EVALUATION OF THE EFFECT OF PURIFIED AQUEOUS EXTRACT OF SHILAJIT IN MODIFYING CARDIOVASCULAR RISK WITH SPECIAL REFERENCE TO ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Niranjan K¹, Ramakanth G.S.H¹*, Nishat Fatima², Usharani P³
¹Senior Resident, ²PhD Student, ³Professor and Head, Department of Clinical Pharmacology and Therapeutics, Nizam’s Institute of Medical Sciences, Punjagutta, Hyderabad, Telangana, India.

ABSTRACT

Context: Shilajit is a natural rock exudate used to prevent and combat problems with diabetes. It also has antioxidant, hypolipidemic and hypoglycaemic properties. Aim: To evaluate the effect of Shilajit on endothelial function in type 2 diabetes mellitus patients. Settings and Design: Randomized, double blind, placebo-controlled study. Methods and Material: After the ethics committee approval and informed consent, forty subjects were randomized to receive either Shilajit 250 mg or placebo (two capsules twice daily for 12 weeks). Endothelial function was evaluated with Reflection index (RI), Augmentation index (AIx), Subendocardial viability ratio (SEVR), Ankle Brachial Index (ABI), Pulse wave velocity(PWV) and Systemic vascular resistance (SVR) at baseline,4,8,12 weeks. Lipid profile and biomarkers Nitric oxide, MDA, Glutathione, hsCRP were evaluated at baseline and post treatment. Statistical analysis used: Data was expressed as mean ±SD. Paired and unpaired t-tests were performed for within group and between groups analysis, respectively. A p value < 0.05 was considered statistically significant. Results: After 12 weeks of treatment, Shilajit produced statistically significant increase in mean RI from baseline (-2.29±1.43 to -8.61±2.70; p<0.001) and in mean SEVR (145.5±24.89 to 150.9±24.08; p<0.05). Compared to placebo, Shilajit produced statistically significant increase in mean percentage change with RI, AIx, SEVR, and SVR, suggesting improvement in endothelial function. There was also statistically significant reduction in hsCRP, MDA, total cholesterol, LDL-C, triglycerides and increase in NO, GSH, HDL-C. The drug was well tolerated and no subjects discontinued due to adverse drug reactions. Conclusion: Shilajit showed significant improvement in endothelial function as evidenced with change in reflection index. It also improved other cardiovascular parameters and biomarker levels. Further studies are warranted in more number of subjects.

KEYWORDS: Augmentation index, reflection index, cardiovascular disease, Shilajit.

INTRODUCTION

Cardiovascular disease (CVD) is the number one cause of death globally.[1] Smoking, hypertension, high LDL cholesterol, low HDL cholesterol and diabetes mellitus are the five major risk factors for CVD.[2] Diabetes is associated with an increased risk of atherosclerosis, which may result in coronary artery disease.[3] Physiological changes seen in Diabetes mellitus (DM) patients, include platelet hyper-reactivity, a tendency for negative arterial remodelling, impaired fibrinolysis, increased inflammation, and endothelial dysfunction.

Endothelial dysfunction is the cause of atherogenesis and associated with late-stage adverse outcomes.[4] This endothelial dysfunction results from reduced bioavailability of the vasodilator nitric oxide (NO) mainly due to accelerated NO degradation by reactive oxygen species.[5] The superoxide production due to oxidative stress is the common pathogenic factor in development of diabetes mellitus and complications associated with DM. Most of the therapies aimed at reducing stress would benefit patients with type 2 DM and those at risk for developing diabetes.[6,7,8]

Many herbs possess potent antioxidant, anti-inflammatory and cardio-protective properties and are used by patients with increased risk of cardiovascular morbidity and mortality. Shilajit, a natural rock exudate containing various bioactives, finds extensive use in Ayurveda for diverse clinical conditions. The active constituents of Shilajit include dibenzo-alpha-pyrones and related metabolites, small peptides (constituting non-protein amino acids), some lipids and carrier molecules (fulvic acids).[9,10,11] For centuries people living in the isolated villages in Himalayas and adjoining regions have used Shilajit alone or in combination with other plant remedies to prevent and combat problems with diabetes.[12] Also, being an antioxidant Shilajit prevents damage to the pancreatic islet cell induced by the cytotoxic oxygen radicals.[13,14]

It has been proposed that the derangement of glucose, fat and protein metabolism during diabetes results into the development of hyperlipidemia.[15] In a study, Shilajit produced significant beneficial effects in lipid profile in diabetic rats by reducing total cholesterol, triglycerides and increasing HDL significantly.[16] But very less information is available about the effects of Shilajit in human diabetic patients. Therefore the present study was planned to evaluate the effect of Shilajit on endothelial function in type 2 diabetes mellitus patients and to further study the probable mechanism of action.
Objective
1). To evaluate the effect of Shilajit on endothelial function in type 2 diabetes mellitus patients and to further study the probable mechanism of action.
2). To study the biomarkers responsible for endothelial dysfunction with change in levels of free radical and inflammatory biomarkers (hsCRP).
3). To evaluate the safety and tolerability of study medications.

Materials and Methods
This was a prospective, randomized, double blind multi-dose, cross-over, placebo controlled study conducted after approval of the Institutional Ethics Committee of Nizam’s Institute of Medical Sciences (NIMS), Hyderabad, India. All subjects gave written informed consent prior to participation in the study.

Study participants
A total of 50 patients were screened for eligibility to participate in this study. Forty patients of either sex, aged 18-75 years were screened for their eligibility to participate in the study with complete medical history, physical examination, hematological and biochemical screening, electrocardiogram and chest X-ray. Patients of either sex, aged 18-75 years, with fasting plasma glucose of ≥110 mg/dl, a glycosylated haemoglobin (HbA1c) between 7 % and 9 % and taking stable dose of anti diabetic treatment (Metformin 1500-2500mg/day) for the past 8 weeks prior to the screening visit and having endothelial dysfunction defined as ≤ 6% change in reflection index (RI) on post salbutamol challenge test were included in the study. Patients with severe uncontrolled hyperglycaemia, uncontrolled hypertension, cardiac arrhythmia, impaired hepatic or renal function, history of malignancy or stroke, smoking, chronic alcoholism, any other serious disease requiring active treatment and treatment with any other herbal supplements, were excluded from the study. The subjects were excluded from study if there was any evidence of physical illness, drug abuse or abnormal laboratory parameters.

Eligible subjects were trained on the test procedure on two prior occasions to make them familiar with the testing device and test procedure. All the recordings were carried out in the morning between 7.30 am and 10:00 am after a light breakfast.

Study medication
The study medications included capsules of Shilajit (250 mg strength) and placebo. Each Shilajit 250mg capsule consisted of purified aqueous extract of rock exudates containing dibenzo-ɑ-pyrones, dibenzo-ɑ-pyrene chromoproteins and fulvic acids as bioactives. Purified Shilajit was manufactured by a totally aqueous extraction process using raw material obtained from the Himalayas at about 10,000 feet altitude. After multiple extractions and removal of heavy metals, the liquid extract was dried by rotary vacuum drying and milled to specified particle size.

Each placebo capsule contained microcrystalline cellulose (49.7% w/w), lactose (49.5%) and magnesium stearate (0.69% w/w). Both study medications were supplied by Natreon, Inc USA.

Study Procedure
After screening, all the eligible subjects were randomized to receive either one of the two treatments for a duration of 12 weeks. Subjects in Group1 received one capsule of Shilajit 250mg twice daily and subjects in Group 2 received one capsule of placebo twice daily. Subjects were asked to review for follow up visits at 4, 8 and 12 weeks of therapy. At each visit they were evaluated for efficacy and safety. Pharmacodynamic evaluation for endothelial function was conducted at every visit. Blood sample was collected for evaluation of biomarkers before and at end of treatment. Safety lab investigations for haematological, hepatic and renal biochemical parameters were conducted before and at the end of the study and also as and when required. Subjects were enquired for the presence of any ADRs and the same was recorded in the case report form. Compliance to therapy was assessed by pill count method.

Procedure for Assessment Of Endothelial Function
A salbutamol challenge test employing digital volume plethysmography was used to assess endothelial function as reported by Chowienczyk et al.[17] and Naidu et al.[18]. The patients were examined in supine position after 5 minutes of rest. A digital volume pulse (DVP) was obtained using photo plethysmograph (Pulse Trace PCA2, PT200, Micro Medical, Gallingham, Kent, UK) transmitting infra red light at 940 nm, placed on the index finger of right hand. The signal from the plethysmograph was digitized using a 12 bit analogue to digital converter with a sampling frequency of 100 Hz. DVP waveforms were recorded over 20 second period and the height of the late systolic / early diastolic portion of the DVP was expressed as a percentage of the amplitude of the DVP to yield the reflection index (RI), as per the procedure described in detail by Millasseau et al.[19] After DVP recordings had been taken, three measurements of reflection index (RI) were calculated and the mean value was determined. Subjects were then administered 400μg of salbutamol by inhalation. After 15 minutes three measurements of RI were obtained again and the difference in mean RI before and after administration of salbutamol was used for assessing endothelial function. A change of ≤ 6% in RI post salbutamol was considered as endothelial dysfunction.

Measurement of wave reflection indices
Arterial stiffness was measured by using a validated, commercially available system (SphygmoCor; AtCor Medical, Australia) that employs the principle of applanation tonometry and appropriate acquisition and analysis software for non-invasive recording and analysis of the arterial pulse. Augmentation index (AIx) and augmented pressure of the central (aortic) pressure waveforms were measured as indices of wave reflections. The AIx is a composite measure of the magnitude of wave reflections and arterial stiffness, which affects timing of wave reflections. Because the augmentation index is influenced by changes in heart rate (HR), it was also accordingly corrected. The central (aortic) arterial pressure was derived from radial artery recordings, with the use of a generalized transfer function that has been
shown to give an accurate estimate of the central arterial pressure waveform and its characteristics. Waveforms of radial pressure were calibrated according to sphygmonomanometric systolic and diastolic pressure measured in the brachial artery because there is practically negligible pressure pulse amplification between the brachial and the radial artery. The subendocardial viability index, an indicator of myocardial workload and perfusion (O₂ supply vs. demand) was calculated as the ratio of the integral of diastolic pressure and time to the integral of systolic pressure and time.

Brachial-ankle pulse wave velocity (baPWV) was also used to evaluate arterial stiffness. Pulse wave velocity is the speed at which the blood pressure pulse travels from the heart to the peripheral artery after blood rushes out during contraction. It is mainly used to evaluate stiffness of the artery wall. Pulse wave velocity increases with stiffness of the arteries. The PTT (Pulse Transit Time) of each segment is calculated from the waveform taken from each sensor. It calculates heart-brachial PWV of both upper limbs, heart-ankle PWV of both lower limbs, brachial-ankle PWV of both right and left limb pairs and effective estimated carotid-femoral PWV is calculated.

Brachial Ankle Pulse Wave Velocity (baPWV), Ankle Brachial Index (ABI) and Blood Pressure (BP) were measured using an automatic waveform analyzer (BP-203 RPE; Colin, Japan). Measurements were taken with patients lying in a supine position after 5 minutes of rest in that position. Pressure waveforms of the brachial and tibial arteries were then recorded simultaneously by an oscillometric method. Measurement of right and left baPWV was obtained for an average of 10 seconds. The average of left and right baPWV was used for analysis.

**Method for recording of Cardiac output (Lt/min)**

Recording of cardiac output was performed using L&T Nivomon monitor, that works on the features of impedance plethysmography principle.

**Biomarker evaluation**

Nitric oxide, Malondialdehyde (MDA) and Glutathione levels were estimated spectrophotometrically and hsCRP (high sensitivity C-reactive protein) by ELISA method.

After the baseline test measurements, the subjects were discharged with study medications for 12 weeks and were instructed to take 2 capsules twice daily with 240 ml of water. The same test procedure was again repeated after 12 weeks of treatment to obtain post treatment values. Samples were collected after an overnight fast of 12hrs after the last dose of medication for determination of haemoglobin, HbA1c, blood urea and serum creatinine, liver function test and lipid profile. A washout period of 10 days was given between the treatments. Subjects were then crossed over to receive the second formulation of 2 capsules twice daily for 12weeks for Run II. All the test procedures described for Run I were repeated pre and post treatment.

**Efficacy Parameters**

The primary efficacy measure was a change in endothelial dysfunction as assessed by more than 6% change in reflection index at 12 weeks in all the treatment groups. Secondary efficacy measures included change in oxidative stress markers, serum levels of nitric oxide at 12 weeks in all the treatment groups and also evaluation of safety and tolerability of the test medications.

**Safety Assessments**

All the subjects had undergone complete physical examination, safety lab evaluations at baseline and at the end of the treatment.

**Statistical Analysis**

Data was expressed as mean ± SD. Paired and unpaired t-tests were performed for within group and between groups analysis, respectively. A p-value < 0.05 was considered to be statistically significant. All statistical analysis was performed using the Graphpad Prism 5, Sandiego, CA, USA.

**Results**

A total of 50 subjects were screened and 40 eligible subjects, 20 each in Shilajit 250mg and placebo groups completed the study. The demographic characteristics of both the groups are shown in Table 1. There was no significant difference between treatment groups in the baseline characteristics.

### Table 1: Demographic characteristics of the two study Groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Shilajit (A)</th>
<th>Placebo (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No.</td>
<td>n=20</td>
<td>n=20</td>
</tr>
<tr>
<td>Gender(M/F)</td>
<td>16/4</td>
<td>14/6</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>54.85±9.32</td>
<td>55.75±7.62</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>64.01±9.23</td>
<td>64.35±6.46</td>
</tr>
<tr>
<td>BMI(Kg/m²)</td>
<td>24.68±2.93</td>
<td>24.70±2.42</td>
</tr>
</tbody>
</table>

### Table 2: Effect of Shilajit and Placebo on pharmacodynamic parameters after 12 weeks of treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Shilajit (A)</th>
<th>Placebo (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RI (%)</td>
<td>-2.29±1.43</td>
<td>144.54±12.93</td>
</tr>
<tr>
<td>Aix (%)</td>
<td>145.3±24.89</td>
<td>145.3±24.89</td>
</tr>
<tr>
<td>SEVR (%)</td>
<td>1.05±0.07</td>
<td>1569±194.09</td>
</tr>
<tr>
<td>ABI</td>
<td>1525±136.2</td>
<td>1525±136.2</td>
</tr>
<tr>
<td>PWV(cm/s)</td>
<td>4.76±1.02</td>
<td>4.76±1.02</td>
</tr>
<tr>
<td>SVR (dyne.sec/cm²)</td>
<td>1564±437.67</td>
<td>1564±437.67</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Shilajit (A) (n=20)</th>
<th>Post-treatment</th>
<th>Absolute Change</th>
<th>Mean Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>RI (%)</td>
<td>-8.61±2.70</td>
<td>-6.32±2.54</td>
<td>-273.9±92.85</td>
</tr>
<tr>
<td>Aix (%)</td>
<td>139.30±10.30</td>
<td>-5.24±8.40</td>
<td>-3.36±5.47</td>
</tr>
<tr>
<td>SEVR (%)</td>
<td>150.9±24.08</td>
<td>5.55±10.76</td>
<td>4.28±8.51</td>
</tr>
<tr>
<td>ABI</td>
<td>1525±136.2</td>
<td>0.017±0.09</td>
<td>3.95±9.20</td>
</tr>
<tr>
<td>PWV(cm/s)</td>
<td>1569±194.09</td>
<td>-43.75±148.9</td>
<td>-1.06±9.47</td>
</tr>
<tr>
<td>SVR (dyne.sec/cm²)</td>
<td>4.76±1.02</td>
<td>0.2±0.41</td>
<td>1.09±9.36</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Placebo (B)</th>
<th>Post-treatment</th>
<th>Absolute Change</th>
<th>Mean Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>RI (%)</td>
<td>144.54±12.93</td>
<td>-5.24±8.40</td>
<td>-3.36±5.47</td>
</tr>
<tr>
<td>Aix (%)</td>
<td>145.3±24.89</td>
<td>5.55±10.76</td>
<td>4.28±8.51</td>
</tr>
<tr>
<td>SEVR (%)</td>
<td>1.05±0.07</td>
<td>0.017±0.09</td>
<td>3.95±9.20</td>
</tr>
<tr>
<td>ABI</td>
<td>1525±136.2</td>
<td>-43.75±148.9</td>
<td>-1.06±9.47</td>
</tr>
<tr>
<td>PWV(cm/s)</td>
<td>1569±194.09</td>
<td>0.2±0.41</td>
<td>1.09±9.36</td>
</tr>
<tr>
<td>SVR (dyne.sec/cm²)</td>
<td>4.76±1.02</td>
<td>0.2±0.41</td>
<td>1.09±9.36</td>
</tr>
</tbody>
</table>

**Safety Assessments**

All the subjects had undergone complete physical examination, safety lab evaluations at baseline and at the end of the treatment.
Available online at: [http://ijapr.in](http://ijapr.in)
Treatment with Shilajit significantly reduced total cholesterol (p<0.01), LDL-cholesterol (p<0.0), triglycerides (p<0.001), VLDL-cholesterol (p<0.05) and HbA1c (p<0.001) levels and increased HDL-cholesterol (p<0.05) at the end of 12 weeks, compared to baseline (Table 4). When compared to placebo, treatment with Shilajit for 12 weeks produced a favourable lipid profile and improved HbA1c levels, as observed by the significant differences in absolute change and mean percentage change of metabolic parameters in the two treatment groups.

**Safety**

At post treatment, there were no significant changes in vital, hematological, renal and hepatic functions. Three patients in Shilajit treatment group complained of headache mild in intensity and two with dyspepsia in placebo group. Both the treatments were well tolerated. There was no serious adverse event recorded in the study.

**DISCUSSION**

Type 2 diabetes is a global epidemic and studies have revealed an associated two- to fourfold increased risk of cardiovascular disease. This has been attributed to the adverse effects of hyperglycemia and oxidative stress on vascular biology. Also, patients with impaired fasting glucose and impaired glucose tolerance are at increased risk of cardiovascular disease.\(^2^0\) One of the important risk factors for the development of cardiovascular pathology is endothelial dysfunction. The physiology of endothelium has been actively researched in the last few years and evidence suggests that endothelium has an important role in regulating vascular tone and structure. A healthy endothelium has been shown to inhibit platelet and leukocyte adhesion to the vascular surface thus maintaining a balance of profibrinolytic and prothrombotic activity.\(^2^1\) Endothelial dysfunction, which refers to an impairment of the ability of the endothelium to properly maintain vascular homeostasis, \(^2^2\) significantly contributes to the pathogenesis and clinical manifestation of atherosclerosis and has been linked to Type 2 diabetes mellitus and insulin resistance in experimental and clinical studies.\(^2^3\)

The characteristic feature of endothelial dysfunction is reduction of the bioavailability of vasodilators, especially nitric oxide (NO), and an increase in endothelium-derived contracting factors.\(^2^4\) This leads to an impairment of endothelium-dependent vasodilation and development of a specific state of endothelial activation, resulting in pro-inflammatory, proliferative, and pro-coagulatory states that favour all stages of atherogenesis.\(^2^5\) Thus, endothelial function may serve as a marker of an unfavourable cardiovascular prognosis.\(^2^6\)

Treatment of endothelial dysfunction includes use of cholesterol lowering drugs, antioxidants, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers, fibrates, thiazolidinediones, estrogen replacement therapy, L-Arginine supplementation, tetrahydrobiopterin, or stimulators of endothelial progenitor cells.\(^2^7, 2^8\)

Studies conducted by the practitioners of Ayurvedic, Chinese and Unani medicine to manage the cardiovascular complications in diabetic patients have indicated that it is rational to use our natural resources along with current therapy to identify inexpensive and safer strategies for managing cardiovascular disease.\(^2^9\) Shilajit is a natural rock exudate that possesses antioxidant activity.\(^3^0\) In this study, we evaluated the effect of Shilajit 250 mg and placebo on endothelial function in patients with type 2 diabetes.

Shilajit treatment for 12 weeks improved the arterial stiffness in patients which was evident by a significant increase in the reflection index (RI) and subendocardial viability ratio (SEVR) and a reduction in augmentation index (Alx), compared to baseline and placebo. Subendocardial viability ratio (SEVR) is an index of myocardial oxygen supply and demand.\(^3^1\) Alx has been shown to be predictive for coronary artery disease.\(^3^2\) The improvement in the parameters of arterial stiffness can be attributed to the cardioprotective property of Shilajit mediated by it’s anti-oxidant effects.\(^3^3\) Experimental studies have further demonstrated the elevation of endogenous antioxidants on treatment with Shilajit.\(^3^3\) Also, Shilajit treatment was shown to have beneficial effect against experimentally induced myocardial necrosis,\(^3^3\) which possibly explains it’s probable beneficial role in coronary artery disease. Interestingly, results from recently concluded experimental studies evaluating the cardioprotective activity of Shilajit indicate that other mechanisms than reinforcements of antioxidant system are involved in the cardioprotective beneficial effect of Shilajit.\(^3^4\)

The effect of Shilajit treatment on oxidative stress biomarker levels was evaluated to elucidate the anti-oxidant activity of Shilajit formulation. There was a significant increase from baseline in the levels of nitric oxide (vasodilatory and anti-oxidant) and glutathione (anti-oxidant) and significant reductions in the levels of malondialdehyde (MDA, oxidative stress marker) and high sensitivity C-reactive protein (inflammatory marker) in patients who were treated with Shilajit for 12 weeks, thus demonstrating the anti-oxidant and anti-inflammatory properties of Shilajit. The anti-oxidant property of Shilajit has been extensively studied under experimental conditions with convincing results.\(^3^5\) Evidence shows that Shilajit is a source of natural antioxidants.\(^3^5\) Further, it has been shown that Shilajit has potent scavenging activity against lipid peroxidation products.\(^3^5\) In our study, Shilajit significantly reduced MDA levels, which is a marker of lipid peroxidation.\(^3^5\) By increasing the levels of nitric oxide, Shilajit has demonstrated inherent vasodilator property that is further possibly responsible for the restoration of imbalance between vasodilator and vasoconstrictor effects of damaged endothelium in diabetes patients. It has also been shown that Shilajit increases glutathione levels when it has been decreased by experimentally induced oxidative stress.\(^3^6\) In our study there was a significant increase in glutathione levels in Shilajit group at the end of 12 weeks. The anti-inflammatory activity of Shilajit has been demonstrated under experimental conditions.\(^3^7\) High sensitivity C reactive protein (HSCRP) is an inflammatory biomarker that is a potent independent predictor of myocardial infarction and stroke in healthy men and women.\(^3^8\) Treatment with Shilajit in our study has significantly reduced the levels of HSCRP, thus...
demonstration anti-inflammatory and cardioprotective properties.

Metabolic indicators including lipid parameters and glycosylated haemoglobin were also evaluated in patients of both study groups. In our study, treatment with \textit{Shilajit} significantly improved the lipid profile and glycemic control at the end of 12 weeks. Studies in experimental models suggest that the beneficial effects of \textit{Shilajit} on lipid profile in subjects with diabetes is due to better glycemic control induced by it.\cite{39} However, direct beneficial effects of \textit{Shilajit} on lipid profile also exist.\cite{39} The most probable mechanism of hypoglycaemic effects of \textit{Shilajit} is its ability to protect pancreatic beta cell function secondary to its anti-oxidant effect.\cite{40} Gupta et al suggested that long-term treatment with \textit{Shilajit} increases the number of \( \beta \)-cells of pancreas (pancreatotropic action), which may result in better sensitivity of pancreatic \( \beta \)-cells with prompt secretion of a large quantity of insulin in response to hyperglycemia.\cite{40} \textit{Shilajit} was well tolerated by patients in our study with no serious adverse events.

\textbf{CONCLUSION}

The purified aqueous extract of \textit{Shilajit} showed significant improvement in endothelial function as evidenced with change in reflection index, SEVR and augmentation index. It also improved other cardiovascular & metabolic parameters and biomarker levels, demonstrating cardioprotective, anti-oxidant, anti-inflammatory, hypoglycaemic and lipid friendly effects. However, further studies are warranted to evaluate these beneficial effects of \textit{Shilajit} in more number of subjects.

\textbf{ACKNOWLEDGEMENTS}

The authors would like to thank Natreon Inc, USA for providing study medications (Shilajit and Placebo) and literature. Authors thank ICMR (New Delhi) for extramural grant to develop test equipments and Dr. I. V. Sranvanti (Ayurvedic Physician) for her expert advice. Authors also thank Mr. N. Muralidhar for helping in carrying out study related procedures.

\textbf{Declarations}

\textbf{Funding:} This study was supported by Natreon Inc., USA.

\textbf{Conflict of Interest:} None declared.

\textbf{REFERENCES}


\textit{Available online at: http://ijapr.in}
Assessment in the coronary flow

Special Reference to Endothelial Dysfunction in Patients with Type 2 Diabetes

of Purified Aqueous Extract of Shilajit in Modifying Cardiovascular Risk with Niranjan K, Ramakanth Cite this article as:

reserve in hypertensives without significant coronary viability ratio as an index of impaired co

Dimitriadis K et al. 

Gaur B, Misra N. 

Gupta SS. Effect of Shilajit, Ficus Bengalensis & ant. Pituitary extract on glucose tolerance in rats. Indian J 


Cite this article as:


*Address for correspondence

Dr Ramakanth G.S.H
Senior Resident,
Department of Clinical Pharmacology and Therapeutics, Nizam’s Institute of Medical Sciences (NIMS), Pun jagutta, Hyderabad, Telangana, India - 500082.
Email: grklinpharma@gmail.com
Mobile: 09703633788