HOW GOOD IS RED CABBAGE EXTRACT FOR LOWERING HIGH BLOOD GLUCOSE AND ALLEVIATING PAIN? A PRELIMINARY EVALUATION OF *BRASSICA OLERACEA* L. VAR. *CAPITATA* F. *RUBRA*

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**ABSTRACT**

**Background.** *Brassica oleracea* L. var. *capitata* f. *rubra* (red cabbage) is cultivated in Bangladesh for its edible leaves, which are taken raw in salad or in the cooked form. It was of interest to determine the antihyperglycemic and analgesic properties of the leaves of the plant.

**Methods.** Antihyperglycemic activity was determined through oral glucose tolerance tests (OGTT). Analgesic activity was determined by observed decreases in abdominal constrictions (writhings) in intraperitoneally administered acetic acid-induced pain model in mice.

**Results.** Administration of methanol extract of red cabbage leaves led to significant dose-dependent reductions in blood glucose levels in glucose-loaded mice. At doses of 50, 100, 200 and 400 mg per kg body weight, the extract reduced blood glucose levels by 27.5, 32.9, 39.6, and 56.0%, respectively compared to control animals. By 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%. In analgesic activity tests, the extract at doses of 50, 100, 200 and 400 mg per kg body weight dose-dependently reduced the number of abdominal constrictions by 7.4, 22.2, 37.0, and 55.6%, respectively. A standard pain relieving (analgesic) drug, aspirin, reduced the number of writhings by 37.0 and 55.6%, respectively.
when administered at doses of 200 and 400 mg per kg body weight. **Conclusion.** Red cabbage leaves can be beneficial in lowering blood glucose and for alleviating pain.

**KEYWORDS:** Antihyperglycemic, *Brassica oleracea* var. *capitata* f. *rubra*, analgesic, Brassicaceae, red cabbage.

**BACKGROUND**

The red cabbage or *Brassica oleracea* var. *capitata* f. *rubra* (Brassicaceae) is characterized by its purple color leaves but otherwise looks similar to the more common green cabbage or *Brassica oleracea* var. *capitata*. The plant is grown during the winter months of November to February in Bangladesh, primarily for it edible leaves, which are consumed raw in salads or cooked and eaten as vegetable. We have previously noted antihyperglycemic activity in methanol extract of green cabbage leaves.[1] The leaves of red cabbage have been reported to contain biologically potent anthocyanins and reportedly ameliorated dyslipidemia and hepatic injury induced by exogenous cholesterol administration.[2] Red cabbage is also known to contain glucosinolates,[3] these types of compounds being reported to possess antidiabetic activity.[4]

Other variants of the *Brassica oleraceae* species have also been reported for their beneficial effect in diabetes. It has been reported that consumption of broccoli sprouts improved insulin resistance in type-2 diabetic patients.[5] It has been reported that presence of sulforaphane makes broccoli sprouts an excellent choice for management of type 2 diabetes and its complications.[6] The hypoglycemic and hypolipidemic effect of cabbage has been noted in alloxan induced diabetic rabbits.[7]

Diabetes and pain are common afflictions throughout the world. Search for new drugs to treat diabetes is a vital necessity for existing drugs can only treat the symptoms like high blood glucose levels or slow down progress of complicated factors associated with the disease, but cannot cure the disease. Over the counter drugs exist for pain relief, but drugs like aspirin suffer from adverse effects like causing gastric ulceration, while acetaminophen can lead to hepatic toxicity through over-dosage or overuse. Thus better pain relieving drugs are also needed without the adverse effects. Towards that, we had been systematically screening various types of plants of Bangladesh for their antihyperglycemic and analgesic activities.[8-24] The objective of the present study was to evaluate the antihyperglycemic potential of...
methanol extract of red cabbage leaves (through oral glucose tolerance tests) and analgesic potential of the leaves (through acetic acid induced pain model) in Swiss albino mice.

METHODS

Plant material collection
Red cabbage leaves were collected during April 2014 from a local market in Dhaka city, Bangladesh. The leaves were taxonomically identified at the Bangladesh National Herbarium (Accession Number 39,515).

Preparation of methanolic extract of leaves
Leaves were sliced into small pieces and thoroughly dried in the shade and 100g of dried and powdered leaves were extracted with methanol (w:v ratio of 1:5, final weight of the extract 10g).

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 were carried out as per the procedure previously described by Joy and Kuttan (1999).[25] with minor modifications. Briefly, fasted mice were grouped into six groups of five mice each. The various groups received different treatments like Group 1 received vehicle (1% Tween 80 in water, 10 ml/kg body weight) and served as control, Group 2 received standard drug (glibenclamide, 10 mg/kg body weight). Groups 3-6 received methanolic red cabbage leaf extract (MERC) at doses of 50, 100, 200 and 400 mg 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.\textsuperscript{26} The percent lowering of blood glucose levels were calculated according to the formula described below.

Percent lowering of blood glucose level = \((1 – W_e/W_c) \times 100\),
where \(W_e\) and \(W_c\) represents the blood glucose concentration in glibenclamide or MERC administered mice (Groups 2-6), and control mice (Group 1), respectively.

**Analgesic activity evaluation through abdominal writhing test**

Analgesic activity of MERC was examined as previously described.\textsuperscript{27} Mice were divided into seven groups of five mice each. Group 1 served as control and was administered vehicle only. Groups 2 and 3 were orally administered the standard analgesic drug aspirin at doses of 200 and 400 mg per kg body weight, respectively. Groups 4-7 were administered MERC at doses of 50, 100, 200 and 400 mg per kg body weight, respectively. Following a period of 60 minutes after oral administration of standard drug or MERC, 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\textsuperscript{28}, 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 = \((1 – W_e/W_c) \times 100\)
where \(W_e\) and \(W_c\) represents the number of writhings in aspirin or MERC administered mice (Groups 2-7), and control mice (Group 1), respectively.

**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.\textsuperscript{15}

**RESULTS**

**Antihyperglycemic activity evaluation results**

In oral glucose tolerance tests (OGTT), MERC at doses of 50, 100, 200 and 400 mg/kg caused, respectively, 27.5, 32.9, 39.6, and 56.0\% reductions in blood glucose levels. The results were dose-dependent and statistically significant. Glibenclamide (a standard antihyperglycemic drug), when administered at a dose of 10 mg/kg lowered blood glucose by
51.0%, which was lower than that observed with the highest dose of MERC. The results are shown in Table 1 and suggest that MERC possess antihyperglycemic activity, with the highest dose of the extract being better than glibenclamide.

**Analgesic activity evaluation results**

Dose-dependent reductions in the number of abdominal constrictions induced by intraperitoneal administration of acetic acid were observed with MERC. At doses of 50, 100, 200 and 400 mg per kg body weight, MERC was observed to reduce the number of constrictions, respectively, by 7.4, 22.2, 37.0, and 55.6%. The results obtained with 50 mg per kg MERC were not statistically significant. A standard analgesic drug, aspirin, when administered to experimental animals at doses of 200 and 400 mg per kg body weight, reduced the number of constrictions by 37.0 and 55.6%, respectively. Thus, a dose of 200 mg/kg MERC was equivalent to 200 mg/kg aspirin, while a dose of 400 mg/kg MERC was equivalent to 400 mg per kg aspirin. The results are shown in Table 2 and suggest that MERC possesses significant analgesic properties.

**Table 1: Effect of crude methanol extract of red cabbage leaves (MERC) on blood glucose level in hyperglycemic mice following 120 minutes of glucose loading.**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose (mg/kg body weight)</th>
<th>Blood glucose level (mmol/l)</th>
<th>% lowering of blood glucose level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10 ml</td>
<td>5.96 ± 0.49</td>
<td>-</td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>10 mg</td>
<td>2.92 ± 0.29</td>
<td>51.0*</td>
</tr>
<tr>
<td>(MERC)</td>
<td>50 mg</td>
<td>4.32 ± 0.15</td>
<td>27.5*</td>
</tr>
<tr>
<td>(MERC)</td>
<td>100 mg</td>
<td>4.00 ± 0.38</td>
<td>32.9*</td>
</tr>
<tr>
<td>(MERC)</td>
<td>200 mg</td>
<td>3.60 ± 0.27</td>
<td>39.6*</td>
</tr>
<tr>
<td>(MERC)</td>
<td>400 mg</td>
<td>2.62 ± 0.25</td>
<td>56.0*</td>
</tr>
</tbody>
</table>

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

**Table 2: Analgesic effect of crude methanol extract of red cabbage leaves (MERC) in acetic acid-induced pain model mice.**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose (mg/kg body weight)</th>
<th>Mean number of abdominal constrictions</th>
<th>% inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10 ml</td>
<td>5.4 ± 0.24</td>
<td>-</td>
</tr>
<tr>
<td>Aspirin</td>
<td>200 mg</td>
<td>3.4 ± 0.40</td>
<td>37.0*</td>
</tr>
<tr>
<td>Aspirin</td>
<td>400 mg</td>
<td>2.4 ± 0.60</td>
<td>55.6*</td>
</tr>
<tr>
<td>(MERC)</td>
<td>50 mg</td>
<td>5.0 ± 0.32</td>
<td>7.4</td>
</tr>
<tr>
<td>(MERC)</td>
<td>100 mg</td>
<td>4.2 ± 0.58</td>
<td>22.2*</td>
</tr>
<tr>
<td>(MERC)</td>
<td>200 mg</td>
<td>3.4 ± 0.06</td>
<td>37.0*</td>
</tr>
<tr>
<td>(MERC)</td>
<td>400 mg</td>
<td>2.4 ± 0.51</td>
<td>55.6*</td>
</tr>
</tbody>
</table>
All administrations (aspirin and extract) were made orally. Values represented as mean ± SEM, (n=5); *P < 0.05; significant compared to control.

DISCUSSION
Glucosinolate type of compounds present in red cabbage leaves [3] can be responsible for the observed antihyperglycemic activity.[4] The variants of Brassica oleracea species are also known to contain sulforaphane and glucoraphin, which can also be responsible for the antihyperglycemic effects.[29-32] Additionally, red cabbage leaves are known to contain anthocyanins. Anthocyanins and ursolic acid in Cornelian cherry (Cornus mas) has been shown to ameliorate obesity and glucose intolerance in high-fat-fed C57BL/6 mice. [33] Antihyperglycemic effect of blackberry and mulberry fruits as observed in diabetic rats can be due to presence of anthocyanins.[34] The preventive effects of Morus alba anthocyanins on diabetes in Zucker diabetic fatty rats has been reported. [35] It has been reported that anthocyanin-rich purple corn extract ameliorated insulin resistance and reduced diabetes-associated mesangial fibrosis and inflammation.[36] Thus anthocyanins present in red cabbage have the potential not only to reduce blood glucose but also ameliorate other diabetes-related complications.

Anthocyanins and anthocyanidins have also been implicated in demonstrating analgesic effects. Analgesic action has been seen with cacao and avocado proanthocyanidins.[37] Analgesic and antiinflammatory activity of the proanthocyanidin shellegueain A from Polypodium feei has been reported.[38] □-Sitosterol has been reported for leaves of red cabbage.[39] □-Sitosterol has reportedly both antidiabetic and analgesic properties.[40,41] Taken together, red cabbage leaves contain a number of compounds, which has demonstrated usefulness in alleviating high blood glucose levels as well as pain, and so can be considered a substitute for blood glucose lowering and pain alleviating drugs.

CONCLUSION
The results suggest that methanolic extract of red cabbage leaves can be used for lowering blood glucose and for alleviating pain.

Conflicts of interest
The author(s) declare that they have no competing interests.
REFERENCES


