ejpmr, 2022, 9(4), 418-422

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

IN VITRO ANTIDIABETIC AND ANTI-INFLAMMATORY ACTIVITY OF METHANOLIC AND AQUEOUS EXTRACTS OF *SCHEFFLERA ARBORICOLA*

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Article Received on 20/02/2022 **Article Revised on 10/03/2022** **Article Accepted on 30/03/2022**

ABSTRACT

The nature has provided abundant plant wealth for all the living creatures, which possess medicinal virtues. Therefore, there is a necessity to explore their uses and to ascertain their therapeutic properties. **Objective:** The objective of the present study was carried out to evaluate the *in vitro* antidiabetic and anti-inflammatory activity of methanol and aqueous extracts of leaves and stems of *Schefflera arboricola*. **Materials and methods:** Antidiabetic activity was determined by α-amylase inhibition assay, here acarbose used as a positive control and *in vitro* anti-inflammatory activity by albumin denaturation method, standard drug for anti-inflammatory activity was diclofenac sodium. The absorbance values were measured spectrophotometrically at 405 nm. **Results:** The results suggests that the dose dependent α-amylase inhibition percentage of methanol leaf from 1.53 - 72.43 µg/mL, aqueous leaf from 0.51 - 50.05 µg/mL, methanol stem from 1.22 - 79.96 µg/mL and aqueous stem from 0.10 - 72.84 µg/mL as compared to acarbose at sequential concentrations. Further results found that methanol leaf, methanol stem, aqueous leaf and aqueous stem extracts at concentration from 20 - 120 µg/mL showed inhibition of albumin denaturation was 11.46% - 71.90%, 6.12% - 84.77%, 5.65% - 55.89% and 0.47% - 76.30% respectably, as compared with standard diclofenac. **Conclusion:** The findings showed that the maximum α-amylase inhibition activity as well as albumin denaturation activity of *Schefflera arboricola* was observed in methanol stem, hence the extract can be a potential source of antidiabetic and anti-inflammatory agent.

KEYWORDS: *Schefflera arboricola*, Antidiabetic activity, Anti-inflammatory activity, Alpha amylase inhibition assay, Albumin denaturation assay, Acarbose, Diclofenac.

INTRODUCTION

Diabetes is a disease caused by the malfunctioning of the hormone insulin. The term diabetes refers to a whole group of diseases, all characterized by the unusual thirst, and in consequence, an unusual output of urine. Ordinarily the body most of its glucose in liver in the form of glycogen keeping a small quantity of glucose in the bloodstream to serve the immediate energy needs of the cell. Maintaining this level of glucose is insulin work. Diabetes mellitus is a heterogeneous metabolic disorder characterized by altered carbohydrate, fat and protein metabolism[1], resulting pancreatic insulin deficiency in all age groups of human being all over the world. Treatment of diabetes involves lowering blood glucose through different mechanisms, including insulin secretion, glucose absorption, and metabolism.[2] The number of people in the world with diabetes has increased dramatically over recent years. It is also predicted that by 2030 in India, China and the United states will have the largest number of people with diabetes.[3] Some hypoglycemic drugs such as metformin, rosiglitazone, proglitazone, biguanide and sulfonylurea are used clinically in the treatment of diabetes.[4] The empagliflozin, insulin Icodec and tirzepatide are the recent drugs for treatment of diabetes. These drugs may have adverse side effects and may lose their effectiveness in long diabetic treatment. Recently natural compounds of plant origin are gaining attention in place of chemical drugs to cure diabetes.[5] The World Health Organization (WHO) also recommended the traditional phytomedicines for diabetes treatment. The diabetic patients prefer to use natural plant products with antidiabetic activity.[6] Natural foods are replacing the drugs to control diabetes and its complications.[7]

Inflammation is a normal response of the body to protect tissues from infection, injury or disease. The inflammatory response beings with the production and release of chemical agents by cells in the infected, injured or diseased tissue. These agents cause redness (Rubor), swelling (Tumor), pain (Dolor), heat (Calor) and loss of function (Functio laesa). This inflammatory response usually promotes healing but, if uncontrolled, may become harmful. Conventional anti-inflammatory

drugs are either non-steroidal or steroidal in nature. The non-steroidal anti-inflammatory drugs (NSAIDs) such as Aspirin, Indomethacin and Ibufrogen inhibit early steps in the pathway of prostaglandins by inhibition of cyclooxygenase enzymes. These drugs are used to reduce the outward consequences of inflammation.[8] For instance, use of NSAIDs associated with several serious adverse effects like gastric injury and ulceration, renal damage and bronchospasm due to their non-selective inhibition of both isoforms of the Cyclooxygenase (COX) enzyme.[9] In the current scenario, Several plants like *Lawsonia inermis*, *Cassia fistula*, *Phyllanthus emblica*, *Lantana camara* contained Curcumin, Bromelain, Epigallocatechin that have been reported for their potent anti-inflammatory activity.[10] The anti-inflammatory activity of most the plants in attributed to the presence of polyphenols in them.[11] The investigations of the efficacy of plant based drugs used in the traditional medicine have great interest owing to their lesser side effects.

Schefflera arboricola is a species of flowering plant from Araliaceae family, native to Taiwan, it is a popular indoor plant, because of its tolerance to various poor growing conditions, and also grown in outdoor plant. Previously *S. arboricola* Hayata is used as a folk medicine for treatment of pain, rheumatic arthritis, fracture, sprain and traumatic bleeding in the southern provinces of China. Previous phytochemical study on leaves of *S. arboricola* has led to isolation of triterpene glucosides.[12] It has been reported that the ethyl acetate extraction of this crude drug exhibited potent inflammatory and analgesic activities.[13]

The objective of the present work is to study the *in vitro* antidiabetic and anti-inflammatory activity of *Schefflera arboricola* (Hayata) Merr. by alpha amylase and albumin denaturation assays.

MATERIALS AND METHODS

Plant material

Leaves and stems of *Schefflera arboricola* (Hayata) Merr. of family Araliaceae were collected at Acharya Nagarjuna University and authenticated by the taxonomist, Department of Botany, Acharya Nagarjuna University, Nagarjuna Nagar, Guntur, on January-18-2018. Collected plant materials were then cleaned with fresh water for to eliminate dirt and other pollutants, and dried for several days with periodic sun drying, dried samples were grind into rough powder by a grinding machine and stored in an air tight container at room temperature 40°C for extraction.

Chemicals

2-Chloro-4-nitrophenyl-α-D-maltotrioside (CNPG3), Acarbose, Dimethylsulfoxide (DMSO), Porcine pancreative α-amylase (PPA). Bovine serum albumin, 1N HCl, Diclofenac sodium and all other reagents used were of LR grade purchased from Merk chemicals PVT LTD, Mumbai, India.

Plant extraction

25 g of each sample, was uniformly extracted with 100 ml quantity of solvents (methanol and aqueous) in soxhlet extractor. The process continues till the solvent in siphon tube of an extractor become colorless. The extracts were taken in a beaker and kept it for air dry till the solvent got evaporated. Dried extracts were refrigerator at 40°C for their future use in phytochemical studies.

Alpha amylase inhibition assay

In-vitro α-Amylase inhibition activity of all extracts was determined based on the spectrophotometric assay using acarbose as the reference compound.[14] The extracts were dissolved in DMSO to give concentrations from 5 to 150 µg/ml. The enzyme α- amylase solution was prepared by mixing of α- amylase in 50 ml of 40 mmol/L phosphate buffer, pH 6.9. Positive control, acarbose was obtained by dissolving in phosphate buffer. The assay was conducted by mixing 80 µL of methanol leaf extract, 20 µL of α-amylase solution and 1 ml of 2- chloro-4-Nitrophenyl-α-D-Maltotrioside. The mixture was incubated at 37°C for 5 min. The absorbance was measured at 405 nm spectrophotometrically. Similarly, a control reaction was carried out without the plant extract/acarbose. The same procedure was followed for all the extracts.

Percentage inhibition was calculated by the expression:
Percentage inhibition = [(Absorbance $_{Control}$ - Absorbance $_{Test}$) / Absorbance $_{Control}$] × 100

Inhibition of albumin denaturation assay

The anti-inflammatory activity of *Schefflera arboricola* was studied using inhibition of albumin denaturation assay which was developed according to Mizushima et al.[15] and Sakat et al.[16] followed with minor modifications. The extracts were dissolved in DMSO solution. 2ml of 1% Bovine serum albumin (BSA) was mixed with 400 µL of methanol leaf extract in different concentrations (20 - 100 µg/ml) and the pH of the reaction mixture was adjusted to 6.8 using 1N HCl. The mixture was incubated at room temperature for 20 min and then heated to 55°C for 20 min in a water bath. The mixture was cooled to room temperature and the absorbance values were recorded at 660 nm. Diclofenac sodium in different concentrations was used as a standard. The experiment was performed in triplicate. The procedure is same for other extracts (aqueous leaf, methanol and aqueous stems extracts).

Percent inhibition was calculated using the following formula:

$$\% \text{ Inhibition} = \frac{\text{Control O.D.} - \text{Sample O.D.}}{\text{Control O.D.}} \times 100$$

Control O.D = Optical density of control
Sample O.D = Optical density of test sample

Statistical analysis: All analysis were performed in triplicate and data were expressed as Mean ± SD. IC_{50}

values were calculated using regression analysis, and the graphs were drawn MS Excel software.

RESULTS AND DISCUSSION

In vitro antidiabetic activity (Alpha-amylase inhibition)

The inhibitory of pancreatic alpha amylase is one of the therapeutic targets for delaying oligosaccharide digestion to absorbable monosaccharides in the intestinal brush border, resulting in reduced postprandial hyperglycemia.[17] Some of the compounds effectively inhibit alpha-amylase activity based on the ability to form quinine with the 4-oxopyrane structure of the enzyme via the hydroxyl group at C-3 and C-4 of ring B. **Table 1** shows the percent of alpha amylase (AA) inhibition by the methanol and aqueous crude extracts, the result showed that methanol leaf, methanol stem, aqueous leaf and aqueous stem extracts were able to inhibit the enzyme by from 1.53 - 72.43, 1.22 - 79.96, 0.51 - 50.05, and 0.10 - 72. 84 µg/mL respectively, the alpha-amylase inhibition (AAI) was not significant as compared with the acarbose but showed that the extracts contained bioactive compounds that can inhibit AA since less starch converted to maltose. The IC_{50} values of standard acarbose leaf, methanol leaf, aqueous leaf, acarbose stem, methanol stem, and aqueous stem extracts were 61.53, 80.07, 135.51, 62.51, 68.36, 77.53µg/ml respectably. Percentage inhibition of all extracts of *S. arboricola* with standard acarbose at different concentrations was shown in **Figure 1.** High percentage amylase inhibition was shown at 79. 96 of methanol stem extract compared with acarbose.

In vitro anti-inflammatory activity (Albumin denaturation inhibition)

Albumin denaturation is a process in which most biological proteins lose their biological function when denatured. As part of the investigation on the mechanism of the anti-inflammatory activity of methanol and aqueous extracts of *Schefflera arboricola*. Inhibition percentage of methanol leaf, aqueous leaf, methanol stem and aqueous stem extracts were ranging from 11.46% - 71.90%, 5.65% - 55.89%, 6.12% - 84.77%, 0.47% - 76.30 % respectively at the concentrations from 20 - 120 µg/ml, as compared to diclofenac from 15.86% - 86.34% and the IC_{50} values of methanol leaf, aqueous leaf, methanol stem and aqueous stem extracts were 89.07, 119.34, 75.92 and 85.32 respectively, and the IC_{50} value obtained for the standard drug was 69.81µg/ml was shown in **Table 2.** Maximum albumin denaturation inhibition of 84.77% observed at 120 µg/ml concentration of methanol stem extract as compared to diclofenac (86.34%) was shown in **Figure 2.**

Table 1: α-amylase activity and IC_{50} of standard acarbose, methanol and aqueous extracts of *Schefflera arboricola.*

Concentration (µg/mL)	% Inhibition					
	Acarbose		Methanol		Aqueous	
	Leaf	Stem	Leaf	Stem	Leaf	Stem
5	7.12 ± 0.01	1.93 ± 0.01	1.53 ± 0.01	1.22 ± 0.05	0.51 ± 0.01	0.10 ± 0.05
10	15.36 ± 0.01	15.36 ± 0.01	9.05 ± 0.01	12.61 ± 0.02	4.68 ± 0.04	7.93 ± 0.05
15	23.80 ± 0.01	23.80 ± 0.01	17.29 ± 0.01	21.06 ± 0.01	12.41 ± 0.01	18.51 ± 0.01
20	35.40 ± 0.01	35.40 ± 0.01	28.99 ± 0.01	30.72 ± 0.01	17.29 ± 0.01	27.98 ± 0.01
25	47.30 ± 0.01	47.30 ± 0.01	39.47 ± 0.01	44.35 ± 0.01	23.80 ± 0.01	40.69 ± 0.01
50	59.92 ± 0.01	59.92 ± 0.01	51.07 ± 0.01	56.77 ± 0.01	33.16 ± 0.01	51.98 ± 0.01
100	74.26 ± 0.01	74.26 ± 0.01	62.26 ± 0.01	69.68 ± 0.01	39.57 ± 0.01	66.63 ± 0.01
150	81.28 ± 0.01	81.28 ± 0.01	72.43 ± 0.01	79.96 ± 0.01	50.05 ± 0.005	72.84 ± 0.01
IC_{50} (µg/mL)	61.53	62.51	80.07	68.36	135.5	77.53

The data are expressed in Mean ± STD, IC_{50} – Inhibitory concentration at 50%

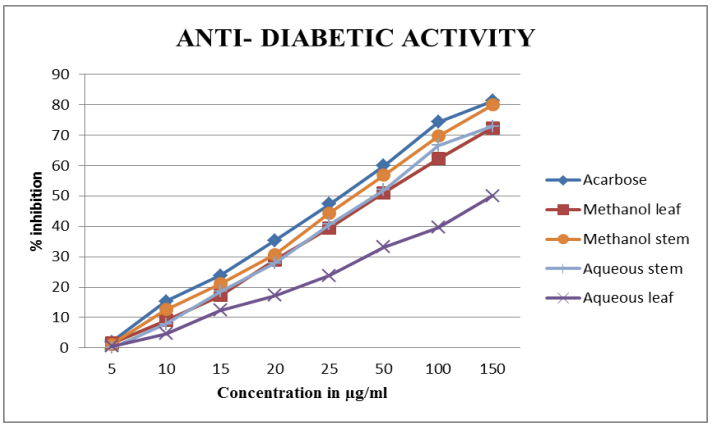

Figure 1: α –amylase percent inhibition of standard acarbose, leaf and stem extracts of *Schefflera arboricola.*

Table 2: Albumin denaturation activity and IC_{50} of standard diclofenac, methanol and aqueous extracts of *Schefflera arboricola.*

Concentration (µg/mL)	% Inhibition of denaturation				
	Diclofenac	Methanol		Aqueous	
		Leaf	Stem	Leaf	Stem
20	15.86 ± 0.01	11.46 ± 0.01	6.12 ± 0.01	5.65 ± 0.01	0.47 ± 0.01
40	27.63 ± 0.01	19.47 ± 0.01	21.98 ± 0.01	6.28 ± 0.01	16.64 ± 0.01
60	44.27 ± 0.01	28.10 ± 0.01	40.03 ± 0.01	13.97 ± 0.01	32.65 ± 0.005
80	57.14 ± 0.01	40.19 ± 0.01	52.75 ± 0.01	22.61 ± 0.01	47.72 ± 0.01
100	69.54 ± 0.01	58.40 ± 0.01	66.88 ± 0.01	41.29 ± 0.01	58.08 ± 0.01
120	86.34 ± 0.01	71.90 ± 0.01	84.77 ± 0.01	55.89 ± 0.01	76.30 ± 0.01
IC_{50} (µg/mL)	69.81	89.07	75.92	119.34	85.32

The data are expressed in Mean ± STD, IC_{50} – Inhibitory concentration at 50%

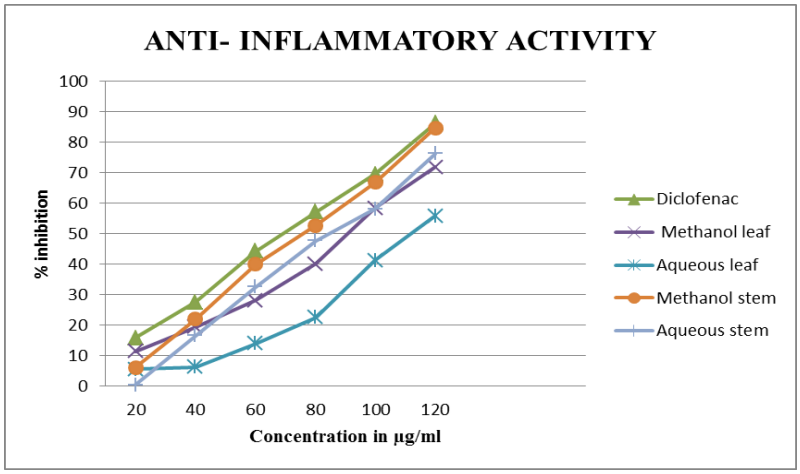

Fig. 2: % inhibition of standard diclofenac and different extracts from leaf and stem of *Schefflera arboricola.*

CONCLUSION

The present study investigated the antidiabetic and anti-inflammatory activity of methanol and aqueous extracts of leaves and stems of *Schefflera arboricola* by *in vitro* methods. Results revealed that all the extracts possess antidiabetic and anti-inflammatory properties at different levels, and this could be due to the differences in the composition and concentration of bioactive compounds. Among the extracts methanol stem extract showed the antidiabetic activity at maximum amylase inhibition of 79.96 µg/mL and anti-inflammatory activity at maximum albumin denaturation inhibition of 84.77%. Finally, it can be concluded that methanol stem extract of *Schefflera arboricola* possess *in vitro* diabetic and inflammatory activities.

CONPETING OF INTERESTS

The authors declare that they have no competing of interests.

ACKNOWLEDGEMENT

The authors are thankful to the Head, Department of Zoology & Aquaculture for providing the necessary facilities to carry out the present work.

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