Comparative Antidiabetic Investigation of Talapotaka Churna and Avartaki Churna in STZ-Induced Diabetic Rats

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Abstract

Aim: To compare the antidiabetic effect of Talapotaka Churna and Avartaki Churna in experimental animals.

Materials and Methods: Talapotaka Churna (Avartaki [Cassia auriculata L.], Amalaki [Emblica officinalis G.], Haridra [Curcuma longa L.], and Daruharidra [Berberis aristata]) and Avartaki Churna (C. auriculata L.) were prepared by the standard procedure of Churna Kalpana. Diabetes was induced by streptozotocin (35 mg/kg) solution (intra-peritoneal). After assessment of hyperglycemia as an approximate induction of diabetes, a group of animals (TP300 and AV300) were treated with a dose of 300 mg/kg of Talapotaka Churna and Avartaki Churna each. For treatment comparison, Group III animals were treated with a standard antidiabetic drug, glibenclamide 1 mg/kg. Blood sugar and lipid profile level were estimated biochemically. Results: Talapotaka Churna and Avartaki Churna both reduced fasting blood glucose significantly on various doses in STZ-induced diabetic rats. Talapotaka Churna and Avartaki Churna also showed a reduction in the levels of total cholesterol, triglycerides, low-density lipoprotein-cholesterol, very low-density lipoprotein-cholesterol but it increases the levels of high-density lipoprotein-cholesterol in diabetic rats. Conclusion: Talapotaka Churna and Avartaki Churna have significant antidiabetic and antihyperlipidemic activities in Type 2DM rats, which seem to scientifically validate its traditional uses and might be promising drugs in the therapy of diabetes mellitus and its hyperlipidemic complications.

Key words: STZ, Talapotaka Churna, Avartaki, hyperlipidemia

INTRODUCTION

Diabetes is characterized by increased glucose level and affected metabolic system supported by genetic and lifestyle changes.¹ Noninsulin-dependent diabetes mellitus (Type-2 DM) is associated with damaged β-cell of pancreas leading to decreased insulin productivity² and increased insulin resistance.³ Physiological and biochemical changes were observed in experimentally induced diabetic rodents which were characterized by variation in lipid profile along with glucose level.⁴ Elevated lipid peroxidation, conversion of free fatty acid, formation of triglycerides (TGs), and cholesterol are associated with hyperlipidemias.⁵

Due to various factors involved in DM, there is a need of integrated approach for its management. In this context, medicinal plants have been employed since the inception of Ayurveda to cure chronic disorders such as diabetes.⁶ Prameha/Madhumeha can be considered as DM by different perspectives based on clinical symptoms, and attempts have been made by Ayurvedic physicians and researchers to treat these two entities using classical formulations mentioned in Prameha Chikitsa.⁷ Acharya Vallabhacharya of the 15th century, who wrote “Vaidya Chintamani” a classical text, has quoted the formulation Talapotaka Churna in the

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20th chapter, *Prameha Prakarana*. In Vaidya Chintamani, it is mentioned that *Talapotaka Churna* has “Sarvaprameha hara” property.[9] Kaiyadeva Nighantu, a classical text of *Ayurveda* has elaborately described the *Avartaki* as a *Pramehoghana/Madhumehoghana* plant.[10] Various Siddha and *Ayurvedic* herbo-mineral antidiabetic formulations such as Aavarai Kudineer, SUGNIL, Avarai Panchaga Choornam, Kalpa herbal tea, Diasulin, Diasakthi, and Avaribeej Choornam containing *Avartaki* as major ingredient available in the market.[11]

*Talapotaka Churna* contains *Avartaki*, *Amalaki*, *Haridra*, and *Daruharidra* in a specific ratio 4:2:1:1, respectively. *Avartaki* is a major ingredient of *Talapotaka Churna*. Furthermore, *Kaiyadeva Nighantu* a classical text has mentioned the wide therapeutics of *Avartaki* in *Prameha*. The view of an ancient *Ayurveda* scholar Vallabhacharya for selecting *Avartaki* as a major ingredient of *Talapotaka Churna* is cleared. In this study, an attempt was made to search out the scientific reason behind such permutation and to compare the antidiabetic and antihyperlipidemic activity of *Talapotaka Churna* and *Avartaki Churna* in STZ-induced diabetic rats.

**MATERIALS AND METHODS**

**Collection of plant materials**

The *Talapotaka Churna* contains four ingredients. Among these, *Avartaki* was collected from the peripheral region of Satara District, Maharashtra, India. The rest three raw drug samples (*Amalaki*, *Haridra*, and *Daruharidra*) were procured from Gola Dinanath (Raw drug market), Varanasi, Uttar Pradesh, India.

**Identification of plant materials**

All the collected samples were pharmacognostically identified and confirmed in Department of Dravyaguna, Faculty of Ayurveda, IMS, Banaras Hindu University, Varanasi.

**Churna preparation**

The collected plant materials of *Talapotaka Churna* including *Avartaki Churna* were cleaned and dried in the sunlight. The dried plant material was then ground into a fine powder using a mechanical pulverizer in Ayurvedic Pharmacy, Banaras Hindu University, Varanasi, India. This sample was used for the antidiabetic study.

**Chemicals**

Streptozotocin was sponsored by Department of Rasa-Shastra, Faculty of Ayurveda, IMS, Banaras Hindu University, Varanasi, which was purchased from Himedia Laboratories Pvt. Ltd., Dindori, Nashik, India. Batch number was 000022052, manufacturing date was November 2014, and Expiry date is February 2017. Glibenclamide was purchased from Emcure SANOFI, trade name Daonil (Manufacturing date April 2015 and Expiry date 2016) in India, for use as the standard antidiabetic agent.

**Animals**

Thirty Charles Foster albino rats of either sex weighing between 180 ± 30 g were used for the experimental study. The animals were obtained from the Central Animal House, Institute of Medical Sciences, Banaras Hindu University, Varanasi. The animals were freely allowed to eat pellet chow (Amrut Laboratory Animal Feed, Pranav Agro Industries Limited, Sangali) and ad libitum water during the study periods. Principles of laboratory animal care as per NIH guidelines were always followed and prior approval of Institutional Animal Ethical Committee (Reg. No. Dean/2014-15/EC/1057) of Banaras Hindu University (BHU) was obtained before commencing experiments.[12,13]

**Experimental design**

The experimental study was conducted at the Department of Pharmacology, IMS, BHU. Animals were kept under standard laboratory condition during the study. Thirty animals were divided into five groups, and for each group, six animals were taken.

Group I: Normal control (NC) (vehicle-treated).

Group II: Diabetic control (DC) (vehicle-treated).

Group III: Diabetic rats + standard (glibenclamide 1 mg/kg/day/oral).

Group IV: Diabetic rats + treated with 300 mg *Talapota Churna*.

Group VI: Diabetic rats + Treated with 300 mg *Avartaki Churna*

On day $t = -1$, before induction of hyperglycemia as an approximate induction of DM, the rats were kept fasting from all food; only water was given.

**Preparation of STZ solution**

Immediately before injection, STZ was dissolved in 50 mg of sodium citrate buffer (pH 4.5) to a final concentration of 1 mg/ml. The STZ solution was freshly prepared for each rat and was injected within 5 min after being dissolved.

**Induction of diabetes**

Hyperglycemia was induced (in-Group II to V) by STZ solution intra-peritoneal using a dose of 35 mg/kg through insulin syringes.
Biochemical assay

After 72 h, blood sugar level was measured by Optium Xceed glucometer (Abbott). For investigation of blood glucose, blood of rats was withdrawn through a tail central vein. Hyperglycemia was confirmed by the elevated glucose level in the blood by glucometer, determined after 72 h. On the 7th day after confirmation of hyperglycemia, animals of Groups IV (TP300) and V (AV300) were treated with Talapotaka Churna 300 mg/kg and Avartaki Churna 300 mg/kg, respectively. Animals of Group III were treated with hypoglycemic drug glibenclamide 1 mg/kg. Glibenclamide stimulates the pancreatic beta cells of the pancreas and increasing the sensitivity of the peripheral tissue to insulin. Data of blood sugar were collected every 7th day of duration for 4 weeks and compared among groups.

Dose schedule

Thirty Charles Foster rats were divided into five groups, namely NC (Group I), DC (Group II), standard group treated with glibenclamide in dose of 1 mg/kg body weight (Group III), and treated group with Talapotaka Churna (Group IV) and Avartaki Churna (Group V) in the doses of 300 mg/kg body weight each. The test drugs Talapotaka Churna and Avartaki Churna; standard drug glibenclamide were administered according to the body weight of the animal by oral route with the help of intragastric tube.

Statistical analysis

Statistical analysis of data was performed using SPSS 16.0 and one-way analysis of variance (ANOVA). The results were expressed as a mean ± standard deviation from six rats in each group. P < 0.05 was considered statistically significant and <0.001 were considered highly significant in the results of this study.

RESULTS [TABLE 1]

In this study, antidiabetic effect of Avartaki and Talapotaka Churna was accessed and treatment groups show significant effect on diabetic rats. Table -1 refers to differed study groups with treatment plans. Five groups were taken for this study and diabetes induced by STZ.

Blood glucose

Results are expressed as mean ± standard deviation (SD) (n = 6). The data were analyzed using One-way ANOVA followed by Dunnett's test (*P < 0.05, **P < 0.001 vs. control).

Hyperglycemia was significantly induced compared to NC fasting blood glucose after 72 h and was confirmed on the 7th day following STZ administration [Figure 1].

Blood sugar level was reduced significantly in Groups IV (TP300) and V (AV300) as compared to Group II (DC) [Figure 2]. Talapotaka Churna (TP300) and Avartaki Churna (AV 300) produced a maximum reduction of blood glucose of 54.59% (P < 0.001) and 57.11% (P < 0.001) 1 h, respectively [Figure 2].

In a 4 weeks study, Talapotaka Churna (TP300) and Avartaki Churna (AV300) produced a significant reduction in blood glucose compared to glibenclamide as shown in Table 2. Glibenclamide (1 mg/kg) produced a maximum reduction of 63.36% (1 h, P < 0.001) compared to DC Group II [Figure 3, Tables 3 and 4].

The results are expressed as mean ± SD (n = 6). The data were analyzed using One-way ANOVA followed by Dunnett’s test (*P < 0.05, **P < 0.001 vs. control).

Table 1: Groups and treatment

<table>
<thead>
<tr>
<th>Groups</th>
<th>Treatment</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal control (normal saline)</td>
<td>1 ml/100 g</td>
</tr>
<tr>
<td>II</td>
<td>Diabetic control (STZ)</td>
<td>35 mg/kg</td>
</tr>
<tr>
<td>III</td>
<td>Glibenclamide (standard)</td>
<td>1 mg/kg</td>
</tr>
<tr>
<td>IV</td>
<td>Talapotaka Churna</td>
<td>300 mg/kg</td>
</tr>
<tr>
<td>V</td>
<td>Avartaki Churna</td>
<td>300 mg/kg</td>
</tr>
</tbody>
</table>

Figure 1: The effect on fasting blood sugar in streptozotocin-induced albino rats, where values are given as mean ± standard deviation (n = 6 in each group). Values are statistically significant at P < 0.05, P < 0.001 compared with normal control group

Figure 2: The effect of dose of Talapotaka Churna and Avartaki Churna on fasting blood sugar in streptozotocin-induced albino rats, where values are given as mean ± standard deviation (n = 6 in each group). Values are statistically significant at P < 0.05, P < 0.001 compared with diabetic control group
The effect of *Talapotaka Churna*, *Avartaki Churna* and glibenclamide on Lipid profile has been shown in Figure 4.

**DISCUSSION**

DM is such a worldwide problem, whose solution still remains within the queue of medical scientific progress. Developed medical science is searching alternative therapies to treat a disorder like DM. As multiple factors involved in the pathology of DM, it is somewhat difficult to treat by single drug remedy. Ayurvedic herbal drug remedies are very well known for their different wide range therapeutic actions due to numerous phytoconstituents. Efficacy of phytotherapy depends on mixture of substances constituting the medicinal plants, also the polyherbal formulations composed of many ingredients having specific time proven therapeutic values.[15]

The treatment with *Talapotaka Churna*, *Avartaki Churna* and glibenclamide lowered elevated blood glucose level, which was high in DC animals. Within the first week, maximum reduction in the blood glucose level was noted with *Avartaki Churna*. While during next 3 weeks, blood glucose level was gradually decreased with *Talapotaka Churna* and glibenclamide. *Talapotaka Churna*, *Avartaki Churna* and glibenclamide significantly decreased the serum lipids level.
Talapotaka Churna is a poly-herbal formulation containing Avartaki as a major ingredient along with other three herbs, each reported in the Ayurvedic classics to have the action of reducing Prameha. These herbs have also been studied in modern science and showed a significant reduction in blood glucose levels and antihyperlipidemic activity in DM animal models. Gupta et al. found that Cassia auriculata leaf extract has insulinogetic action in streptozoatin-induced diabetic rats. Latha et al. found C. auriculata L. flower extract suppresses enhanced gluconeogenesis and enhances utilization of glucose through increased glycolysis in streptozotocin-induced diabetic rats. Abesundara et al. showed that C. auriculata flower extract exerts a strong antihyperglycemic effect in rats comparable to the therapeutic drug acarbose. Venkatchalam et al. found that an aqueous extract of flowers of C. auriculata has PTP-1B inhibitory activity in alloxan-induced diabetic rats. Brahmacahari et al. showed that aqueous extract of the whole plant of C. auriculata has hypoglycemic effect in STZ-induced diabetic rats. Uma Devi et al. found the hypolipidemic effect of aqueous extract of flowers of C. auriculata in alloxan induced diabetic rats. Pari et al. showed that an aqueous extract of C. auriculata flowers has preventive effects on lipid peroxidation in rats treated with streptozotocin. Gupta et al. showed the hypolipidemic activity of aqueous extract of C. auriculata leaves in experimental diabetes. Patel et al. found fruit juice of Emblica officinalis showed decreased glucose level by enhancing insulin sensitivity and inhibit the production of reactive oxygen species by elevating the levels of antioxidant enzymes in diabetic heart. Kumar et al. found fruit juice of E. officinalis (mixed with fresh bitter gourd juice) stimulate the islets of Langerhans. Jacob et al. found that dry powder of E. officinalis has antihyperlipidemic effect in men aged 35-55 years. Tirgar et al. showed fruit juice of E. officinalis improves deranged lipid metabolism in STZ induced Type-I DM in rats. Qureshi et al. reported that aqueous extract of E. officinalis fruit possess hypoglycemia in action in alloxan-induced diabetic rats. Santoshkumar et al. showed antidiabetic effects of aqueous extract of Curcuma longa rhizome in alloxan-induced diabetic rats. Krishnaswamy found C. longa has increased plasma insulin and hepatic glycokine activity levels in STZ-induced diabetic rats. Rezq found that curcumin has pancreatic islet regeneration capacity in STZ-induced diabetic rats. Pari et al. reported that curcumin present in C. longa possess antihyperlipidemic effect in experimental type 2 diabetic rats. Soudamini et al. found the hypolipidemic effect of curcumin in type 2 diabetic-induced mice. Singh et al. showed berberine reduces blood sugar by inhibiting absorption of sugars from the intestine. Furthermore, enhances production of insulin. It lowers elevated blood total cholesterol, LDL cholesterol, TGs, and atherogenic apolipoproteins. Mall et al. found root bark powder of Berberis aristata stimulates pancreas to secret insulin. Upwar et al. reported hypolipidemic activity of methanolic extract of B. aristata dc stem on normal and streptozotocin-induced diabetic rats.

All ingredients of Talapotaka Churna including Avartaki have different phytochemicals. It is believed that the basis of the chemical constitution of different herbal drugs and various medicinal/plant extracts contain active flavonoids, alkaloids, phenolic compounds, terpenoids, saponins, and phytosterol type chemical constituents that are effective in the management of diabetic complications. This effect might be attributed to the amelioration of persistent hyperglycemia, oxidative stress, deranged lipid metabolism, and modulations of the various metabolic pathway involved in the pathogenesis of diabetic complications.

In our study, Avartaki Churna showed sudden fall in blood glucose level in the 1st week of 28 days study as compared to Talapotaka Churna and glibenclamide which reported gradual decrease in blood glucose level in succeeding weeks. Talapotaka Churna and Avartaki Churna showed a significant decrease in blood sugar level along with antihyperlipidemic activity both compared to a diabetic non-treated control group and to a group treated with a standard anti-diabetic drug, glibenclamide in an animal model. This study attempts to show that the mode of action of Talapotaka Churna as a polyherbal drug and Avartaki Churna as a single herbal drug may be similar to the mode of action of glibenclamide, i.e., by stimulating the pancreatic beta cells of the pancreas and increasing the sensitivity of the peripheral tissue to insulin.
CONCLUSION

Avartaki Churna and Talapotaka Churna showed significant hypoglycemic and hypolipidemic activity in experimental animals induced by STZ. Talapotaka Churna reduced blood sugar level gradually. However, there is need to evaluate antidiabetic effect in vivo and clinical level to determine effects of the drug.

Future prospects

Ayurvedic polyherbal drugs are gaining popularity because of several advantages such as fewer side-effects, better patient tolerance, relatively less expensive, and acceptance due to a long history of use. The more important cause is that herbal medicines provide rational means for the treatment of many diseases which are incurable and obstinate in other systems of medicine.[45]

REFERENCES


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