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Evaluation of Antioxidant Activity of Pioglitazone: Hydrogen Peroxide scavenging Activity (*In-Vitro* Method).

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ABSTRACT

Diabetes mellitus (DM) is an endocrine disorder characterized by abnormal carbohydrate, lipid and protein metabolism along with specific long-term complications which are associated with oxidative stress. Hence, it is important to discover a hypoglycemic drug that reduces oxidative stress in diabetic patients. This study, therefore, was performed to investigate the antioxidant potential of Pioglitazone (PIO) by hydrogen peroxide scavenging activity, an in –vitro method. Pioglitazone antioxidant property was analyzed with varying concentration from 100 to 1000 µg/ml using spectrophotometer while keeping butylatedhydroxyltoluene (BHT)as the standard. The results of this study show that Pioglitazone, oncomparisonwith butylatedhydroxyl toluene, has dose dependent antioxidant property.

Keywords: Diabetes mellitus, pioglitazone, antioxidant, Hydrogen peroxide

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INTRODUCTION

Free radicals are atoms or groups of atoms with an odd (unpaired) number of electrons and can be formed when oxygen interacts with certain molecules. Once formed these highly reactive radicals can start a chain reaction. Their chief danger comes from the damage they can do when they react with important cellular components such as DNA, or the cell membrane which may lead to cellular death. To prevent free radical damage the body has a defense system of antioxidant [1-3].

Antioxidants are molecules which can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. Therefore, antioxidant has potential to prevent aging, cancer , cardiovascular disease, Alzheimer's disease [4,5].

Free radicals production is increased in diabetes mellitus. The increase in glucose level leadsto increase in oxidative stress thereby changing in antioxidant capacity. This plays a vital role in complication of diabetes [6].

Thiazolidinediones, a group of oral hypoglycemic agents effectively improves the glycemic control in diabetes mellitus type 2. They act as agonist for nuclear transcriptase factor peroximase proliferative activator gamma which improves insulin sensitivity [7,8].

MATERIALS AND METHODS

- Test sample: crude drug of Pioglitazone (15mg)
- Reference antioxidant: BHT (ButylatedHydroxy Toluene)
- Solvent: Phosphate buffer
- Reagent: Hydrogen peroxide
- Spectrophotometer

Hydrogen Peroxide Scavenging Effect

Procedure: A solution of hydrogen peroxide (40 mM) was prepared in phosphate buffer (pH 7.4). Plant extracts at the concentration of 10mg/10µl were added to 0.6ml of H2O2 solution [9,10]. The total volume was made up to 3ml with phosphate buffer. The absorbance of the reaction mixture was recorded at 230nm. The blank solution contained phosphate buffer without H_2O_2 [11].

Calculation

The percentage of scavenging activity by the drug was calculated using the formula:

$$\% \text{ scavenged hydrogen peroxide} = \frac{(A_O - A_1) \times 100}{A_O}$$

where, Ao - Absorbance of control

A1 - Absorbance in the presence of Drug

RESULTS

Table 1: In-vitro antioxidant activity by Hydrogen peroxide Scavenging Activity

Sl.No.	% of Inhibition		
	Concentration (µg/ml)	Pios-15	BHT
1	100	1.2±4.36	40±2.6
2	200	2.4±3.12	65.6±1.4
3	400	4.36±2.46	77.21±3.42
4	600	5.46±1.06	84±1.62
5	800	8.42±4.37	92.2±6.13
6.	1000	11.04±1.2	99.2±6.13

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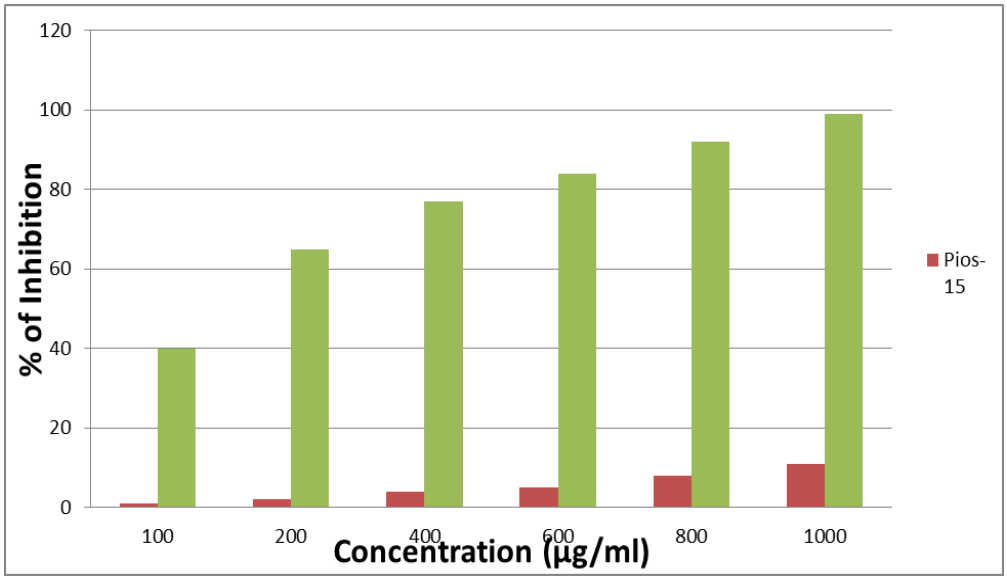

Figure 1: Bar Chart Comparing Percentage Inhibition Pioglitazone With BHT At Various Concentrations

The hydrogen peroxide scavenging activity was recorded in terms of percentage Inhibition. It was observed from that pioglitazone (1000 µg /ml) has shown dose dependent hydrogen peroxide scavenging activity (11.04%) (Table 1). The Results obtained were comparative to BHT (ButylatedHydroxy Toluene) standard. Higher Percentage Inhibition indicates better scavenging activity or antioxidant potential. The given sample showed the dose dependent activity in scavenging the free radicals but insignificant when compared to that of the BHT (ButylatedHydroxy Toluene) standard.

DISCUSSION

The antioxidant property of pioglitazone was assessed by percentage of scavenged hydrogen peroxide (Table 1). As the concentration of the drug increases, the percentage of scavenged hydrogen peroxide increases, but insignificant when compared to ButylatedHydroxy Toluene standard(Figure 1).Therefore, this study shows that Pioglitazone has minimal dose dependentAntioxidant property.

The 2, 4-thiazolidinedione structure is common in a variety of agents and difference in side chain modifications influences their pharmacological actions. Thiazolidinediones are believed to mediate their effects via a variety of targets: peroxisome proliferator activated receptor (PPAR), protein tyrosine phosphate 1B (PTP 1B), mitochondria. Their therapeutic attestation as antidiabetic, antioxidant, anti-inflammatory, antibacterial, anti-obesity agents point toward biodynamic nature of 2,4-thiazolidinedione [12].

A series of 5-arylidene-2, 4-thiazolidinediones and its geranyloxy or prenyloxy derivative were synthesized and studied for their radical scavenging activity using 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay. Their comparable scavenging activities were expressed as IC50 value. Compounds 2c, 2d, 4d, and 6a showed appreciable radical scavenging activities. The vanillin based thiazolidinedione compound 2c displayed highest activity comparable to that of alpha-tocopherol. But in vivo, compound 6a showed better results in inducing phase II detoxifying/antioxidative enzyme [13].

CONCLUSION

Thiazolidinediones have been cited as the most costly oral anti-diabetic medications [14]. Limiting glucose lowering efficacy (20% maximum decrease in fasting plasma glucose at the maximum recommended dose) and side effect profile (chiefly weight and fluid retention) confines the use of currently available thiazolidinediones [15].

Therefore, novel thiazolidinediones compounds which have superior glucose lowering efficacy coupled with antioxidant activity are needed. This will help in the development of thiazolidinediones derivatives possessing a broad spectrum of activities as to counter major components of metabolic syndrome.

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