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COMPARATIVE STUDY OF TWO DIFFERENT MARKETED PREPARATION (TABLETS) CONTAINING EMPAGLIFLOZIN & LINAGLIPTIN AND DEVELOPING NOVEL METHOD FOR SIMULTANEOUS ESTIMATION OF EMPAGLIFLOZIN AND LINAGLIPTIN USING UV VISIBLE SPECTROPHOTOMETER

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ABSTRACT

A simple, precise, accurate and economic simultaneous UV spectrophotometric method has been developed for the estimation of Empagliflozin & Linagliptin in combination in bulk and tablet. The estimation was based upon measurement of absorbance at absorbance maxima of (λ_{max}) 233nm for Empagliflozin (API) and 277 nm for Linagliptin (API) in **Ethanol:** Distilled Water (1:1 ratio) as a solvent respectively in bulk mixture and tablet. The Beer Lambert's law obeyed in the concentration range 5-25 µg/ml, 10-50 µg/ml for Empagliflozin & Linagliptin respectively. The estimation of bulk mixture and tablet was carried out by simultaneous equation, Q-analysis and area under curve method for estimation of Empagliflozin & Linagliptin. Method was validated with respect to specificity, linearity, range, accuracy, precision, Limit Of Detection, Limit Of Quantitation. Validation was performed as per ICH guidelines the results were found out to be for Empagliflozin & Linagliptin. (As per Label Claim). Comparative Study was done using Two Different Marketed Preparation (Tablet) Containing Empagliflozin & Linagliptin.

(**GLYXAMBI (10/5) TABLET**: BOEHRINGER INGELHEIM LTD, **AJADUO (10/5)TABLET**: LUPIN LTD)

KEYWORDS: Empagliflozin, Linagliptin, Comparative Study , Simultaneous Estimation.

INTRODUCTION

Empagliflozin: Empagliflozin chemically,(1-chloro-4-[b-D-glucopyranos-1-yl]-2-[4-([S]-tetrahydrofuran-3-yl-oxy) benzyl]-benzene. Empagliflozin is a sodium glucose co-transporter-2 (SGLT-2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 Empagliflozin is sodium glucose cotransporter (SGLT)-2 inhibitor; by inhibiting the glucose transporter in the kidney , empagliflozin increases the secretion of glucose and has an antihyperglycemic effect.Empagliflozin is an inhibitor of the sodium glucose co-transporter-2 ,which is found almost exclusively in the proximal tubules of nephronic components in the kidneys.SGLT-2 accounts for about 90 percent of glucose reabsorption into the blood. BlockingSGLT-2 reduces blood glucose by blocking glucose reabsorption in the kidney.

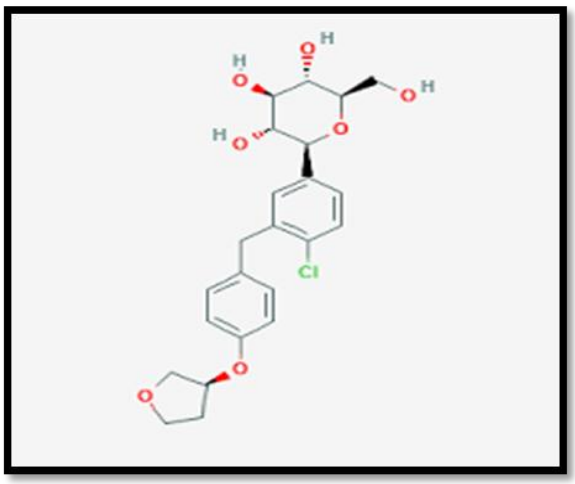

Fig.1 Stucture of Empagliflozin

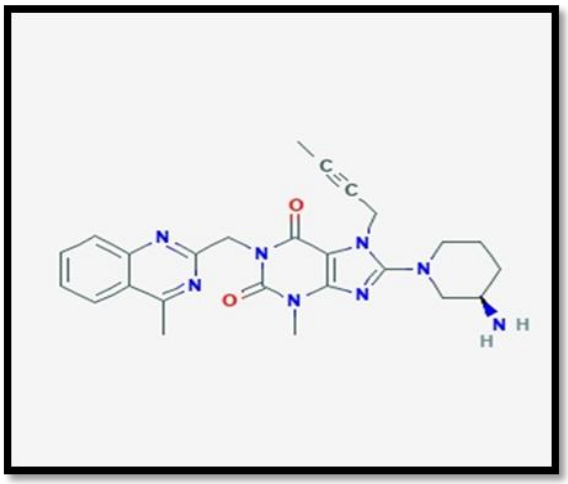

Fig.2 Stucture of Linagliptin.

EXPERIMENTAL

Reagent and Materials

All the reagents in this assay along with triple distilled water were of analytical grade. Empagliflozin & Linagliptin were obtained as a gift sample from Lupin Ltd, Mumbai & Macleod Pharmaceutical Pvt. Ltd. Gujrat, India. The marketed tablets used were purchased from local market. (**GLYXAMBI (10/5) TABLET**: BOEHRINGER INGELHEIM LTD, **AJADUO (10/5)TABLET**: LUPIN LTD)

Apparatus

Spectral analysis were made on a Jasco Spectrophotometer, Model- V-630 (Japan), was employed with spectral bandwidth of 1nm and wavelength accuracy of ±0.3nm with automatic wavelength correction with a pair of 10mm quartz cells. Glass wares used in each procedure were soaked overnight in a mixture of chromic acid and sulphuric acid rinsed thoroughly with double distilled water and dried in hot air oven.

Preparation of stock solution

Accurately weighed Empagliflozin & Linagliptin (10 mg each) was transfer two separate 100ml volumetric flask, dissolved in 100ml of Ethanol: Distilled Water (1:1 ratio) as a solvent and make up the volume up to the mark.

Preparation of working standard

Take required quantity of stock solution of Empagliflozin & Linagliptin diluted with Ethanol: Distilled Water (1:1 ratio) to obtained working standard of both solution.

Picture No. 1: Working on UV –VISIBLE Spectrophotometer.

Selection of Detection Wavelength

Solutions of drug were scanned over the range of 200-400nm. It was observed that both the drug showed considerable absorbance at 233nm for Empagliflozin and 277nm for Linagliptin was selected as the wavelength for detection.

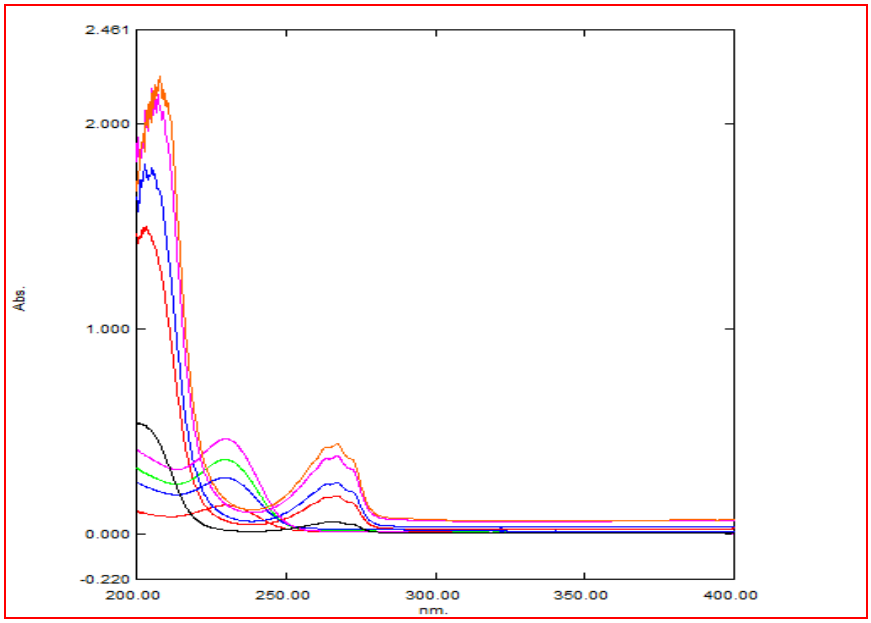

Fig 3: Calibration UV spectra of Empagliflozin & Linagliptin.

METHOD VALIDATION

Linearity

Working standard solution of Empagliflozin and Linagliptin was taken in different 10 ml volumetric flasks and diluted up to mark with distilled water to obtained concentrations 50, 60, 70, 80, 90µg/ml of Empagliflozin and 2, 4, 6, 8, 10µg/ml of Linagliptin. A calibration curve was constructed by plotting concentration versus absorbance and line equation was calculated for both the drugs.

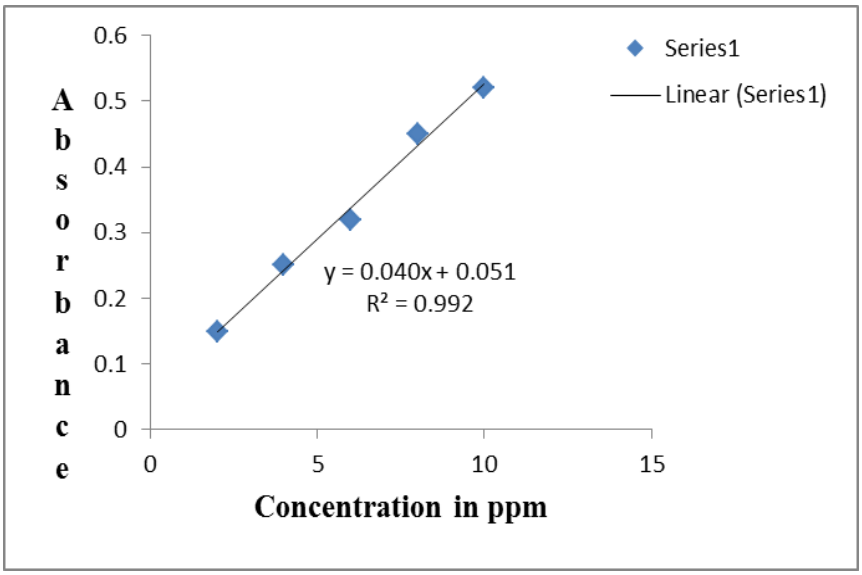

Fig.4 Calibration Curve of Empagliflozin.

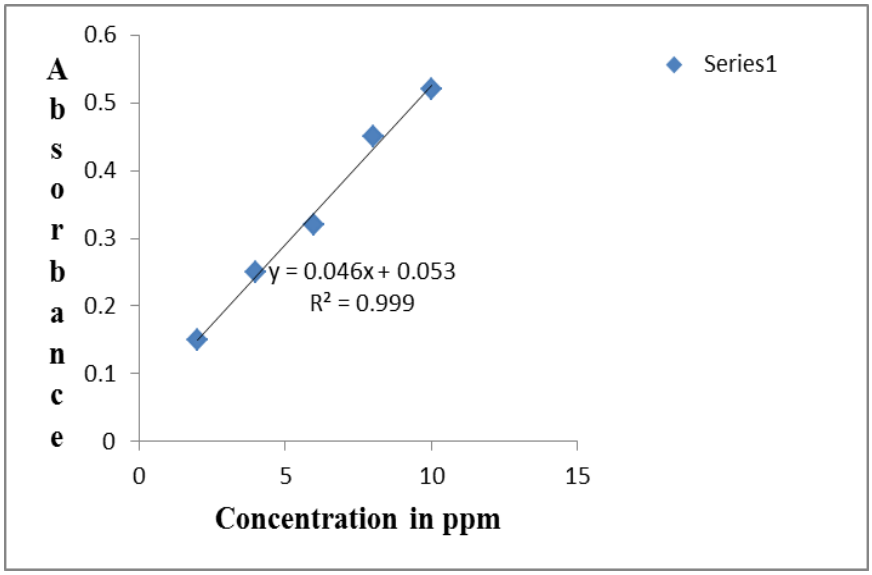

Fig.5 Calibration Curve of Linagliptin.

Precision

The repeatability studies were carried out by estimating response of Empagliflozin and Linagliptin five times and results are reported in terms of relative standard deviation. The intermediate precision were carried out by estimating the corresponding responses 3 times on the same day and 3 different days for 3 different concentrations of Empagliflozin and Linagliptin and results are reportred in terms of relative std. deviation.

Accuracy

Recovery studies of Empagliflozin and Linagliptin were performed to judge the accuracy of the method by standard additions at three different levels 80, 100, 120 %. Mean percentage recovery was determined. Recovery values were calculated shown in table 1.

Table.1 Recovery Studies (API).

Amount of drug sample used Empagliflozin	Obtained(µg) Empagliflozin (n=3)	% Recovery	Amount of drug sample used Linagliptin	Theoretical amount added (%)	Obtained (µg) Linagliptin (n=3)	% recovery
10µg	10.05	100.22	5µg	80	5.01	100.01
10µg	10.85.	100.55	5µg	100	5.96	102.38
10µg	10.01	100.08	5µg	120	5.75	101.05
	Mean % recovery	100.20			**Mean % recovery**	100.80

Assay of Drug Formulation (Tablet Dosage Form)

Fig.6 Two tablet brands containing Empagliflozin and Linagliptin.

Table 2 Assay of Combined Dosage.

Sr. No.	Brand Name	Drug	Label Claim (mg/Tablet)	Amount Estimated (mg/Tablet)*	Percentage Label Claim (%)
1	Glyxambi Tablet : Boehringer Ingelheim Ltd,	Empagliflozin	10	10	100
		Linagliptin	5	4.99	99.99
2	Ajaduo Tablet: Lupin Ltd	Empagliflozin	10	10	100
		Linagliptin	5	5	100

***Mean of five reading

Detection Limit

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitative as an exact value.

$$LOD = 3.3\sigma/S$$

Where,σ = Relative std. deviation of the response, S = slope of calibration curve.

Quantitation Limit

The quantitation limit of an analytical procedure is the lowest amount of analyte in a sample, which can be quantitatively determine with suitable precision and accuracy.

$$LOQ = 10\sigma/S$$

Where,σ = Relative std. deviation of the response, S = slope of calibration curve.

Table.3 Method Validation Parameters.

Parameter	Result	
	Empagliflozin	**Linagliptin**
Linearity range (µg/ml)	2-8	50-80
Sensitivity(mg/cm2/.001 absorbance unit)	0.015	0.199
Correlation Coefficient (r^2)	0.991	0.989
Slope (m)	0.051	0.013
Intercept (c)	0.036	0.0415
Accuracy	99.99 %	100.10 %
Precision (% RSD)		
Repeatability	0.300	0.600
Intraday	0.32	0.62
Interday	0.52	0.81
LOD (µg)	1.2	6.1
LOQ (µg)	2.2	20.56

RESULTS AND DISCUSSION

Comparative Study of Two Different Marketed Preparation (Tablets) Containing Amlodipine Besylate and Valsartan Shows that near about 100% of Label Claim. The developed UV-Visible Spectrophotometric method for the simultaneous estimation of Empagliflozin and Linagliptin was found to be simple and useful with high accuracy, precision, LOD, LOQ as per ICH guidelines. Sample recoveries in all formulations using the above method was in good agreement with their respective label claim or theoretical drug content, thus suggesting the validity of the method and non-interference of formulation excipients in the estimation. In the selected solvent system Ethanol: Distilled Water (1:1 ratio), drugs were stable for more than 48 hours, thus suggesting that samples need not be estimated immediately after collection. The method was successfully used for determination of drugs in their pharmaceutical formulation.

CONCLUSIONS

The developed UV-Visible Spectrophotometric method for the simultaneous estimation of Amlodipine Besylate and Valsartan in the tablet dosage form in the solvent system Ethanol: Distilled Water (1:1 ratio) give proper estimation of percentage label claim of marketed product.

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