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Research Article

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Antihyperglycemic and analgesic studies with methanol extract of a mixture of *Cuminum cyminum* and *Coriandrum sativum* seeds

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ABSTRACT

In oral glucose tolerance tests with methanolic extract of Cuminum cyminum and Coriandrum sativum seeds (1:1), the extract significantly and dose-dependently reduced blood glucose concentrations in glucose-loaded mice. At extract doses of 100, 200 and 400 mg/kg (i.e. 100, 200 and 400 mg each of extract from each plant seeds), the reductions in blood glucose levels were, respectively, 37.6, 44.0 and 48.7%. In comparison, a standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg, reduced blood glucose level by 51.0%. In analgesic activity tests with acetic acid induced pain model mice, the extract at the afore-mentioned three doses, significantly and dose-dependently reduced acetic acid induced abdominal constrictions in mice by 25.9, 44.4, and 59.3%, respectively, versus the 55.6% reduction obtained with a standard analgesic drug, aspirin, administered at a dose of 400 mg per kg. In both antihyperglycemic and analgesic activity studies, the effect of combined extract was greater than that obtained with extract from individual plants. The individual or combined extracts when administered to mice did not cause any acute toxicity when administered at doses up to 3000 mg per kg. Thus the seeds of the two plants may be used for controlling both high blood sugar as well as pain.

Key words: *Cuminum cyminum*, *Coriandrum sativum*, analgesic, antihyperglycemic

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INTRODUCTION

Cuminum cyminum L. (Apiaceae) and *Coriandrum sativum* L. (Apiaceae) are two of the most widely used spice plants in Bangladesh. In English, the seeds of the plants are known, respectively, as cumin and coriander, while in Bengali, they are known, respectively, as jeera and dhonia. The seeds of both plants are used as spices in literally hundreds of vegetable, fish and meat dishes throughout the country. The leaves of *C. sativum* are also used as spice.

The hypolipidemic effect of *C. cyminum* has been observed in alloxan induced diabetic rats [1]. Methanol extract of seeds of *C. cyminum* have been shown to exhibit antihyperglycemic activity and inhibition of formation of advanced glycation end product in streptozotocin induced diabetic rats [2]. Incorporation of coriander in diet and drinking water has been found to reduce hyperglycemia in streptozotocin diabetic mice [3]. Coriander seed extract has been observed to increase the activity of pancreatic beta cells and so stimulate insulin increase in streptozotocin induced diabetic rats [4]. A single dose of coriander seed extract has been observed to suppress hyperglycemia in obese-hyperglycemic-hyperlipidemic (OHH) Meriones shawi rats [5]. The antioxidant, antihyperglycemic and antihyperlipidemic effects of *C. sativum* leaf and stem has been reported in alloxan induced diabetic rats [6].

Diabetes and pain are common afflictions in Bangladesh; the first from a possible change in life style and food habits of the people, and the second arising from multiple causes including hard labor under the sun because most rural people are agricultural workers. Towards alleviation of these two disorders, we had been systematically screening various plants of Bangladesh for their antihyperglycemic and analgesic activities [7-18]. The objective of the present study was to evaluate the antihyperglycemic and analgesic activities of methanolic extract of cumin and coriander both individually as well as in combination.

EXPERIMENTAL SECTION

Seed collection

Cumin and coriander seeds were collected from a local market in Dhaka during August 2014.

Preparation of methanolic extract of seeds

100g of powdered seeds were extracted with methanol (w:v ratio of 1:5, final weight of the extract 9.97g for cumin and 3g for coriander). Extracts were dissolved in 1% DMSO prior to use.

Chemicals and Drugs

Glibenclamide, aspirin, and glucose were obtained from Square Pharmaceuticals Ltd., Bangladesh. All other chemicals were of analytical grade.

Animals

Swiss albino mice, which weighed between 14-18g were used in the present study. The animals were obtained from International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B). The animals were acclimatized for three days prior to actual experiments. The study was conducted following approval by the Institutional Animal Ethical Committee of University of Development Alternative, Dhaka, Bangladesh.

Oral glucose tolerance tests for evaluation of antihyperglycemic activity

Oral glucose tolerance tests (OGTT) were carried out as per the procedure previously described by Joy and Kuttan [19] with minor modifications. Briefly, fasted mice were grouped into nine groups of five mice each. The various groups received different treatments like Group 1 received vehicle (1% DMSO in water, 10 ml/kg body weight) and served as control, Group 2 received standard drug (glibenclamide, 10 mg/kg body weight). Groups 3 and 4 received methanolic seed extract of cumin (MECC) at doses of 200 and 400 mg per kg body weight. Groups 5 and 6 were administered methanolic seed extract of coriander (MECS) at doses of 200 and 400 mg per kg body weight. Groups 7-9 received, respectively, (100 mg each of MECC and MECS), (200 mg each of MECC and MECS), and (400 mg each of MECC and MECS) per kg body weight. All substances were orally administered. Following a period of one hour, all mice were orally administered 2g glucose/kg of body weight. Blood samples were collected 120 minutes after the glucose administration through puncturing heart. Blood glucose levels were measured by glucose oxidase method [20]. The percent lowering of blood glucose levels were calculated according to the formula described below.

Percent lowering of blood glucose level = $(1 – W_e/W_c)$ X 100,

where W_e and W_c represents the blood glucose concentration in glibenclamide or MECC and MECS administered mice (Groups 2-9), and control mice (Group 1), respectively.

Antinociceptive activity evaluation through abdominal writhing test

Antinociceptive activity of MECC, MECS and (MECC + MECS) was examined as previously described [21]. Mice were divided into nine groups of five mice each. Group 1 received vehicle (1% DMSO in water, 10 ml/kg body weight) and served as control, Group 2 received standard drug (glibenclamide, 10 mg/kg body weight). Groups 3 and 4 received methanolic seed extract of cumin (MECC) at doses of 200 and 400 mg per kg body weight. Groups 5 and 6 were administered methanolic seed extract of coriander (MECS) at doses of 200 and 400 mg per kg body weight. Groups 7-9 received, respectively, (100 mg each of MECC and MECS), (200 mg each of MECC and MECS), and (400 mg each of MECC and MECS) per kg body weight. All substances were orally administered. Following a period of 60 minutes after oral administration of standard drug or extract(s), all mice were intraperitoneally injected with 1% acetic acid at a dose of 10 ml per kg body weight. A period of 5 minutes was given to each animal to ensure bioavailability and onset of chemically induced irritation of acetic acid [22],

following which period, the number of abdominal constrictions (writhings) was counted for 10 min. The percent inhibitions of abdominal constrictions were calculated according to the formula given below.

Percent inhibition = $(1 – W_e/W_c) X 100$,

where W_e and W_c represents the number of abdominal constrictions or writhings in aspirin or extract administered mice (Groups 2-9), and control mice (Group 1), respectively.

Acute toxicity test

Acute toxicity test was conducted as previously described [23]. Mice were divided into nine groups, each group consisting of six animals. Group 1 was given 1% Tween 80 in normal saline (2 ml per kg body weight). The other eight groups (Groups 2-9) were administered, respectively, 100, 200, 300, 600, 800, 1000, 2000 and 3000 mg of MECC or MECS or (MECC + MECS) per kg body weight. All animals were closely observed for the next 8 hours to notice any behavioral changes or mortality and were kept under close observation for the next two weeks.

Statistical analysis

Experimental values are expressed as mean ± SEM. Independent Sample t-test was carried out for statistical comparison. Statistical significance was considered to be indicated by a p value < 0.05 in all cases [14].

RESULTS AND DISCUSSION

Toxicity evaluation

The crude extract (MECC, MECS, MECC + MECS) did not show any toxicity in mice even at the highest dose tested.

Antihyperglycemic activity evaluation through OGTT

Dose-dependent and significant reductions in blood glucose levels in glucose-loaded mice were observed both with MECC and MECS. At doses of 200 and 400 mg per kg body weight, MECC lowered blood glucose levels, respectively, by 19.5 and 33.9%. At the same doses MECS, respectively, lowered blood glucose levels by 28.2 and 30.9%. However, the reductions in blood glucose levels were significantly higher with the combination of MECC and MECS. At doses of 100, 200, and 400 mg each of MECC and MECS, blood glucose levels were lowered, respectively, by 37.6, 44.0 and 48.7%. In comparison, a standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced blood glucose level by 51.0%. Thus the combination of the highest dose of 400 mg each of MECC and MECS gave blood glucose lowering effects comparable to that of glibenclamide. The results are shown in Table 1 and suggest that the combination can be used for lowering blood glucose in hyperglycemic subjects.

Table 1: Effect of crude methanol extract of MECC, MECS, and (MECC + MECS) on blood glucose level in hyperglycemic mice following 120 minutes of glucose loading

Treatment	Dose (mg/kg body weight)	Blood glucose level (mmol/l)	% lowering of blood glucose level
Control	10 ml	5.96 ± 0.49	-
Glibenclamide	10 mg	2.92 ± 0.29	51.0*
(MECC)	200 mg	4.80 ± 0.25	19.5*
(MECC)	400 mg	3.94 ± 0.27	33.9*
(MECS)	200 mg	4.28 ± 0.48	28.2*
(MECS)	400 mg	4.12 ± 0.0.12	30.9*
(MECC + MECS)	100 mg	3.72 ± 0.31	37.6*
(MECC + MECS)	200 mg	3.34 ± 0.26	44.0*
(MECC + MECS)	400 mg	3.06 ± 0.24	48.7*

*All administrations were made orally. Values represented as mean ± SEM, (n=5); *P < 0.05; significant compared to hyperglycemic control animals.*

The exact mechanism through which the extracts individually or in combination lowered blood glucose levels were not ascertained in the present study. The nature of the bioactive component or components was also not determined in this preliminary work. However, *C. cuminum* is known to contain cuminaldehyde and cuminol with demonstrated insulinotropic action in streptozotocin induced diabetic rats [24]. That such other bioactive component(s) with hypoglycemic action is present in both plants and seeds can be reasonably deduced from the other studies conducted

with seeds as well as other plant parts like leaves and stems in previous studies [1-6]. Our results are in conformity with these studies and suggest that the two spices individually or in combination can be used by diabetic patients for blood glucose control.

Antinociceptive activity evaluation results

Dose-dependent and significant reductions ($P < 0.05$) in the number of abdominal constrictions (writhings) induced by intraperitoneal administration of acetic acid were observed with MECC and MECS as well as the combination of (MECC + MECS). At doses of 200 and 400 mg per kg body weight, MECC was observed to reduce the number of writhings, respectively, by 48.1, and 51.9%. At doses of 200 and 400 mg per kg body weight, MECS was observed to reduce the number of writhings, respectively, by 29.6, and 44.4%. A standard analgesic drug, aspirin, when administered to experimental animals at a dose of 200 per kg body weight, reduced the number of constrictions by 29.6%. Thus, a dose of 200 or 400 mg/kg MECC or MECS was equivalent to or better than that of 200 mg/kg aspirin regarding antinociceptive potential. When the extracts were used in combination, (MECC + MECS) produced a higher antinociceptive effect at 400 mg/kg than MECC or MECS alone at 400 mg/kg; furthermore, the percent reduction in the number of writhings was double than that observed with 200 mg/kg aspirin. The results are shown in Table 2 and suggest that the extracts individually or in combination possess significant antinociceptive properties and can be used for alleviating pain.

The antinociceptive effect of *C. cyminum* fruit essential oil has been shown in rats in both formalin and thermal test models [25]. The analgesic and anti-inflammatory effect of *C. cyminum* seeds aqueous and ethanolic extracts has also been demonstrated in Swiss albino mice using different pain and inflammation models [26]. The analgesic effects of different extracts of aerial parts of *C. sativum* have been shown [27]. Aqueous and ethanolic extracts of seeds of *C. sativum* reportedly showed analgesic effect against thermal pain stimulus in rats [28]. The various reports alongside the present one strongly indicates that the two spices cumin and coriander can produce pain relieving activity, while the present study goes further in demonstrating that in combination the analgesic effects are greater. The isolation and identification of the responsible bioactive component(s) remains to be determined and further studies are ongoing in our laboratory towards such isolation and identification.

Table 2: Antinociceptive effect of crude methanol extract of MECC, MECS and (MECC + MECS) in acetic acid-induced pain model mice

Treatment	Dose (mg/kg body weight)	Mean number of abdominal constrictions	% inhibition
Control	10 ml	5.4 ± 0.40	-
Aspirin	200 mg	3.8 ± 0.37	29.6*
(MECC)	200 mg	2.8 ± 0.37	48.1*
(MECC)	400 mg	2.6 ± 0.51	51.9*
(MECS)	200 mg	3.8 ± 0.20	29.6*
(MECS)	400 mg	3.0 ± 0.0.32	44.4*
(MECC + MECS)	100 mg	4.0 ± 0.55	25.9*
(MECC + MECS)	200 mg	3.0 ± 0.45	44.4*
(MECC + MECS)	400 mg	2.2 ± 0.20	59.3*

*All administrations were made orally. Values represented as mean ± SEM, (n=5); *P < 0.05; significant compared to hyperglycemic control animals.*

CONCLUSION

The experimental results suggest that the methanolic extract of seeds of *Cuminum cyminum* and *Coriandrum sativum* possess antihyperglycemic and analgesic potential and may be used for lowering blood sugar and alleviating pain individually or in combination.

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REFERENCES

[1] S Dhandapani; VR Subramanian; S Rajagopal; N Namasivayam, *Pharmacol. Res*., **2002**, 46(3), 251-255.
[2] AG Jagtap; PB Patil, *Food Chem. Toxicol*., **2010**, 48(8-9), 2030-2036.
[3] AM Gray; PR Flatt, *Br. J. Nutr*., **1999**, 81(3), 203-209.

[4] M Eidi; A Eidi; A Saeidi; S Molanaei; A Sadeghipour; M Bahar; K Bahar, *Phytother. Res*., **2009**, 23(3), 404-406.
[5] A Aissaoui; S Zizi; ZH Israili; B Lyoussi, *J. Ethnopharmacol*., **2011**, 137(1), 652-661.
[6] S Sreelatha; R Inbavalli, *J. Food Sci*., **2012**, 77(7), T119-T123.
[7] A Morshed; MH Hossain; S Shakil; K Nahar; S Rahman; D Ferdausi; T Hossain; I Ahmad; MH Chowdhury; M Rahmatullah, *Adv. Nat. Appl. Sci*., **2010**, 4(2), 193-7.
[8] M Rahmatullah; S Sultan; TT Toma; SS Lucky; MH Chowdhury; WM Haque; MEA Annay; R Jahan, *Afr. J. Trad. Complement. Altern. Med*., **2010**, 7(2), 109-12.
[9] F Ahmed; S Rahman; N Ahmed; M Hossain; A Biswas; S Sarkar; H Banna; MA Khatun; MH Chowdhury; M Rahmatullah, *Afr. J. Trad. Complement. Altern. Med*., **2011**, 8(1), 79-81.
[10] S Shahreen; J Banik; A Hafiz; S Rahman; AT Zaman; MA Shoyeb; MH Chowdhury; M Rahmatullah, *Afr. J. Trad. Complement. Altern. Med*., **2012**, 9(2), 287-91.
[11] M Rahmatullah; M Hosain; S Rahman; S Rahman; M Akter; F Rahman; F Rehana; M Munmun; MA Kalpana, *Afr. J. Trad. Complement. Altern. Med*., **2013**, 10(5), 408-11.
[12] M Rahmatullah; M Hossain; A Mahmud; N Sultana; SM Rahman; MR Islam; MS Khatoon; S Jahan; F Islam, *Afr. J. Trad. Complement. Altern. Med*., **2013**, 10(4), 1-5.
[13] ME Haque; S Rahman; M Rahmatullah; R Jahan, *BMC Complement. Alternat. Med*., **2013**, 13, 296-9.
[14] AI Hossain; M Faisal; S Rahman; R Jahan; M Rahmatullah, *BMC Complement. Alternat. Med*., **2014**, 14, 169-73.
[15] F Akhter; M Al-Razi; FB Chowdhury; N Ara; MM Rahman; M Rahmatullah, *J. Chem. Pharmaceut. Res*., **2014**, 6(9), 322-327.
[16] AKMM Haque; MZ Kabir; S Rahman; MM Rahman; R Jahan; MS Hossan; M Rahmatullah, *J. Chem. Pharmaceut. Res*., **2014**, 6(9), 397-402.
[17] BA Labib; S Roy; S Rahman; MM Rahman; M Rahmatullah, *J. Chem. Pharmaceut. Res*., **2015**, 7(4), 393-396.
[18] MSH Khan; MF Molla; S Sultana; S Rahman; M Rahmatullah, *J. Chem. Pharmaceut. Res*., **2015**, 7(4), 420-424.
[19] KL Joy; RJ Kuttan, *J. Ethnopharmacol*., **1999**, 67(2), 143-148.
[20] S Venkatesh; GD Reddy; YSR Reddy; D Sathyavathy; B Reddy, *Fitoterapia*, **2004**, 75(3-4), 364-367.
[21] P Shanmugasundaram; S Venkataraman, *Afr. J. Tradit. Complement. Altern. Med*., **2005**, 2(1), 62- 69.
[22] M Akter; IZ Mitu; JJ Proma; SM Rahman; MR Islam; S Rahman; M Rahmatullah, *Adv. Nat. Appl. Sci*., **2014**, 8(8), 70-74.
[23] S Ganapaty; GK Dash; T Subburaju; P Suresh, *Fitoterapia*, **2002**, 73(1), 28-31.
[24] SB Patil; SS Takalikar; MM Joglekar; VS Haldavnekar; AU Arvindekar, *Br J Nutr*., **2013**, 110(8), 1434-1443.
[25] M Sayyah; A Peirovi; M Kamalinejad, *Iranian Biomed. J*., **2002**, 6(4), 141-145.
[26] SP Bhat; W Rizvi; A Kumar, *J. Nat. Remedies*, **2014**, 14(2), 187-192.
[27] SF Kazempor; SV Iangehbiz; M Hosseini; MN Shafei; A Ghorbani; M Pourganji, *Int. J. Biomed. Sci*., **2015**, 11(1), 23-28.
[28] SP Bhat; W Rizvi; A Kumar, *J. Phytopharmacol*., **2014**, 3(4), 254-258.