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Research Article

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Evaluation of anti-oxidant properties of linagliptin

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ABSTRACT

Linagliptin is a dipeptidyl peptidase-4 (DPP-4)inhibitor used in the treatment of type-2 Diabetes Mellitus. Antioxidant property is one of the beneficial effects in Diabetic patients having cardiovascular and neurological complications. This study aims to evaluate the antioxidant property of Linagliptin using DPPH scavenging property compared with that of Vitamin C. The test was done using the 2, 2 diphenyl 2 picrylhydrazyl hydrate (DPPH) assay. DPPH reacts with an antioxidant compound, which can donate hydrogen, and reduce DPPH. The reaction mixture containing 3ml of DPPH solution with different concentrations of the drug Linagliptin (100, 200, 400, 600, 800 and 1000 µg/1ml) was shaken and incubated in dark for 15 min at room temperature. The change in colour (from deep violet to light yellow) denoting the antioxidant property was measured at 517 nm on a UV visible light spectrophotometer. The percentage of inhibition by Linagliptin was 3.9, 4.5, 7.12, 15.6, 25.8, and 38 respectively. The percentage inhibitions by the standard antioxidant (ascorbic acid) at the same concentrations were 38,46,54,65, 78, 86respectively.This study showed dose dependent Anti-Oxidant property of Linagliptin.

Key words: Linagliptin, Oxidative stress, Antioxidant, Ascorbic Acid, DPPH assay

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INTRODUCTION

Diabetes Mellitus is a highly prevalent chronic metabolic disorder in which oxidative stress plays an important role in its pathogenesis. Persistent hyperglycaemia leads to production of highly reactive oxygen species .Drugs which possess antioxidant properties helps in controlling hypoglycaemia at the same time it will reduce the apoptosis of beta cells of pancreas and reduces the complications of Diabetes Mellitus[1]. Linagliptin is dipeptidyl peptidase-4 (DPP-4) inhibitor approved by FDA on 2nd may 2011 for the treatment of type-2 Diabetes Mellitus. It is a Xanthine based molecule with long duration of action. It inhibits DPP-4 enzyme competitively by acting extracellularly. Linagliptin has got high selectivity for DPP-4 enzyme than other gliptins. At a 5mg oral dose it inhibits DPP-4 activity by 80 %. So many studies has showed that Linagliptin has a role in reducing oxidative stress and inflammation and improving vascular function[2]. Antioxidant properties of Linagliptin has a beneficial role in diabetic patients with cardiovascular disease[3].

The aim was to evaluate the antioxidant property of Linagliptin using DPPH scavenging property compared with that of Ascorbic acid (Vitamin-C)

EXPERIMENTAL SECTION

1.Test sample: Crude drug of Linagliptin- 5mg
2. Reference antioxidant: Ascorbic acid
3. Solvent: Methanol
4. Reagent: DPPH (2, 2-Diphenyl-2-picryl hydrazyl)

5. Spectrophotometer

PROCEDURE.
The DPPH assay procedure was done using methodology of Brand-williams et al 1995 [4]
1.Test sample tablet Linagliptin 5mg was crushed in to fine powder and stock solution was prepared using methanol as solvent.
2. Reference Antioxidant- Ascorbic Acid.
3. The solution of DPPH in methanol 6 ×10-5 M was prepared fresh daily before UV measurements.
4. Test samples were prepared from stock solution to attain a concentration of 100µg/ml ,200µg/ml ,400µg/ml and 600µg/ml 800µg/ml ,1000µg/ml.
5. Similar concentrations of Ascorbic acid were also prepared from its respective stock solution.
6. The reaction mixture containing 3ml of DPPH solution with different concentrations of Linagliptin was shaken and incubated in dark for 15mins at room temperature.
7. Similarly concentrations of the Standard (Ascorbic Acid) were also taken.
8. The change in colour (from deep violet to light yellow) was measured at 517 nm on a UV visible light spectrophotometer

Percentage of Inhibition = [(A B –A A)/A B] × 100

Where A B = absorption of blank sample (t= 0 min)
A A = absorption of test extract solution (t=15 mins)

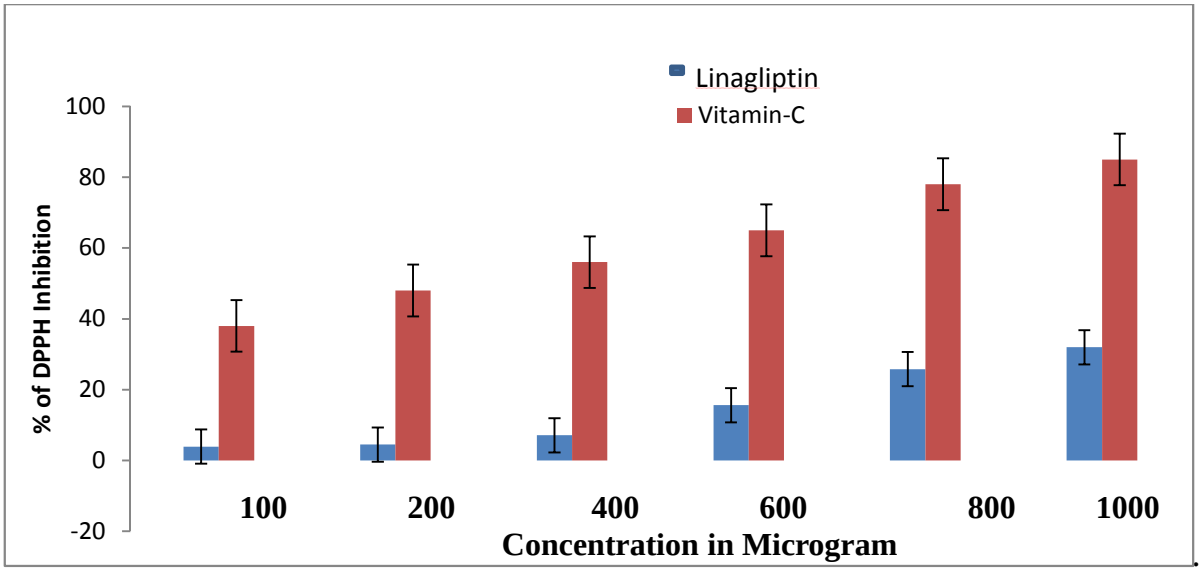
RESULTS

After incubation period of 15 minutes, there was a change in the colour of the reaction mixture which was appreciable in both the test and reference mixtures. At concentrations of 100, 200, 400, 600, 800and 1000 µg/1ml. The percentage of inhibition by Linagliptin was 3.9, 4.5,7.12,15.6, 25.8,and 38 respectively. The percentage inhibitions by the standard antioxidant (ascorbic acid) at the same concentrations were 38, 46,54, 65, 78,86 respectively. The results are shown in table-1 and graph-1 below.

Table-1

SL. NO	% OF INHIBITION		
	Concentration(ug/ml)	Linagliptin	Ascorbic Acid
1	100	3.9	38
2	200	4.5	46
3	400	7.12	54
4	600	15.6	65
5	800	25.8	78
6	1000	38	86

Graph-1



DISCUSSION

Linagliptin inhibits the action of DPP-4, an enzyme that destroys the hormone GLP-1, which helps the body to produce more insulin when it is needed. Linagliptin can be used as monotherapy and in combination for the treatment of Type2 DM.Two pharmacological characteristics that sets Linagliptin apart from other DPP-4 inhibitors is that it has a non-linear pharmacokinetic profile and is not primarily eliminated by the renal system. Linagliptin has got good antioxidant property compared to other drugs in the same class which reduces the oxidative stress of the metabolic disorder[5].The antioxidant property of the drug is dose dependant.

CONCLUSION

The study concludes that Linagliptin has got Dose-Dependent antioxidant property, which can be used to prevent micro and macro Angiopathic complications of Diabetes Mellitus and thereby extrapolated to be used to reduce the morbidity and mortality due to Diabetes mellitus**.**

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