POLYHERBAL FORMULATION FOR LOWERING BLOOD GLUCOSE LEVELS: EVALUATION OF A COMBINATION OF 
FOeniculum vulgare and brassica alba SEEDS

Md. Saydur Rahman Sayeed¹, Hossain Ahmed¹, Shahnaz Rahman¹, Ishtiaq Ahmad², 
Md. Moshiur Rahman², Md. Shahadat Hossan², Mohammed Rahmatullah²*

¹Department of Biotechnology & Genetic Engineering, University of Development 
Alternative, Dhanmondi, Dhaka-1209, Bangladesh. 
²Department of Pharmacy, University of Development Alternative, Lalmatia, 
Dhaka-1207, Bangladesh.

ABSTRACT

Background. We have previously evaluated the antihyperglycemic potential of seeds of Foeniculum vulgare and Brassica alba separately. It was of interest to determine whether a combination of the seeds demonstrates synergistic antihyperglycemic effects and so can be more useful in lowering blood glucose. Methods. Antihyperglycemic activity was determined through oral glucose tolerance tests (OGTT). Results. Administration of 200 mg/kg of methanol extract of Foeniculum vulgare seeds led to 33.1% reduction in blood glucose levels in glucose-loaded mice. At the same dose, methanol extract of Brassica alba seeds reduced blood glucose levels by 38.8%. Administration of a combination of the extracts (1:1, w/w) at doses of 100, 200 and 400 mg/kg led to, respectively, 34.2, 43.1, and 47.7% reductions in blood glucose levels. By comparison, a standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced blood glucose level by 48.0%. The results demonstrate that a formulation containing extracts from seeds of both plants can give synergistic effects in lowering of blood glucose, and at the highest dose tested of the combination, is equivalent to that of glibenclamide. Conclusion. A polyherbal formulation containing extracts of Foeniculum vulgare and Brassica alba seeds is comparable to glibenclamide in lowering blood glucose levels.

BACKGROUND

*Foeniculum vulgare* Mill. (Apiaceae), known in English as ‘sweet fennel’ and in Bengali as ‘mouri’ is cultivated in Bangladesh for its seeds which are used for both culinary and medicinal purposes. *Brassica alba* Rabenh., is an annual plant belonging to the Brassicaceae family and cultivated in Bangladesh for culinary uses of its seeds, and is known as ‘white mustard’ in English and ‘shada shorisha’ in Bengali. Diabetes is widely prevalent in Bangladesh. The overall age-adjusted prevalence of diabetes and prediabetes has been found to be 9.7% and 22.4%, respectively.[1] In another study, it has been observed that the prevalence of diabetes in Bangladesh was 10.6% in men and 11.3% in women.[2] Despite the prevalence, a study on prescribing physicians has observed that a large proportion of prescriptions in Bangladesh related to diabetes care still lack standardization and acceptable quality.[3] When these facts are coupled with other factors like the general illiteracy of the population as well as the lack of access to modern doctors and the lack of affordability to modern medicines by a large section of the rural population, it does not present an overall satisfactory picture of diabetes treatment. As a result, localized treatment methods need to be found for lowering high blood sugar levels present in diabetic conditions, and medicinal plants which are locally available and affordable can fill this gap. We had been systematically screening various types of plants of Bangladesh for their antihyperglycemic and analgesic activities[4-20] We had previously reported the antihyperglycemic activity, individually, of methanol extract of *Foeniculum vulgare* and *Brassica alba* seeds.[21,22] The major objective of the present study was to determine whether a polyherbal formulation containing seeds from both the plants can produce a synergistic effect in lowering blood glucose levels in glucose-loaded mice.

METHODS

*Plant material collection*

*Foeniculum vulgare* and *Brassica alba* seeds were collected during August 2014 from a local market in Dhaka city, Bangladesh.

*Preparation of methanolic extract of leaves*

Seeds were thoroughly dried in the shade and 100g of dried and powdered seeds each were individually extracted with methanol (w:v ratio of 1:5, final weight of the extract 3g for
**Foeniculum vulgare** and 5.881g for **Brassica alba**. For the polyherbal extract preparation, individual extract of seeds of the two plants were mixed in a ratio of 1:1 (w/w).

**Chemicals and Drugs**

Glibenclamide 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). with minor modifications. Briefly, fasted mice were grouped into seven 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). Group 3 received methanolic extract of **Brassica alba** seeds (MEBA) at a dose of 200 mg per kg body weight. Group 4 received methanolic extract of **Foeniculum vulgare** seeds (MEFV) at a dose of 200 mg per kg body weight. Groups 5-7 received the polyherbal formulation (methanolic extract of seeds of **Brassica alba** and **Foeniculum vulgare** seeds combined in a w:w ratio of 1:1, MEPH) at doses of 100, 200 and 400 mg per kg body weight, respectively. 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. The percent lowering of blood glucose levels were calculated according to the formula described below.

\[
\text{Percent lowering of blood glucose level} = (1 - \frac{W_e}{W_c}) \times 100, \\
\text{where } W_e \text{ and } W_c \text{ represents the blood glucose concentration in glibenclamide or MEBA, MEFV or MEPH administered mice (Groups 2-7), and control mice (Group 1), respectively.}
\]
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{[11]}

RESULTS
Administration of MEBA at a dose of 200 mg per kg led to a 38.8% reduction in blood glucose levels in glucose-loaded mice in oral glucose tolerance tests. MEFV, at the same dosage, caused blood glucose levels to fall by 33.1%. On the other hand, the polyherbal formulation i.e. the combination of the two extracts, namely MEPH, when administered at doses of 100, 200 and 400 mg per kg, respectively, caused blood glucose levels to drop by 34.2, 43.1, and 47.7%. Thus the polyherbal formulation was more effective than either MEBA or MEFV alone in reducing blood sugar. For instance, the 200 mg per dose of MEPH (which contained 100 mg each of MEBA and MEFV) was more effective than 200 mg dose per kg of MEBA or MEFV alone in reducing blood glucose levels. The same effect was noticed with 400 mg MEPH (containing 200 mg each of MEBA and MEFV), which reduced blood glucose levels by 47.7% versus 200 mg each of MEBA or MEFV alone in reducing blood glucose levels (43.1% versus 38.8 and 33.1%, respectively). A standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg, caused reductions in blood glucose levels by 48.0%. Thus the highest dose of MEPH was equivalent to that of glibenclamide. The results are shown in Table 1, and suggest a synergistic interaction between MEBA and MEFV in producing antihyperglycemic effects.

<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>5.62 ± 0.31</td>
<td>-</td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>10 mg</td>
<td>2.92 ± 0.29</td>
<td>48.0*</td>
</tr>
<tr>
<td>(MEBA)</td>
<td>200 mg</td>
<td>3.44 ± 0.40</td>
<td>38.8*</td>
</tr>
<tr>
<td>(MEFV)</td>
<td>200 mg</td>
<td>3.76 ± 0.25</td>
<td>33.1*</td>
</tr>
<tr>
<td>(MEPH)</td>
<td>100 mg</td>
<td>3.70 ± 0.48</td>
<td>34.2*</td>
</tr>
<tr>
<td>(MEPH)</td>
<td>200 mg</td>
<td>3.20 ± 0.33</td>
<td>43.1*</td>
</tr>
<tr>
<td>(MEPH)</td>
<td>400 mg</td>
<td>2.94 ± 0.34</td>
<td>47.7*</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.
DISCUSSION
In our earlier papers,[21,22] we have postulated that phenolic compounds present in Brassica alba seeds, and unknown component(s) present in Foeniculum vulgare seeds may be responsible for the observed antihyperglycemic effects. In this respect, further work needs to be done in elucidating the nature of the phytochemicals present in both seeds with blood glucose lowering effects. The essential oil of Foeniculum vulgare has been reported to demonstrate hypoglycemic activity in streptozotocin diabetic rats.[25] The major point of interest of the present study is the observation of the synergistic effect and which is comparable to glibenclamide. Since both seeds are readily available to the rural people, they can, in combination, easily form a substitute for glibenclamide or other blood glucose lowering allopathic drugs, which may be difficult to obtain in rural areas. Thus, this polyherbal formulation may constitute an alternative approach to lower blood sugar and which may be of benefit to the diabetic patients of rural areas of Bangladesh.

CONCLUSION
The results suggest that the seeds of Brassica alba and Foeniculum vulgare, in combination, can synergistically lower blood glucose levels in glucose-loaded mice.

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

REFERENCES


