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Evaluation of *In Vitro* Antidiabetic Activity of Synthesized Acetohydrazide Compounds

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Abstract: *The aim of the current work is to screen in vitro inhibition of alpha-amylase enzyme activity in* ***S1*** *((E) – 2 – cyano – N'- (3-methyl-2,6-diphenylpiperdine-4-ylidene) acetohydrazide),* ***S2*** *((E) – 2-cyano-N'-(3-methyl-2,6, di-p-tolypiperidin – 4-ylidene) acetohydrazide) and* ***S3*** *((E) – 2-cyano-N'-(3-methyl-2,6, di-o-tolypiperidin – 4-ylidene) acetohydrazide). This in vitro study explores the antidiabetic properties of S1, S2 and S3 and it can be considered as a potential candidate for the management of type-II diabetes mellitus. The present findings exhibited a concentration dependent inhibition of α-amylase activity by S1, S2 and S3. The half inhibition concentration (IC_{50}) of S1, S2, S3 and Acarbose tested against α-amylase were 1.240 0.648 0.2730.274mg/ml^{-1} respectively. The results of the study revealed that the antidiabetic activity of the S3 is much higher than that of S1 and S2 and near to the standard.*

Key words: *Diabetes mellitus, S1, S2, S3, Acarbose, α-amylase*

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I. Introduction

Diabetes mellitus results from the defects in the insulin secretion and action, this may be characterized by chronic hyperglycemia, which is connected with the carbohydrates, protein and lipid metabolism [1]. Globally mortality rate 9% is recorded due to the diabetes. Diabetes mellitus a well-known endocrine disorder and it is most common in India now a day. The reason may be life style and genetic factors [2]. Due these factors the diabetic monocytes produce increased superoxide anion. (O_2) [3]. In premature atherosclerosis and oxidative stress patient's diabetes is a major risk factor. The treatment of diabetes need to spent vast amount of resources including medicines, diets, physical training and along with serious complications often resulting in high death rate. Therefore there is a need for searching of a new class of compounds to overcome diabetic problems [4]. Thus taken above into considerations synthesized compounds were screened for their in-vitro antidiabetic activity and to find out the comparative potential of the compounds. In the present study is to screen for *in vitro* inhibition of alpha-amylase enzyme activity of **S1, S2 and S3** and compared with standard as Acarbose.

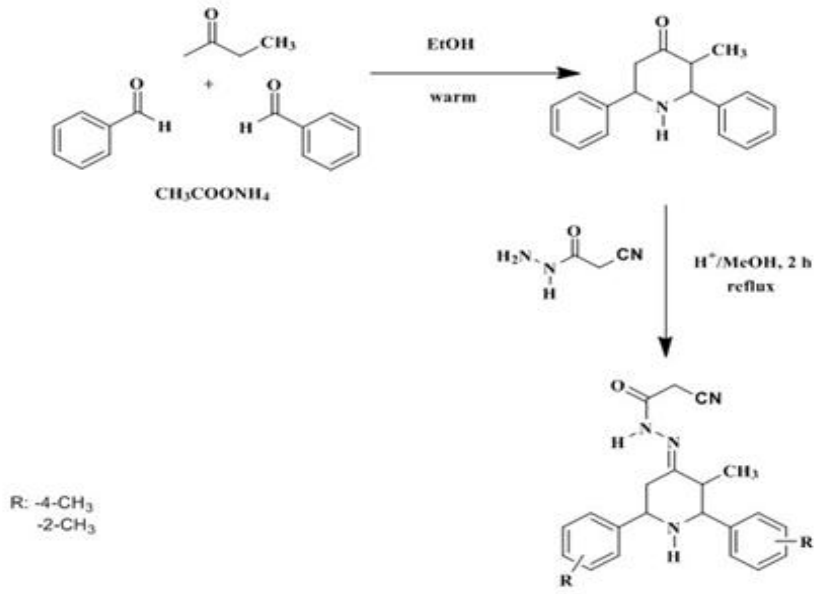
II. Materials And Methods

Preparation of S1, S2 and S3

3-methyl-2,6-diphenylpiperidin-4-one was prepared by adopting the literature method. Condensation of 2-butanones, benzaldehyde and ammonium acetate in warm ethanol in the ratio of 1:2:1 respectively afforded the formation of 3-methyl-2,6-diphenylpiperidin-4-ones.

Preparation of 3-methyl-2,6-diphenylpiperidin-4-one cyanoacetyl hydrazone

A mixture of 3-methyl-2,6-diphenylpiperidin-4-one (0.1 mol), cyanoacetic hydrazide (0.1 mol) in the presence of few drops of concentrated acetic acid in methanol was refluxed for 2 hours. After the completion of reaction, the reaction mixture was cooled to room temperature. The solid product was separated by filtration and washed with warm water and recrystallized by methanol to afford 3-methyl-2,6-diphenylpiperidin-4-one cyanoacetyl hydrazone.



***In vitro* antidiabetic activity**

In vitro α-amylase inhibition assay was carried out by the method of Apostolidis [5].

III. Results And Discussion

In the preset study to investigate the anti-diabetic activity of **S1, S2 and S3** tested against alpha-amylase enzyme. There are several possible mechanisms through which these herbs can act to control the blood glucose level [6]. In that one of the mechanism is that an alteration of the activity of some enzymes that are involved in glucose metabolism. The intestinal enzymes like α-amylase and α- glucosidase are found to be very important in carbohydrate digestion and glucose absorption. The suppression of the activity of such digestive enzymes would delay the degradation of starch and oligosaccharides, which would in turn cause a decrease in the absorption of glucose and consequently in the reduction of postprandial blood glucose level elevation [7]. Alpha amylase and glucosidase inhibitors are the potential targets in the development of lead compounds for the treatment of diabetes [8].Thus in this study, S1, S2 and S3 were used as inhibitors of these intestinal enzymes.

Alpha amylase is an enzyme that hydrolyses alpha bonds of large alpha linked polysaccharide such as lycogen and starch to yield glucose and maltose. Alpha amylase inhibitors bind to alpha-bond of polysaccharide and prevent break down of polysaccharide in mono and disaccharide [9]. The α-amylase inhibitors act as an anti-nutrient that obstructs the digestion and absorption of carbohydrates [10]. The present findings exhibited a concentration dependent inhibition of α-amylase activity by the S1, S2 and S3. The lowest inhibition of α-amylase activity of S1, S2, S3 and Acarbose were 14.15, 21.94, 46.19 and 19.63 in the concentration of 100µg/ml respectively while the highest inhibition of α-amylase activity of S1, S2, S3 and Acarbose were 26.94, 42.47, 61.06 and 86.75% in the concentration of 500µg/ml respectively. The greatest effect of S3 (500 µg/ml) was found to be near to standard Acarbose. The half inhibition concentration (IC_{50}) of S1, S2, S3 and Acarbose were 1.240 0.648 0.273 0.274mg/ml^{-1} respectively. From the present study it can be concluded that S3 showed marked *in vitro* antidiabetic effect against the α-amylase activity (Table 1 and Figure 1). Present finding is in agreement with Gupta [11] study.

Table 1 In vitro α-amylase inhibition (S1, S2 and S3)

Concentrations	S1	S2	S3	Standard Acarbose
	% of inhibition			
100µg/ml	14.15±0.42	21.94±0.75	46.19±0.50	19.63±0.57
200µg/ml	18.26±0.80	24.42±0.74	47.25±0.40	35.61±0.68
300µg/ml	22.37±0.38	31.68±0.87	49.20±0.71	56.84±0.68
400µg/ml	23.51± 0.44	36.63±0.77	50.61±0.09	73.28±0.16
500 µg/ml	26.94±0.97	42.47±0.65	61.06±0.95	86.75±1.02
IC_{50} (mg/ml)	1.240	0.648	0.273	0.274

Values are expressed as Mean ± SD for triplicates

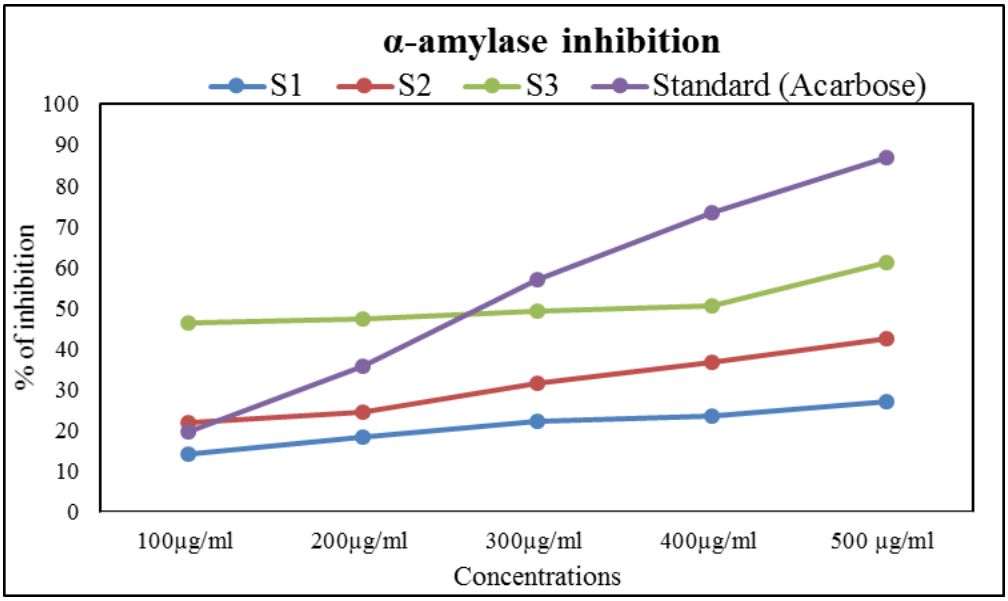


Fig 1 In vitro α-amylase inhibition (S1, S2 and S3)

IV. Conclusion

The synthesized **S1** ((E) – 2 – cyano – N'- (3-methyl-2,6-diphenylpiperdine-4-ylidene)acetohydrazide), **S2** ((E) – 2-cyano-N'-(3-methyl-2,6, di-p-tolypiperidin – 4-ylidene)acetohydrazide) and **S3** ((E) – 2-cyano-N'-(3-methyl-2,6, di-o-tolypiperidin – 4-ylidene)acetohydrazide).compounds possess potential antidiabetic activity compared to commercial drug Acarbose and hence clearly proved their pharmaceutical and medicinal importance of synthesized compounds.

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