EVALUATION OF THERAPEUTIC POTENTIAL OF AEGLE MARMELOS (BILVA) LEAVES IN METABOLIC SYNDROME

Amit Vaibhav1*, Prof. O.P. Singh2
1Dr. Vijay Ayurvedic Medical College Hospital and Research Center, Kaithi, Varanasi, Uttar Pradesh, India.
2Department of Kaya Chikitsa, Faculty of Ayurveda, Institute of Medical Sciences, BHU, Varanasi, Uttar Pradesh, India.

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ABSTRACT

Metabolic Syndrome is a cluster of disease highly prevalent in the sophisticated, modernized and western world. It received increased attention in the past few decades and is the burning problem of today’s world. The metabolic syndrome has been shown to be a powerful risk factor responsible for coronary artery disease, renal failure, neuropathy etc. The conventional treatment option is only limited to managing hyperglycemia, dyslipidemia, hypertension but unable to prevent disease pathogenesis and complications. Long term side effect of artificial chemical drugs are another big problem, keeping these points in the account a pilot study has been framed to evaluate the therapeutic potential of Aegle marmelos (Bilva) leaves in Metabolic Syndrome. Aegle marmelos (Bilva) plant is vividly described in all ancient Ayurvedic texts known for its potent anti-diabetic, antioxidant, anti-inflammatory and anti-hyperlipidaemic activities. The main objective of the present work to evaluate the therapeutic potential of crude leaf powder of Aegle marmelos (Bilva). In this present study, total 30 previously diagnosed MS patients were randomly selected and divided into two groups having 15 patients in each group. In group I (n=15) patient have advised taking starch capsule 500 mg BD as a placebo and in Group II (n=15) crude leaf powder of Aegle marmelos (Bilva) 10 g BD has been given for 3 months with follow-up of 1 month. During the entire course of therapy, patients were advised to continue their ongoing conventional treatment along with the trial drug. The result showed a significant improvement in dyslipidemic state and hyperglycemic state of MS patient as compared to placebo group. The study can be concluded that the crude leaf powder of Aegle marmelos (Bilva) exhibit excellent hypolipidemic and hypoglycemic potential in MS patients, it can be used as natural, safe alternative to conventional management in the management of Metabolic Syndrome (MS).

Corresponding author
Amit Vaibhav
Lecturer, Department of Kaya Chikitsa,
Dr. Vijay Ayurvedic Medical College Hospital and Research Center,
Kaithi, Varanasi, Uttar Pradesh, India.
drvaamit@gmail.com
+919936180929

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INTRODUCTION

Metabolic Syndrome (MS) is a collection of cardiometabolic risk factors that includes obesity, insulin resistance, hypertension and dyslipidemia [1]. MS is recognized as one of the major public health challenges worldwide and especially in Indian sub-continent [2]. It is most common in adult population throughout the world [3]. It is estimated that approximately 25% of the world's population has MS and it will be increased up to 38% by the year 2023 [4]. In the etiopathogenesis of MS reactive oxygen species works as double-edged swords; while they play an essential role in multiple physiological systems, under conditions of oxidative stress, they contribute to cellular dysfunction. Oxidative stress is thought to play a major role in the pathogenesis of a variety of human diseases, including Diabetes, Hypertension, Atherosclerosis, Aging, Alzheimer's disease, kidney disease and malignancies[5]. It has been found that in MS dyslipidemia & elevated extra- and intra-cellular glucose concentrations result in an oxidative stress, which is defined as an imbalance between prooxidants and antioxidants. Several mechanisms seem to be involved in the genesis of this oxidative stress[6]. Due to remarkable side effects of modern synthetic anti-diabetic, anti-hypertensive, anti-obesity and hypolipidemic agents, there is an urgent need to develop eco-friendly, bio-friendly plant based products to replace synthetic chemicals particularly. Ayurveda has listed a number of medicinal plants with their anti-diabetic, antiobesity and hypolipidemic properties. The Aegle marmelos which is also known as Bael or Bilva is one of them. It possesses very good hypoglycemic and hypolipidemic potential acting through different pathways. Keeping in view the above concept, the present research work was carried out at OPD and IPD of Kayachikitsa, Sir Sunderlal Hospital, I.M.S., B.H.U., Varanasi to established the therapeutic role of an ayurvedic plant Aegle marmelos (Bilva) in MS patients.

Objectives:
To evaluate the therapeutic potential of crude leaf powder of Aegle marmelos (Bilva) in Metabolic Syndrome (MS) patients.

Study Design:
Single blind observational study pre test and post test design was adopted.

METHODS:
Total 30 patients of Metabolic Syndrome (MS) were selected for the present study from the Kayachikitsa OPD and IPD of Sir Sunder Lal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi. The case selection was random regardless of age, sex, occupation and socio-economic conditions. Patients fulfilling the diagnostic criteria were included in the present study. The study was undertaken in the duration of September 2013 to June 2014. Patients were randomly divided into two groups, 15 patients in each group with the care of inclusion and exclusion criteria has been taken. All the registered patients were already diagnosed with MS and taking conventional modern medicine for their treatment but they were still in the dyslipidemic and hyperglycemic state, So they came to us for add on ayurvedic treatment. Most of the patients were come to our hospital directly, while some of them were referred cases from other medical centers or from local doctors. Before registration of the case, all the patients were subjected to repeat diagnostic screening for MS. The cases were recorded with the help of a special proforma prepared for this purpose.

Inclusion criteria:
All patients fulfilling 2001 NCEP/ATP III [1] the criteria to define MS (presence of any three of the following five traits) for M.S were taken.
- Age between: 20-60 years of either sex.
- Waist ≥ 102cm (men), > 88cm (women)
- Hypertension > 130/85 or taking T/t
- Triglycerides ≥ 150 mg/dl or taking T/t
- HDL-cholesterol < 40 mg/dl
- Fasting plasma glucose ≥ 100mg/dl
- Patients having clinical signs and symptoms of Sthaulya.
- Patients willing for trial.

Exclusion criteria:
- Age <20yrs. and >70yrs.
- Type I and Type II Diabetes Mellitus (NIDDM) with major complications.
- Obese and Hypertensive patients with other major complications.
- Drug or chemical induced diabetes mellitus e.g. Glucocorticoids etc.
- Certain genetic syndromes e.g. Down’s syndrome, Klinefelter’s syndrome, Turner’s syndrome etc.
- Patients suffering from other severe systemic diseases.

Termination criteria :
- Sudden deterioration in patient’s health status during the period of study.
- Non compliance of the patient.
Availability of trial drug:

*Aegle marmelos* (Bilva) is very common and popular plant in India. Its fruit pulp is frequently used by most of the population across the country in the from sweet recipes and leaves are used to praise lord Shiva. In this study patients were advised to collect fresh healthy leaves of *Aegle marmelos* (Bilva) from nearby gardens after proper identification then wash and dry it properly, make it fine powder and store in airtight containers.

Grouping of Patients:

**Group- I (n=15):**

Patients were advised to take starch capsule 500 mg two times a day orally before meal empty stomach with luke warm water (Placebo group).

**Group- II (n=15):**

Patients were advised to take crude dry leaf powder of *Aegle marmelos* (Bilva) 10g two times a day orally before meal empty stomach with luke warm water.

Both group patients advised to continue their ongoing conventional treatment.

Parameter of assessment:

1) Blood Sugar Fasting (FBS.)
2) Blood Sugar Postprandial (PPBS)
3) Serum Cholesterol
4) Serum Triglycerides (TG)
5) Serum High density lipoprotein (HDL)
6) Serum High density lipoprotein (LDL)
7) Serum Vary low density lipoprotein (VLDL)

Statistical Analysis:

The data obtained was processed on a computer with the help of “SPSS: 16" software package of statistical analysis. Standard statistical methods were used to determine the mean, standard deviation (SD) and the range. Paired t-test was used to compare the results of various biochemical parameters among the patients in the four groups. All value quoted as the mean ± SD and a p-value of < 0.05 was considered to be statistically significant and p-value of <0.01 or p < 0.001 was considered to be statistically highly significant.

Observation:

<table>
<thead>
<tr>
<th>Table 1. Mean change in different biochemical parameters of Group-I patients [n=15]:</th>
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</thead>
<tbody>
<tr>
<td><strong>Groups</strong></td>
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<tr>
<td>-----------</td>
</tr>
<tr>
<td>FBS*</td>
</tr>
<tr>
<td>PPBS**</td>
</tr>
<tr>
<td>CHL†</td>
</tr>
<tr>
<td>TG‡†</td>
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<td>LDL¶</td>
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<tr>
<td>HDL¶¶</td>
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<tr>
<td>VLDL║</td>
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</tbody>
</table>
The overall study showed significant improvement in all the biochemical indices after treatment with Aegle marmelos. This effect is better than conventional allopathic treatment. As we see here in the results, significant improvement noted in fasting and postprandial blood sugar after therapy in both groups but the effect is better in A. marmelos group. A similar result was obtained by Kamalakkanan et al. 2005[7], Modi et al. 2013[8], Sankeshi et al. 2013[9], Panaskar et al. 2013[10] and Sharma et al. 2016[11] in experimental models proves potent hypoglycemic effect of A.marmelos leaves. Aegle marmelos is very good antidiabetic. This antidiabetic effect of A. marmelos probably due to the presence of Coumarins in various parts of this plant, which potentiate the insulin secretion from existing beta cells of the islets of langerhans and by enhancing glucose utilization by tissues. A significant change in lipid profile also noted in both group, The therapeutic effect A.marmelos group performed better as compare to conventional allopathic treatment, similar result has been drawn from previous studies Vidhya et al.1999[12], Rajadurai et al. 2005[13], Vijaya et al. (2009)[14] and Sharma et al. 2016[11] in experimental models. Possibly due to the Ethnopharmacological studies showed that it potentiates glucose utilization in the body and by modulation of lipid peroxides action[13]. The higher level of fatty acid and their metabolites such as acyl carnitine and long chain acyl CoA usually interfere with NA+/K+ATPase activity level resulting in hypolipidemia [7]. A. marmelos possess very good Rejuvenating action this may be due to its potent antioxidant action which helps in preventing the complication of Diabetes mellitus and dyslipidemia. Eugenol and Marmesinin are probably responsible for such activity because these compounds are very good in reducing oxidative stress[12]. At last, we can say that A. marmelos crude dry leaf powder possesses all the potential which counteract the pathogenesis of Metabolic Syndrome.

Table 2. Mean change in different biochemical parameters of Group-II patients [n=15]:

<table>
<thead>
<tr>
<th>Groups</th>
<th>BT†</th>
<th>FU1‡</th>
<th>FU2</th>
<th>FU3</th>
<th>Paired 't' test BTvs FU3</th>
<th>t value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS</td>
<td>133.00±36.94</td>
<td>107.87±27.22</td>
<td>105.93±24.18</td>
<td>102.93±18.51</td>
<td>30.07±30.68</td>
<td>3.795</td>
<td>0.002</td>
</tr>
<tr>
<td>PPBS</td>
<td>174.67±50.05</td>
<td>150.67±38.81</td>
<td>145.47±38.91</td>
<td>149.53±34.28</td>
<td>25.13±38.39</td>
<td>2.535</td>
<td>0.024</td>
</tr>
<tr>
<td>CHL†</td>
<td>244.80±96.69</td>
<td>195.33±60.94</td>
<td>178.20±39.83</td>
<td>166.33±34.46</td>
<td>78.47±87.49</td>
<td>3.473</td>
<td>0.004</td>
</tr>
<tr>
<td>TG†‡</td>
<td>214.67±81.85</td>
<td>178.67±51.88</td>
<td>149.47±37.47</td>
<td>138.87±31.70</td>
<td>75.80±83.69</td>
<td>3.508</td>
<td>0.003</td>
</tr>
<tr>
<td>LDL¶</td>
<td>109.33±29.71</td>
<td>107.47±22.57</td>
<td>93.93±25.26</td>
<td>93.33±21.16</td>
<td>16.00±15.09</td>
<td>4.108</td>
<td>0.001</td>
</tr>
<tr>
<td>HDL¶¶</td>
<td>40.93±7.25</td>
<td>42.60±4.82</td>
<td>43.67±5.83</td>
<td>44.67±5.18</td>
<td>-3.73±5.44</td>
<td>2.656</td>
<td>0.019</td>
</tr>
<tr>
<td>VLDL§</td>
<td>43.33±15.49</td>
<td>35.93±10.22</td>
<td>34.93±10.46</td>
<td>33.07±11.08</td>
<td>10.27±17.71</td>
<td>2.245</td>
<td>0.041</td>
</tr>
</tbody>
</table>

[FBS=Fasting Blood Sugar, PPBS=Postprandial Blood Sugar, CHL= Cholesterol, TG=Triglyceride, LDL=Low density lipoprotein, HDL=High density lipoprotein, VLDL=Very low density lipoprotein, B.T=Before treatment, FU- Follow up, S.D=Standard deviation]

RESULT

In the entire course of study effect the FBS level significantly decreased in both group (p<0.05) but it is maximum in Group-II (BT- FU3) mean + S.D was 30.07±30.68 (p=0.002) than Group-I (BT- FU3) mean + S.D 8.47±10.81(p=0.009). After the therapy PPBS level significantly decreased in Group-II (BT- FU3) mean + S.D was 25.13±38.39 (p<0.05) as compared to Group-I (p>0.05). A similar result has been observed in Serum cholesterol level which is significantly decreased in both groups (p<0.05) but little bit better improvement found in Group-II (BT- FU3) mean + S.D 78.47±87.49. Serum triglyceride level significantly decreased after the therapy in Group-II (t=3.508 and p<0.05) least improvement found in Group-I (t=2.10 and p>0.05). The serum LDL level also showed a significant decrease in both Groups (p<0.05) after the therapy. After the full course of therapy HDL level significantly increased in Group-II (t=2.66 and p<0.05) while in Group-I there was very nominal change present(p>0.05). During the entire study period the serum VLDL level significantly decreased in Group-II (t=2.25 and p<0.05) while in group Group-I (p>0.05).

DISCUSSION

The overall study showed significant improvement in all the biochemical indices after treatment with Aegle marmelos the effect is for better than conventional allopathic treatment. As we see here in the results significant improvement noted in fasting and postprandial blood sugar after therapy in both the groups but the effect is better in A.marmelos group. A similar result was obtained by Kamalakkanan et al. 2005[7], Modi et al. 2013[8], Sankeshi et al. 2013[9], Panaskar et al. 2013[10] and Sharma et al. 2016[11] in experimental models proves potent hypoglycemic effect of A.marmelos leaves. Aegle marmelos is very good antidiabetic. This antidiabetic effect of A. marmelos probably due to the presence of Coumarins in various parts of this plant, which potentiate the insulin secretion from existing beta cells of the islets of langerhans and by enhancing glucose utilization by tissues. A significant change in lipid profile also noted in both group, The therapeutic effect A.marmelos group performed better as compare to conventional allopathic treatment, similar result has been drawn from previous studies Vidhya et al.1999[12], Rajadurai et al. 2005[13], Vijaya et al. (2009)[14] and Sharma et al. 2016[11] in experimental models. Possibly due to the Ethnopharmacological studies showed that it potentiates glucose utilization in the body and by modulation of lipid peroxides action[13]. The higher level of fatty acid and their metabolites such as acyl carnitine and long chain acyl CoA usually interfere with NA+/K+ATPase activity level resulting in hypolipidemia [7]. A. marmelos possess very good Rejuvenating action this may be due to its potent antioxidant action which helps in preventing the complication of Diabetes mellitus and dyslipidemia. Eugenol and Marmesinin are probably responsible for such activity because these compounds are very good in reducing oxidative stress[12]. At last, we can say that A. marmelos crude dry leaf powder possesses all the potential which counteract the pathogenesis of Metabolic Syndrome.
CONCLUSION

Metabolic syndrome (MS) is a cluster of different life threatening diseases like Diabetes, hypertension, dyslipidemia and obesity. It is very difficult to treat metabolic syndrome patients with single medicine so it is a major challenge for the current medical system to minimize the drug load and cost on the body. Complication of MS and hazardous side effect of the medicine is another big issue. Aegle marmelos (Bilva) an ayurvedic plant possess novel quality to treat this disease naturally and without any side effects. In this study Aegle marmelos crude leaf powder has been screened for their hypoglycemic and hypolipidemic in Metabolic Syndrome patients. A significant decline observed in FBS, PPBS, Cholesterol, TG, LDL, VLDL levels and a Significant increase in S.HDL level (p<0.05) in A. marmelos group which is comparable to the conventional allopathic treatment (placebo) group. So we can conclude that Aegel marmelos leaf contains all the possible active ingredients which antagonize the pathogenesis of MS and we can use this plant drug as an alternative or add-on medication for MS patients.

Bottom line:

The present study is basically a time bound educational pilot study cannot be finally conclusive. But the leads available from this work open a new dimension to managing the metabolic syndrome with crude plant drug. Most of the previous herbal drug-related clinical studies based mainly on extracts and very few studies available which based on the whole plant. In this present study, an effort has been made to use the whole essence of the Aegle marmelos (Bilva) plant in crude form to treat Metabolic syndrome (MS). This wholesome natural approach used in this study seems to be effective and completely safe. We sincerely hope that the present study would be a pioneer as an ideal research work in the field of Metabolic syndrome (MS) and would provide a useful lead for coming generations and future research workers.

List of Abbreviations:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>MS</td>
<td>Metabolic syndrome</td>
</tr>
<tr>
<td>FBS</td>
<td>Fasting Blood Sugar</td>
</tr>
<tr>
<td>PPBS</td>
<td>Postprandial Blood Sugar</td>
</tr>
<tr>
<td>CHL</td>
<td>Cholesterol</td>
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<tr>
<td>TG</td>
<td>Serum Triglycerides,</td>
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<td>LDL</td>
<td>Low density lipoprotein</td>
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<td>FU</td>
<td>Follow up</td>
</tr>
<tr>
<td>S.D</td>
<td>Standard deviation</td>
</tr>
</tbody>
</table>

Conflicts of interest:

There are no conflicts of interest

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# REFERENCES


