ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

INHIBITORY EFFECT OF COSTUS IGNEUS LINN (INSULIN LEAF) ON ALPHA AMYLASE, ALPHA GLUCOSIDASE ACTIVITY TO FACILITATE ANTIHYPERGLYCEMIC EFFECT IN TYPE 2 DIABETES MELLITUS

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ARTICLE INFO

Key words:

Diabetes mellitus, acarbose, α glucosidase, Costus igneus, insulin

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Access this article online Website: https://www.jgtps.com/
Quick Response Code:

ABSTRACT

Background: Diabetes Mellitus (DM) is a type of chronic metabolic disorder characterized by a chronic high blood sugar level or hyperglycaemia. The characteristic clinical features are polyuria, polydipsia and polyphagia. The pathophysiology of the common form i.e. type 2 DM is insulin resistance. This component has been addressed by a lot of drugs and herbs. Alpha glucosidase inhibitors like acarbose form a part of pharmacological armamentarium of innumerable drugs. We wanted to try the leaves of costus igneus which are called insulin leaves on the amount of inhibition of Alpha glucosidase. **Methods:** The clean leaves of Costus igneus have been gathered in the month of November 2019 from the local areas of kumbakonam, Tamilnadu, India. The plant was diagnosed and authenticated by the Department of Botany of our university. Leaf extracts and the inhibitory concentrations of extracts of such leaves on α amylase and α glucosidase were analysed**.** The results were compared with the drug acarbose**.** **Results:** On analyses of such leaves, only methanolic extract revealed 20 bioactive compounds. Methanolic leaf extract of *Costus igneus* at concentration ranging from 100 to 500µg/ml was used to find its inhibitory effect on α amylase and α glucosidase. The half-maximal inhibitory concentration (IC 50) value for α amylase and α glucosidase was found to be 273.99µg/ml and 298.03µg/ml which was higher when compared to acarbose. **Conclusion:** The leaf extract of *Costus igneus* can be projected as a substitute to control postprandial hyperglycaemia to acarbose. The study needs to be validated with human studies with such leaf extracts and glycemic control. This is the pioneer study of such comparisons. As there are no major described side effects, a further research on incretins can be propounded.

INTRODUCTION

Diabetes Mellitus (DM) is one of the commonest non–communicable diseases in the world with India reporting the largest number of cases and named as the capital of diabetes. Strict control of DM from its diagnosis is associated with fewer incidences of complications. The control of diabetes is still unsatisfactory in India with a random community level of around 8.9. [1]Even though newer drugs with more specific targets are continuously being

invented, the side effect profile also extends. To circumvent the problem, the age old described plant products with action on the specific problem of type 2 DM is worthy. The type of drugs can be divided according to the target of action like insulin secretagogues, resistance reductors, incretin mimics and DDP 4 inhibitors.[2]The mechanism of action of acarbose and voglibose are known with evidence. Acarbose is a known as a complex oligosaccharide which acts as a competitive yet reversible inhibitor of the enzymes, pancreatic alpha-amylase and intestinal alpha-glucoside hydrolase or familiarly called alpha glucosidase. The most significant single advantage with this group of drugs is the decreased incidence of hypoglycaemia. [3]The *Costus igneus* plant is recently grown in South India as the insulin plant and belongs to the family Costaceae. The extracts of the leaves of the plants have effect on reduction of blood glucose. We wished to understand the mechanism whether these plant extracts have inhibitory action on alpha amylase and alpha glucosidase and thereby exerts its antidiabetic effect.[4,5] This study was aimed to extract the phytochemicals in the leaves of the insulin plant and an in vitro analysis of the antidiabetic effect through the inhibition of the enzymes alpha amylase and aloha glucosidase.

Material and methods:

The clean leaves of *Costus igneus* have been gathered in the month of November 2019 from the local areas of Tamilnadu, India. The plant was authenticated by the Department of Botany of our university. The methanolic, petroleum and aqueous extract of the leaves were prepared by classically described techniques. All the three extracts were subjected to phytochemical constituent screening by the classically described technique by Raman et al.[6]Gas chromatography and Mass spectrometry was done in the specimens described. In vitro α-amylase inhibition assay was carried out by the method of Apostolidis (2007).[7]By a similar method, α-glucosidase inhibitory activity was determined. Control incubations represent 100% enzyme activity and were conducted in a similar way by replacing extracts. The results were compared with acarbose. Acarbose is an antidiabetic drug with enzyme inhibitory activity of both the enzymes. For blank incubation (to allow for absorbance produced by the extract), enzyme solution was replaced by buffer solution and absorbance recorded. Tests were carried out in triplicate for 3 separate experiments. The result was graphically determined by a linear regression method using MS- Windows based graph pad Instat (version 3) software. Results were expressed as graphically/ mean ± standard deviation.

Results:

The petroleum ether extract confirmed the presence of alkaloids, flavonoids, steroids, and glycosides. In the aqueous extract, carbohydrates, protein, flavonoids, and alkaloids were found, while in ethanolic extract alkaloids, flavonoids, glycosides, steroids, and phenolic compounds were present. It was noticed that the ethanolic leaf extract of *Costus igneus* had shown maximum phytoconstituents while compared to aqueous and petroleum ether extract of *Costus igneus*(see Table 1)

Table 1 showing the metabolites of different extracts of *Costus igneus*

Secondary Metabolites	Petroleum Ether Extract	Methanolic Extract	Aqueous Extract
Alkaloids	-	-	+
Flavonoids	-	-	+
Steroids	+	+	-
Glycosides	+	+	-
Tannins	-	+	-
Phenol	-	+	-
Saponins	-	-	-

Table 2 showing GC MS analyses of methanolic extract of leaves of *costus igneus*

Retention time	Name of the Compound	Molecular formula of the Compound	Area	Height	A/H
11.523	TRIDECANE	$C_{14}H_{30}$	65601	32617	2.01
16.067	2,3,7- Trimethyldecane	$C_{13}H_{28}$	95975	43980	7.56
16.732	Trans-Cinnamic acid	$C_9H_8O_2$	119283	32908	0.82
20.189	Octadecane	$C_{18}H_{38}$	75494	53210	4.98
23.154	Hexadecanoic acid	$C_{16}H_{32}O_2$	110907	55611	4.09
26.015	methyl ester	$C_{17}H_{24}O_{11}$	127736	34526	0.89
26.592	n-Hexadecanoic acid	$C_{16}H_{32}O_2$	2030514	76543	1.89
28.794	Buytanoic acid	CH_3COOH	241871	87543	1.65
28.886	Gamma.-Sitosterol	$C_{29}H_{50}O$	217751	32451	7.43
28.952	Phytol	$C_{20}H_{40}0$	106143	76543	2.34
29.404	Oleic Acid	$C_{18}H_{34}O_2$	2162297	45362	3.24
29.489	Oleic Acid	$C_{18}H_{34}O_2$	4179536	98635	1.43
29.759	Octadecanoic acid	$C_{18}H_{36}O_2$	1040912	54783	2.78
32.654	eicosanoic acid	$C_{20}H_{40}O_2$	146811	74635	0.87
35.327	Docosanoic acid	$C_{22}H_{44}O_2$	186768	43528	0.86
36.228	<NO NAME>		357851	64745	2.32
36.971	9-Octadecenoic acid, 1,2,3-propanetriyl ester, (E,E,E)-	$C_{57}H_{104}O_6$	357851	35334	1.89

Table 3:Alpha amylase inhibition Assay –Comparison between Costus igneus leaf and acarbose

Concentrations (µg/ml)	% of inhibition	
	Insulin leaf	**Standard as Acarbose**
100	18.10±1.26	24.34±1.70
200	36.81±2.57	41.24±2.88
300	57.31±4.01	61.75±4.32
400	74.22±5.19	78.17±5.47
500	86.09±6.02	94.72±6.63
IC_{50} value (µg/ml)	**273.99**	**243.46**

The values expressed are mean ± Standard deviation – expressed in triplicate

Table 4 Alpha glucosidase inhibition assay – comparison between *Costus igneus*leaf and acarbose

Concentrations (µg/ml)	% of inhibition	
	Insulin leaf	**Standard as Acarbose**
100	15.77±1.10	24.16±1.69
200	31.54±2.20	38.25±2.67
300	50.67±3.54	55.03±3.85
400	69.12±4.83	71.14±4.97
500	84.56±5.91	92.95±6.50
IC_{50} value (µg/ml)	**298.03**	**262.96**

The values expressed are mean ± Standard deviation – expressed in triplicate

The present study led to the isolation of 20 bio active compounds in the extract along with its structural elucidation. Presence of oleic acid (41.60%) which is an omega 9 fatty acid in the *Costus igneus* leaf extract indicates its beneficial effect for type2 diabetes patients and insulin sensitivity. Methanolic leaf extract of *Costus igneus* at concentration ranging from 100 to 500µg/ml was used to find its inhibitory effect on α amylase and α glucosidase. The half-maximal inhibitory concentration (IC 50) value for α amylase and α glucosidase was found to be 273.99µg/ml and 298.03µg/ml which was higher when compared to acarbose. The alpha glucosidase inhibition by the leaf was significantly more than the described drug acarbose in similar concentrations.

DISCUSSION:

Diabetes Mellitus (DM) is named as the common non–communicable disease in the world with India reporting the largest number of cases. India is perhaps the diabetic capital of the world. A lot of drugs have been used successfully in the control of the disease. The drug acarbose inhibits alpha amylase and alpha glucosidase and exerts its anti hyperglycaemic action. The insulin leaf *Costus igneus* has been extensively studied for its antidiabetic effects. Bhat et al have established the antidiabetic effect of ethanolic insulin leaf extracts in diabetic rats.[8] They have not clearly deciphered the mechanism of *Costus igneus*. Adiga et al in 2014 have confirmed the findings of ethanolic leaf extracts of *Costus igneus*. [9]These results coincide well with our results. Mani et al have demonstrated antidiabetic, weight reducing and hypolipidemic potential of the leaf extracts in diabetic rats. [10] We have not done any lipid reduction assays in our study. Ziaee A et al [11] have claimed beneficial effects of the drug acarbose even in type 1 DM. In yet another study[12], there is weight reduction and antihyperglycemic effect with the use of acarbose in many human trials. Acarbose has a similar mechanism of action as ethanolic leaf extract of costus igneus. We measured the alpha glucosidase enzyme inhibition of the drug acarbose and found it very close to the extracts of insulin leaf. Acarbose ingestion has got better cardiovascular outcomes along with diabetic control. [13] This gives room to further studies on the leaf with cardiac markers. Apart from antidiabetic action, *Costus igneus* extracts have antioxidant action and diuretic action which will be of immense help in patients with DM. [14]As such, we have compared acarbose and the methanolic extract of leaves of *Costus igneus* and found significant inhibitory action on the enzyme alpha glucosidase. We have not analysed the effect in human trials. In many studies, they have proved that there are no major side effects with the administration of leaf extracts for months together. This gains significance in the upcoming research series of our plant on incretins and diabetic management. This work is the leadoff study of comparing the enzyme inhibition of costus igneus with acarbose.

CONCLUSION:

Various extracts of *Costus igneus* leaves were subjected to phytochemical screening and it revealed that the methanolic leaf extract had shown maximum phytoconstituents viz., alkaloids, flavonoids, glycosides, steroids, and phenolic compounds.GC- MS analysis elucidated the presence of twenty bioactive compounds in the leaf extract.Methanolic leaf extract of *Costus igneus* at concentration ranging from 100 to 500µg/ml was used to find its inhibitory effect on α amylase and α glucosidase to understand the antihyperglycemic effect in patients with Type 2 DM. The IC 50 value for α amylase and α glucosidase was found to be 273.99µg/ml and 298.03µg/ml which was higher when compared to acarbose. As there are no proved side effects, the leaf extracts can be further studied on human trials and added research along the lines of incretin effect may be advocated.

Acknowledgements: Staff of department of chemistry and biosciences SASTRA.

Outside Financial help – NONE

Conflict of interest – NIL for all authors

Contributorship:

MRS – Concept design, **NS and RS** – Data collection, SPS – write up and communication

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