). Coriander is previously reported to stimulate the gastric acid secretion through cholinergic mechanism (Vasudevan et al., 2000). This study explains the use of coriander...
in disorders resulting from delayed gastrointestinal transit including anorexia, indigestion, flatulence and vomiting (Tatsuta and Iishi, 1993), as well as confirms the previous findings. 

Coriander has been used in overactive gut disorders such as abdominal spasm and diarrhea. To see whether it also contains some spasmylotic constituents, Cs.Cr was tested on rabbit jejunum, a spontaneously contracting preparation considered more responsive to spasmylotics (Ghayur and Gilani, 2005). In rabbit jejunum, Cs.Cr caused a dose-dependent spasmylotic effect, followed by relaxation at the higher dose. Pretreatment of the tissue with atropine abolished the contractile effect and the relaxant effect became dominant. In earlier studies, we observed that the spasmylotic effect of medicinal plants is usually mediated through calcium channel blockade (Gilani et al., 2005b). To investigate whether coriander also exhibits its spasmylotic effect through the similar mechanisms, Cs.Cr was studied on high K+-induced contractions. K+ at high concentrations (>30 mM) is known to cause smooth muscle contractions through opening of voltage-dependent slow Ca^{2+} channels, thus allowing influx of extracellular Ca^{2+} causing a contractile effect (Bolton, 1979; Godfraind et al., 1986). Cs.Cr relaxed the high K+-induced contractions, like that caused by verapamil, a standard Ca^{2+} antagonist (Hamilton et al., 1986). The CCB activity of coriander was further confirmed when pretreatment of the tissue with Cs.Cr shifted the Ca^{2+} dose–response curves to the right, like verapamil. Calcium antagonists form an important therapeutic group (Triggle, 1992) and the common characteristic of these drugs is their dose–dependent inhibition of slow entry of Ca^{2+} and their capacity for reversal of this effect by Ca^{2+} (Fleckenstein, 1977). The spasmylotic activity of coriander mediated through Ca^{2+} antagonist effect explains its therapeutic usefulness in hyperactive gut disorders such as abdominal colic and diarrhea, as the CCBs are known to be useful in such disorders (Brunton, 1996).

The combination of cholinergic and CCB components in coriander also suggests its effectiveness in cardiovascular disorders, such as hypertension, as both activities are known to effectively reduce the BP (Furchgott and Zawadski, 1980; Epstein, 1992). Intravenous administration of the aqueous-methanolic extract of coriander fruit produced a dose-dependent fall in both systolic and diastolic BP, which is inline with its medicinal use in hypertension. When repeated in atropinized (1 mg/kg) animal, the BP lowering effect of ACh (1 μg/Kg) was abolished indicating the complete blockade of muscarinic receptors by atropine, whereas the effect of Cs.Cr was partially blocked (Fig. 6). These results suggest that the blood pressure lowering effect of coriander is mediated through cholinergic effect and some additional component(s), probably the CCB activity. Blood pressure is the product of cardiac output and total peripheral resistance (Johansen, 1992), hence Cs.Cr was further studied on heart and aorta for the possible cardiac inhibitory and vasodilator effects.

When tested on spontaneously beating guinea-pig atria, Cs.Cr caused suppression of atrial contractions. Pretreatment with atropine partially blocked the depressant effect of Cs.Cr on heart where M2 receptors are predominant (Eglen et al., 1996), suggesting that the cholinergic constituents in coriander non-specifically
interact with $M_2$ and $M_3$ subtypes of muscarinic receptors. To study the peripheral vascular effect and nature of the additional BP lowering mechanism, Cs.Cr was studied on endothelium denuded rabbit aorta, hence the absence of cholinergic vasodilator effect (Smith and Reynard, 1992). Cs.Cr, relaxed both the phenylephrine and $K^+$ induced contractions, similar to verapamil, thus showing that the BP lowering effect of coriander is mediated through a combination of $Ca^{2+}$ antagonist and cholinergic mechanisms. Coriander, in an earlier study, was shown to lower BP in anesthetized rats, which was however a preliminary study with mode of action remained to be elucidated. The current study reports the presence of cholinergic and $Ca^{2+}$ antagonist combination in coriander mediating the antihypertensive effect and thereby provides rationale for its medicinal use in BP.

The diuretic effect of coriander was tested in view of its use as diuretic as well as the known effectiveness of diuretics in hypertension (Chiu et al., 1986). The effect was confirmed when Cs.Cr caused significant increase in urine output (diuresis) in rats, similar to furosemide, a standard diuretic (Jackson, 1996). Diuretics are considered one of the best choices for the treatment and management of uncomplicated hypertension (Jackson, 2001; Salvetti and Ghiadoni, 2006) and are often prescribed in combinations with antihypertensives for moderate to severe hypertension (Shah et al., 2004). The presence of diuretic activity in coriander is likely to compliment its antihypertensive effect. Coriandrin saturation is previously reported to exhibit diuretic effect through increased urine loss of electrolytes, like furosemide (Aissouei et al., 2008). This study confirms the previous findings and suggests the presence of diuretic effect in this local variety of coriander.

The approximate Na$^+$ and K$^+$ contents reported in the dried fruit of coriander are 11,866–14,781 and 308–430 ppm respectively (Duke et al., 2002). The observed hypotensive and diuretic effects of coriander are not likely to be caused by the direct action of K$^+$ as, at the doses tested in this study, K$^+$ contents are far less that those reported in other plants at which K$^+$ was found pharmacologically inert (Sripandikulchaiti et al., 2001; Camargo et al., 2004).

Activity-directed fractionation of the crude extract showed that the spasmodic (cholinergic) activity of Cs.Cr was separated in its aqueous fraction (Cs.Aq) as it produced atropine sensitive contractile effect in guinea-pig ileum but found devoid of any relaxant effect in isolated rabbit jejenum. The contractile effect of Cs.Aq was more pronounced than the parent crude extract (p < 0.01) apparently due to the shift of the relaxant component(s) in organic fractions. All the three organic fractions i.e. petroleum ether, chloroform and ethyl acetate were devoid of any stimulant effect, while caused concentration-dependent relaxation of both spontaneous and high K$^+$-induced contractions in rabbit jejenum preparations. Ethyl acetate fraction was found most potent in its spasmylocic effect, being 11, 8 and 2 times more potent than the parent extract, petroleum spirit and chloroform fraction respectively. This pattern of separating biological activities among the fractions is in accordance with our previous findings, that the cholinergic activity of crude plant extracts is usually concentrated in the aqueous fractions while the CCB component is concentrated in organic fractions (Bashir et al., 2006; Gilani et al., 2006). Diuretic activity exhibited by the crude plant extract was concentrated in the aqueous fraction, which was found more potent than the parent crude extract. Acute toxicity test revealed no toxicity in Cs.Cr at the doses evaluated in this study, which is inline with wide therapeutic and culinary use of coriander.

5. Conclusion

This study shows that coriander possess gut stimulatory and inhibitory effects mediating through cholinergic and $Ca^{2+}$ antagonist mechanisms respectively and blood pressure lowering effect via combination of cholinergic and CCB components, thus provides sound mechanistic background for its traditional use in dyspepsia, diarrhea, abdominal cramps and hypertension. The presence of diuretic activity in coriander is likely to compliment its antihypertensive effect.

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