Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2015, 7(10):273-275

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Evaluation of radical scavenging property of sitagliptin

Aparna Ravi, N. S. Muthiah, Arul Amudha Elizabeth, Muniappan, Sanitha Philip and Chandrashekar

Department of Pharmacology, Sree Balaji Medical College and Hospital and Research Centre, Chromepet, Chennai, India

---

ABSTRACT

Dipeptidyl peptidase inhibitors, a promising group of antihyperglycemic drugs, inhibits the enzyme, DPP-4, that destroys GLP-1 and GIP and thereby increases the levels as a result by which blood glucose levels fall. Sitagliptin, a newer gliptin acting as dipeptidyl peptidase-4 (DPP-4) inhibitor is used in the treatment of type2 Diabetes Mellitus, combined with diet and exercise to improve blood glucose levels. Antioxidant property is an essential mechanism by which it reduces oxidative stress in Diabetic patients there by preventing further beta cell damage and occurrence of microvascular and macrovascular complications. This study evaluates the antioxidant activity of Sitagliptin by its free radical scavenging activity using DPPH (2,2-diphenyl-1-picrylhydrazyl hydrate)assay. Various Concentrations of Sitagliptin (100 µg/ ml, 200 µg /ml, 400 µg/ml, 600 µg/ml ,800 µg/ ml, and 1000 µg/ml) were evaluated for DPPH free radical scavenging and the following percentage of activity was observed 2.5% , 4.9%, 8.12%,15.54%, 23.3% , 35% respectively which shows considerable antioxidant properties apart from being an effective oral hypoglycemic agent.

Keywords: Dipeptidyl peptidase inhibitor, Sitagliptin, DPPH radical scavenging activity, ascorbic acid, Diabetes Mellitus

---

INTRODUCTION

Free radicals, reactive oxygen species and reactive nitrogen species are generated by our body as a part of our daily metabolic activities. The antioxidant defense mechanism offers protection from the free radicals and from the cellular damage caused by them. This has attracted a great deal of attention, in recent years, towards the field of free radical chemistry. A proper balance between antioxidants and free radicals is essential to maintain normal physiological activities. In case of pathological conditions like Diabetes Mellitus, Alzheimer's Disease, Parkinsonism etc, the antioxidant mechanism is disrupted which leads to the accumulation of free radicals resulting in oxidative stress induced cell damage. In Diabetes Mellitus Type 2, which is one of the leading causes of metabolic and cardiovascular complications, the antioxidant defense mechanism is disrupted, which leads to accumulation of free radicals resulting in increased beta cell damage and increased microvascular and macrovascular complications.

Many new drugs have been introduced for the past few years in the management of type 2 Diabetes Mellitus. The most noted were the oral incretin drugs known as dipeptidyl peptidase 4 inhibitors. Among the effects of incretins, the highlight is its insulinotropic and cytoprotective effects on pancreatic β-cell[1]. DPP-4 inhibitors are considered to have modestly reduced cardiovascular risk, triglycerides, low density lipoprotein cholesterol, high density

lipoprotein cholesterol, and blood pressure[2]. Sitagliptin was the first DPP-4 inhibitor to be marketed in the United States in 2007, followed by saxagliptin in 2009[3]. Sitagliptin acts by inhibiting DPP-4 enzyme, increases the levels of incretins, mainly Glucagon like peptide – 1 (GLP -1).GLP-1 has a very short half life (1-2 min) and is metabolized quickly by DPP -4 enzyme. GLP -1 is produced by the intestinal L cells, which augments glucose dependent – insulin secretion, during the phase of nutrient absorption from gastrointestinal tract. The actions of GLP – 1 are as follows : 1)stimulates insulin secretion from beta cells of pancreas 2)decreases glucagon release 3)slows the rate of nutrient absorption by slowing gastric emptying and 4)decreases appetite by acting at the level of hypothalamus, thereby inducing weight loss.[4]

EXPERIMENTAL SECTION

Radical scavenging activity of plant extracts against stable 2,2 diphenyl 2 picrylhydrazyl hydrate (DPPH) was determined by Brand-Williams et al 1995.DPPH (1, 1-Diphenyl-2-picrylhydrazyl) is a stable free radical with purple colour (absorbed at 517nm).It reacts with an antioxidant compound, which can donate hydrogen, and reduce DPPH.

Materials and methods

The test was done using the DPPH assay which is one of the simple and sensitive assay methods using the methodology of Brand-Williams et al 1995. DPPH reacts with an antioxidant compound, which donates hydrogen, and reduces DPPH. Fresh solution of DPPH in methanol 6 × 10-5 M was prepared daily before UV measurements. Test sample Sitagliptin 100 mg tablet was crushed into fine powder and stock solution was prepared using methanol (200µm) as solvent. Ascorbic acid was used as reference antioxidant.

Test samples were prepared in a concentration of 100µg/mL, 200µg/mL, 400µg/mL, 600µg/mL, 800µg/mL and 1000µg/mL.Three ml of freshly prepared DPPH solution was mixed with the different concentrations of the drug in microgram/ml. The reaction mixture containing DPPH solution (200µM in methanol) with different concentrations of the drug Sitagliptin was shaken and incubated in dark for 15 min at room temperature. The change in color produced (deep violet to light yellow)depends on the strength of free radical scavenging activity and was measured at 517 nm on a UV visible light spectrophotometer. The experiment was carried out in triplicate.

Ascorbic acid was also prepared in similar concentrations from its respective stock solution.

RESULTS AND DISCUSSION

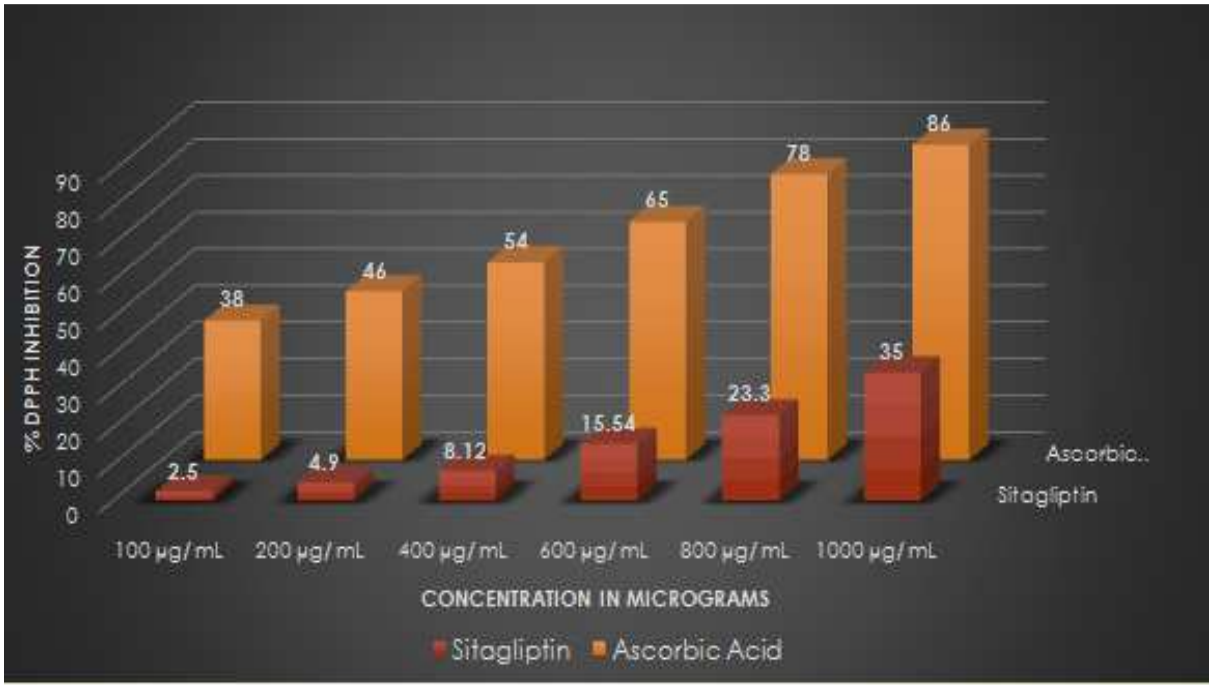
TABLE 1

Sl. No.	% of DPPH Inhibition		
	Concentration (µg/ml)	Sitaglyptin	Ascorbic acid
1	100	2.5	38
2	200	4.9	46
3	400	8.12	54
4	600	15.54	65
5	800	23.3	78
6	1000	35	86

The change in the colour of the reaction mixtures was appreciable in both test and reference mixtures after 15 min of incubation period. At concentrations of 100,200,400,600,800,1000 µg/Ml , the percentage of DPPH inhibition by Sitagliptin was 2.5% ,4.9 %, 8.12%, 15.54%, 23.3% , and 35% respectively. The percentage of DPPH inhibition for the same concentrations by Ascorbic acid was 38% , 46% , 54% , 65% , 78% , 86%.

At multiple concentrations of the drug in µg/ml, percentage of inhibition was noted and evident antioxidant activity was confirmed for Sitagliptin when compared to ascorbic acid.

FIGURE 1



In the present study, Sitagliptin is compared with ascorbic acid and there had been evident antioxidant properties. The readings of DPPH percentage inhibition at different concentrations have clearly shown the considerable free radical scavenging activity of sitagliptin which was dose dependent in action. The activity of Sitagliptin exhibited considerable antioxidant properties when compared with the reference antioxidant, Ascorbic acid. At 1000µg/ml concentration, the percentage of DPPH inhibition by Sitagliptin was 35% and the inhibition of the same by Ascorbic acid is 86%. This dose dependent increase in antioxidant activity protects the beta cells of pancreas from further damage, when taken for a longer duration and prevents the incidence of microvascular and macrovascular complications.

CONCLUSION

Though there have been other similar studies estimating the antioxidant potential of other drugs in this class as well as other oral hypoglycemic agents, not much data is available comparing all possible long term drugs in view of their antioxidant potential .From this study, it has been proved that Sitagliptin apart from being an effective oral hypoglycemic drug exhibits considerable antioxidant properties as measured by DPPH assay. The percentage of DPPH inhibition increases with increasing concentrations of sitagliptin, which shows its dose dependent antioxidant property.

Sitagliptin being a long term prescribed drug, the antioxidant potential is very much helpful as an added advantage for patients in reducing microvascular and macrovascular complications and further damage to pancreas.

REFERENCES

[1] D T Eurich, S Simpson, A Senthilselvan, CV Asche, JK Sandhu-Minhas, FA McAlister, *BMJ*, **2013**; 346
[2]Drucker DJ, Sherman SI, Gorelick FS, Bergenstal RM, Sherwin RS, Buse JB., *Diabetes Care* ,**2010**;33:428-33.
[3]Ávila Dde L1, Araújo GR, Silva M, Miranda PH, Diniz MF, Pedrosa ML, Silva ME, de Lima WG, Costa DC , *Arch Med Res***2013** Apr;44(3):194-202.
[4]Patrick E. MacDonald, Wasim El-kholy, Michael J. Riedel, Anne Marie F. Salapatek, Peter E. *Diabetes*, **2002** Dec;51Suppl 3:S434-42.