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SOLVENT EFFECT ON THE UV ABSORPTION SPECTRA OF EVOGLIPTIN TARTRATE

Gayatri Bahatkar*, Megha S. Kurmi, Monika Jadhao and Vijay M. Waghulkar

Department of Quality assurances, Vidyabharati College of Pharmacy, Amravati.

***Corresponding Author: Gayatri Bahatkar**
Department of Quality assurances, Vidyabharati College of Pharmacy, Amravati.

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ABSTRACT
The current study was designed to investigate the effect of solvents on the UV Absorption spectra of Evogliptin Tartrate. Diabetes is one of the commonly occurring diseases. Evogliptin is the new generation of drugs that was introduced in the year 2015. Evogliptin is used for type 2 Diabetes with or without metformin. The main objective of this study is to understand the effect of solvents on the absorbance of a drug. Trials were taken using different solvents on UV spectrophotometry, Total four solvent were used for this purpose (Water, n-butyl alcohol, DMSO, Ethanol). The spectrum shows little displacement in signals with different solvents.

KEYWORDS: Evogliptin, UV absorbance, solvent effect.

INTRODUCTION

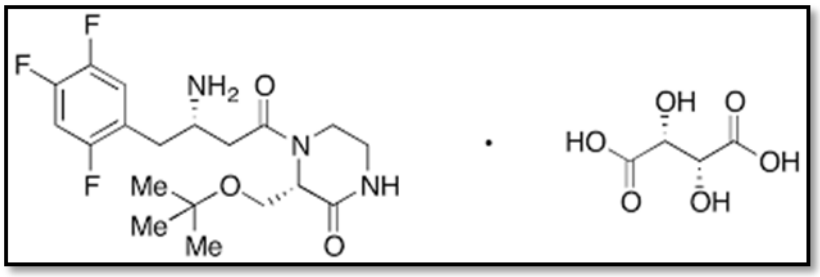

Figure no. 1: Structure of Evogliptin Tartrate.

Evogliptin Tartrate is an antidiabetic agent, used for the treatment of type 2 diabetes mellitus. it is a novel oral DPP-4 inhibitor. It was developed by Dong-A ST for the treatment of type 2 diabetes. It is chemically known as (3R)-4-[(3R)-3-amino-4-(2, 4, 5-trifluorophenyl) butanoyl]-3-[(2-methylpropan-2-yl) oxymethyl] piperazin-2-one ;(2R, 3R)-2, 3-dihydroxybutanedioic acid. The molecular weight of Evogliptin Tartrate is 551.51gram/mol. It is used as the second line of treatment as an adjunct to diet and exercise to improve glycemic control when in monotherapy or combination with metformin. It is used in elderly patients.[1,2]

Mechanism of action

Evogliptin secreted glucagon-like peptide-1(GLP-1) is secreted from alimentary canal in response to meal that promote insulin from the pancreas and reduces the hormones that regulate blood sugar levels post meal by controlling glucagon secretion. It reduces fasting and post-meal sugar levels. Evogliptin also reduces the high-fat diet-induced atherosclerotic plaque area in the ApoE mouse model. It acts by inhibiting the formation of atherosclerotic lesions by reducing Vaso-inflammation and increases plaque stability. Evogliptin exhibit a hypoglycemic effect by controlling the decomposition of GLP-1 by inhibiting dipeptidyl peptidase 4(DPP-4) activity and thereby rises blood concentration of active from GLP-1.

Pharmacodynamic Properties

The glucagon-like peptide -1(GLP-1) is secreted from the alimentary canal in repose to meal that promotes insulin secretion from the pancreas and regulates blood sugar post-meal by controlling glucagon secretion. Evogliptin exhibits a hypoglycaemic effect by decomposing the GLP-1 by inhibiting dipeptidyl peptidase-4(DPP-4) activity and increasing blood concentration of active form GLP-1.[3]

The result from biochemical studies shows that Evogliptin noncovalently binds to the catalytic site of the human DPP4 enzyme in crystal structures complex to human DPP4. the ter-butoxy residue of Evogliptin distinctively interacts with Arg125 of human DPP4, unlike Sitagliptin. This hydrophobic interaction may contribute to the high binding affinity of Evogliptin. Evogliptin is a competitive and reversible inhibitor of dipeptidyl peptidase IV (DPP-IV). The inhibitory activity of Evogliptin is about 10-fold compared to Sitagliptin. The selectivity of Evogliptin for DPP-IV is 6,000-fold higher than DPP8/9. Pre-clinical studies on Evogliptin demonstrated significant DPP-IV inhibitory activity, increased active plasma GLP1 level, reduced blood glucose excursion in a dose-dependent manner. By DPP-IV inhibitory effect, Evogliptin exhibited improvement in the fasting and postprandial blood glucose levels.[3]

Pharmacokinetic properties

The maximum Evogliptin concentrations (Cmax) were observed at 3.0 to 5.5 hours (median value), and the average half-lives (t1/2) were estimated to be 32.5 to 39.8 hours. The average Cmax and AUC values increased as the dose increases while dose-dependent changes were not shown in Tmax and t1/2. The absolute bioavailability of Evogliptin was 50.247%. Plasma protein binding of Evogliptin is 46%.[3]

Drug Interaction:[3]

1. Metformin: Multiple administration of Evogliptin 5 mg and twice daily metformin 1,000 mg until steady state was reached did not show clinically meaningful change in the pharmacokinetics of Evogliptin or metformin.

2. Clarithromycin: Multiple administration of a potent CYP3A4 inhibitor, clarithromycin 1,000 mg/day, until steady state was reached and single administration of evogliptin 5 mg showed increased Cmax of evogliptin by 2.1 times and its AUC by 2.0 times. Caution has to be exercised as pharmacokinetic exposure of evogliptin may increase with concomitant administration of CYP3A4 inhibitors.

3. Rifampicin: Multiple administration of a potent CYP3A4 inducer, Rifampicin 600 mg/day, until steady state was reached and single administration of Evogliptin 5 mg showed no significant change in Cmax of Evogliptin but showed a decrease in AUC by 63%.

Precautions

Precautions should be taken if patients have any renal & hepatic impairment. And if patient have any functional class-1 heart failure.

EXPERIMENTAL

Solvents

Solvents used in UV spectroscopy should not absorb the UV radiation in the same region as the drug whose spectrum is analysed. Some of the commonly used solvents are water, methanol, ethanol, and hexane. Polarity of solvent is very important for determination of the saturation present or not. Polar solvent forms bonding with hydrogen bond with the solute solvent complex that leads to disappearance of fine structure in band. But in non-polar solvent no such complex is formed.[4,5]

Chemicals and Reagents

Evogliptin Tartrate Tablets 5mg (VALERA) was purchased from local pharmacy shop. All the reagents used are of analytical grade from S.D. Fine Chemicals.

Instrumentation

A Shimadzu UV–visible spectrophotometer (Model UV-1800, Shimadzu Corporation, Spectrophotometric Division, Kyoto, Japan) with 10 mm quartz cuvettes were used to record the UV absorption spectraover a wavelength range 200-400 nm. Quartz cuvettes were used for measurements in solution via 1=1 cm. Analytical balance (Shimadzu AX200, Japan).

Preparation of Dilutions

Weigh accurately 5 mg of Evogliptin Tartrate and transfer it to 100 ml volumetric flask. Dissolve it in 50 ml water with constant shaking. Make up the volume with water. This results in 50 µg/ml concentration of the solution. Similarly, Ethanol, DMSO, n-butyl alcohol solution was prepared. The UV spectrum of it was recorded between 200-400 nm.

RESULTS AND DISCUSSION

The different polarity solvents of water, n-butyl alcohol, DMSO, ethanol used affected the behaviour on the absorption spectra of Evogliptin Tartrate. The spectra of Evogliptin Tartrate in water were used as reference. It can be seen that there is bathochromic shift in other solvent as compared to water. The shift was seen from 258.60 nm to 259 nm for ethanol, 264 nm for both n-butyl alcohol and DMSO. It can also be seen that the absorbance increases as the solvents are replaced.

Table no. 1: UV absorbance data for Evogliptin Tartrate.

Sr.no.	Solutions	Wavelength	Absorbance
1	Water	258.60	0.382
2	n-butyl alcohol	264	0.574
3	DMSO	264	0.701
4	Ethanol	259.00	0.844

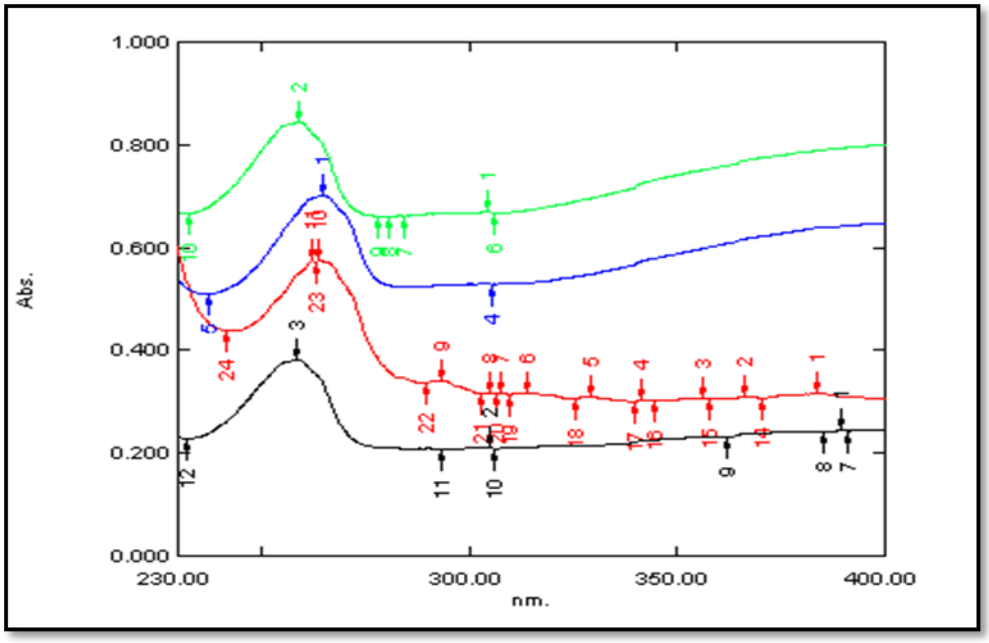

Figure no. 2: Overlain spectra of Evogliptin Tartrate using different solvents.

CONCLUSION

The UV-Visible spectrophotometric method of assay has been employed in Evogliptin tartrate using different solvents. Results obtained from this work shows that different solvent effect on the UV absorption spectra of Evogliptin Tartrate depends on extent of solvent polarity and chemical structure of drug which contains substituents on amino group and carbonyl group. The cause of the spectra is due to lone pair of electrons present that interact with solvent either it stabilizes the charge transfer and increase hydrogen binding capacity of solvents. This leads to shift in longer wavelength.

ABBREVIATION

- ApoE: Apolipoprotein E
- GLP-1: glucagon-like peptide -1
- DPP-4: dipeptidyl peptidase-4
- CYP3A4: Cytochrome P450 3A4
- AUC: Area under Curve

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