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METHOD DEVELOPMENT FOR THE SIMULTANEOUS ANALYSIS OF METFORMIN AND ALOGLIPTIN BY USING UV-VISIBLE SPECTROPHOTOMETER

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Abstract : Alogliptin and metformin are used as combined medication to manage high glucose in type-2 diabetes patient. A simple, rapid, accurate, precise UV spectrophotometric technique for the simultaneous estimation of Alogliptin benzoate and metformin hydrochloride in an exceedingly combined tablet dosage form using the simultaneous equation technique has been developed. The method is based on the equation for analysis of both the drugs using methanol as a solvent. Metformin hydrochloride has absorbance maxima at 231 nm and Alogliptin benzoate has absorbance maxima at 276 nm in methanol. The linearity was obtained within the concentration vary of 5–25 µg/ml and 4–20 µg/ml for Alogliptin benzoate and metformin hydrochloride, severally. The concentrations of the medication were determined by using the simultaneous equations method. The mean recovery was 100.90 ± 1.76 and 100.26 ± 0.71 for Alogliptin salt and Metformin hydrochloride, severally. The strategy was found to be simple, accurate, and precise and was applicable for the simultaneous determination of Alogliptin salt and metformin hydrochloride within the pharmaceutical tablet dosage type. The results of study are valid statistically and by recovery studies. It's a price economical and time saving method that has several applications in stability studies, forced degradation studies, routine analysis, quantification, etc. It will be successfully acquired for daily quality control analysis of Alogliptin and metformin in dosage form.

Keywords: **Alogliptin Benzoate, Metformin Hydrochloride, simultaneous equation, UV spectroscopy, analysis**

I. INTRODUCTION

Metfo Metformin and Alogliptin are employed in the treatment of kind 2 diabetes. Metformin is that the most generally used an antidiabetic agent that could be a biguanide with the chemical name N,N-Dimethylimidodicarbonimidic diamide. These medication were developed from galegine, a by-product of guanidine found in galega officinalis (Fig 1) (Scott, L.J., 2010) (Klepser, T.B. and Kelly, M.W., 1997.).

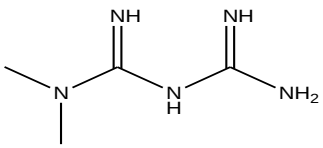

Fig 1 Chemical Structure of Metformin

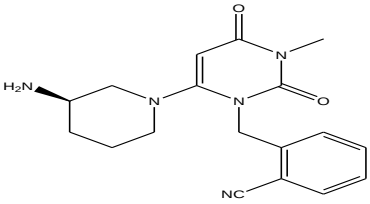

Fig 2 Chemical Structure of Alogliptin

Various analytical methods are developed for metformin in several combos. Mowaka, S. et al developed and compared to a new UHPLC-UV technique and UPLC-MS/MS technique. Kumar, A.P., et al (2013) developed and valid for coinciding determination of Alogliptin and metformin hydrochloride by RP-HPLC in tablet dosage form.

The present analysis work states the rapid, accurate, sensitive, price economical technique for simultaneous estimation of metformin and Alogliptin from the tablet formulation to determine the particular quantification of each drug part within the dosage form and validate the developed technique according to ICH guidelines on varied parameters like Specificity, Accuracy, Precision, Linearity, range and robustness.

II. MATERIALS AND METHODS

Chemicals and Reagents

All reagents utilised during this method were of analytical grade. Alogliptin and metformin API were kindly provided by alembic pharmaceutics limited, Vadodara. For the estimation of a billboard formulation, Kazano [Alogliptin (12.5mg) and metformin (500mg)] manufactured by Takeda Pharms USA was procured from the native market.

Instrument Parameters and Spectroscopic conditions

UV spectroscopy was performed on Shimadzu 1700 uv spectrometer, 1cm cell quartz cuvette. Mode was set as uv mode and Detector wavelength was kept at 231 nm and 276 nm.

Preparation of Alogliptin (5 ppm) and Metformin (10 ppm) standard solution:

5 mg of Alogliptin was weighed and transferred to a 100 ml volumetrical flask and make up with the diluent. Pipette 1 ml and make up with diluents until 10 ml in 10 ml volumetrical flask. 10 mg of metformin was weighed and transferred to a 100 ml volumetrical flask and make up with the diluent. Pipette 1 ml and make up with diluents until 10 ml in 10 ml volumetrical flask.

Analysis of Pharmaceutical dosage form-Tablet by developed method

Preparation of Sample solution:

Tablet powder was weighed equivalent to 10 mg of metformin, and 5 mg of Alogliptin and transferred to 100 ml volumetrical flask, and make up volume with diluent. Pipette 1 ml from above resolution and transferred to a 10 ml volumetrical flask and make up with the diluent.
Analyse above solution on UV Spectrometer.

Analytical Method Validation

The optimized spectroscopic method was valid by evaluating specificity, linearity, precision, accuracy, limit of detection (LOD), limit of quantification (LOQ). The validation of the method was performed as per ICH guidelines.

III. RESULT AND DISCUSSION

Method validation

Specificity

The spectrum of metformin and Alogliptin show no interference with the spectrum of metformin and Alogliptin blank, that the developed method is found to be specific (Fig. 3).

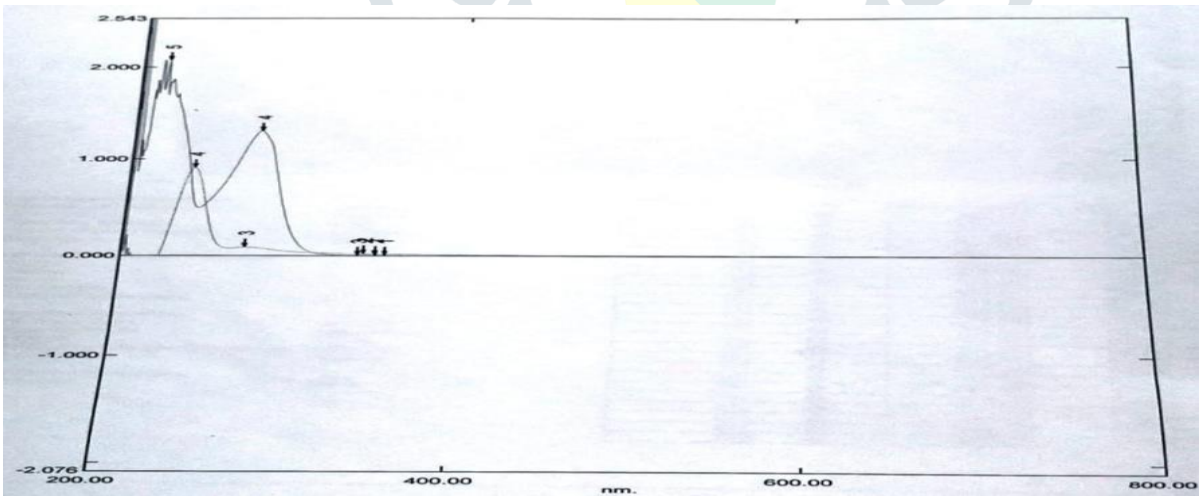

Figure 3 UV Spectra of Metformin and Alogliptin

Linearity

Appropriate volume from Alogliptin and metformin hydrochloride standard solution was transferred to volumetrical flask of 10 ml unit} capacity. The volume was adjusted with mobile phase to allow a solution containing 5–25 µg/ml µg/ml Alogliptin and 5–20 µg/ml metformin hydrochloride. The correlation co-efficient of Alogliptin and metformin was achieved to be 0.998 and 0.999 severally.

Table 1: Linearity data for Alogliptin

Concentration(µg/ml)	Absorbance
5	0.31
10	0.65
15	0.92
20	1.27
25	1.61

Table 2: Linearity data for Metformin

Concentration(µg/ml)	Absorbance
5	0.43
10	0.85
15	1.29
20	1.71
25	2.17

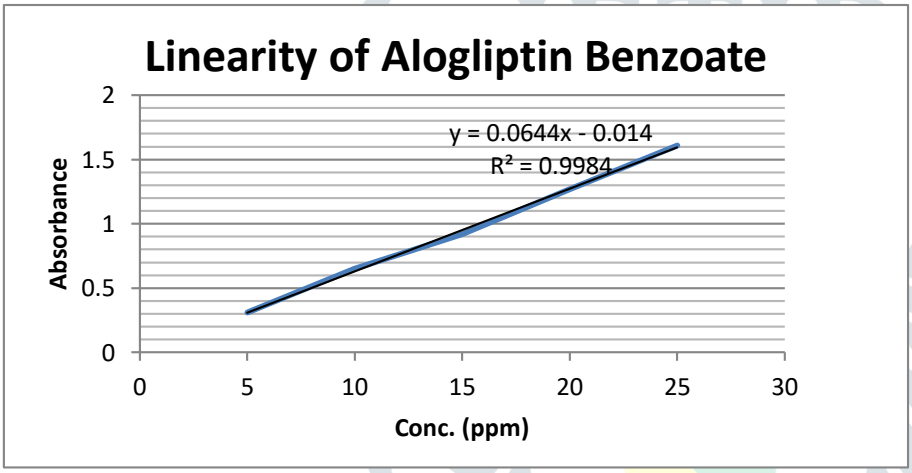

Fig. 4: Linearity of Alogliptin

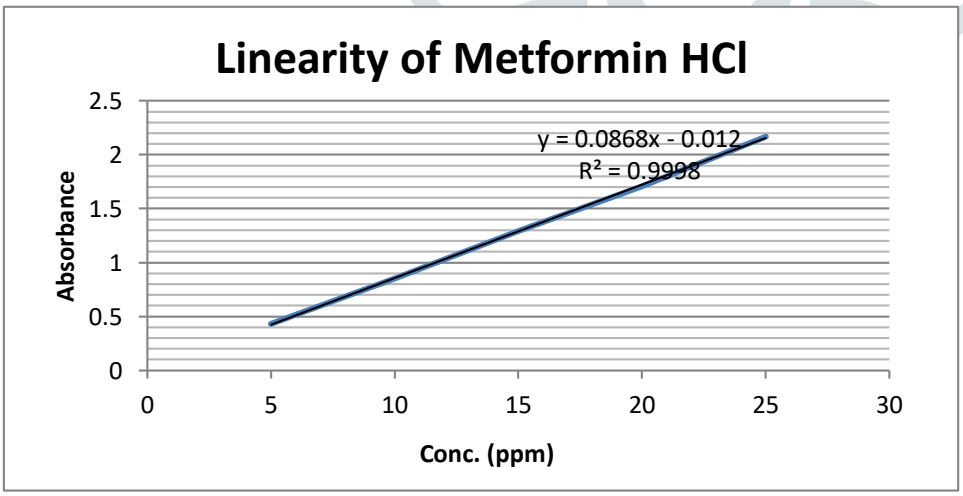

Fig. 5: Linearity of Metformin

Precision

Method Precision

The data for method precision of absorbance measurement for Alogliptin (5 µg/ml) and metformin (10 µg/ml) supported six measurements of the same solution of Alogliptin (5 µg/ml) and metformin (10 µg/ml).The % RSD for Alogliptin and metformin was found to be 1.46 and 1.43 respectively.

Table 3: Method Precision data for Alogliptin

Conc. (µg/ml)	Absorbance	Mean	% R.S.D
5	0.35	0.3533	1.46
	0.35		
	0.36		
	0.35		
	0.37		
	0.35		

Table 4: Method Precision data for Metformin

Conc. (µg/ml)	Area	Mean	% R.S.D
10	0.84	0.8466	1.43
	0.84		
	0.85		
	0.85		
	0.85		
	0.85		

Intraday and Interday precision

Intraday precision was determined through standard solution containing (5, 10, 15 µg/ml) of metformin and (5, 10, 15 µg/ml) of Alogliptin were analyzed thrice on the same day and 2 R.S.D was calculated. Interday precision was resolute through standard solution containing (5, 10, 15 µg/ml) of metformin and (5, 10, 15 µg/ml) of Alogliptin were analyzed three times on totally different day and 2 R.S.D was calculated.

Table 5: Intraday precision data for estimation of Alogliptin

Alogliptin		
Conc. (µg/ml)	**Mean Absorbance**	**% R.S.D**
5	0.33	0.10
10	0.65	0.25
15	0.94	0.25

Table 6: Intraday precision data for estimation of Metformin

Metformin		
Conc. (µg/ml)	**Mean Absorbance**	**% R.S.D**
5	0.44	0.25
10	0.82	1.03
15	1.23	0.25

Table 7: Interday precision data for estimation of Alogliptin

Conc. (µg/ml)	Mean Absorbance	% R.S.D
5	0.34	0.59
10	0.66	0.30
15	0.96	0.35

Table 8: Interday precision data for estimation of Metformin

Conc. (µg/ml)	Mean Absorbance	% R.S.D
5	0.43	1.32
10	0.84	0.96
15	1.25	0.54

Accuracy

Sample solution was taken in 3 completely different flask label A, B and C with different concentration at 80 %, 100%, and 120 % of standard solution spiked in it and diluted up to 10ml. The amount of metformin and Alogliptin was calculated at every level and 2 recoveries were computed.

Table 9: Recovery data for Metformin

Conc. Level (%)	Sample amount (µg/ml)	Recovery	% Recovery	% Mean Recovery
80 %	8	80.363	100.363	100.230
	8	79.804	99.804	
	8	80.524	100.524	
100 %	10	100.700	100.700	99.917
	10	100.114	100.114	
	10	98.938	98.938	
120 %	12	120.539	100.539	99.758
	12	119.276	99.276	
	10	119.458	99.458	

Table 10: Recovery data for Alogliptin

Conc. Level (%)	Sample Amount	% Recovery	% Recovery	% Mean Recovery
80 %	4	80.518	100.518	100.436
	4	79.928	99.928	
	4	80.862	100.862	
100 %	5	100.857	100.857	99.478
	5	98.729	98.729	
	5	99.848	99.848	
120 %	6	120.687	100.687	99.532
	6	119.448	99.448	
	6	119.463	99.463	

LOD and LOQ

LOD and LOQ were evaluated by injecting the dilution of standard solution and the standard deviation (SD) of the intercepts was calculated.

Table 11: LOD data for Metformin and Alogliptin

Metformin	Alogliptin
LOD = 3.648 µg/ml	LOD = 1.456 µg/ml

Table 12: LOQ data for Metformin and Alogliptin

Metformin	Alogliptin
LOQ = 4.486 µg/ml	LOQ = 2.264 µg/ml

Analysis of Marketed Formulation by developed method

Metformin and Alogliptin are out there in combined pharmaceutical dose form for the treatment of diabetes mellitus type 2. Earlier, numerous HPLC and UV methods for metformin and Alogliptin are reported for bulk drug or together with different medication. Some HPLC study has been reported on the mix of metformin and Alogliptin. However there's a requirement for development and validation of a simple and precise UV methodology for simultaneous estimation of metformin and Alogliptin for combined pharmaceutical dose form. The estimation results were corresponding to labeled value of each drug within the combined dose kind. These results indicate that the developed methodology is correct, precise, simple and rapid which can be used for routine quality control of the dose form in industries.

Table 13 Analysis of Marketed Formulation

Tablet	**Kazano**	
Label claim	**Metformin (500 mg)**	**Alogliptin (12.5 mg)**
Assay	100.487	100.154

IV. CONCLUSION

A simple, rapid, accurate, sensitive and cost economical methodology for simultaneous estimation and precise ultraviolet radiation methodology has been developed and valid as per ICH guidelines for simultaneous Estimation of metformin and Alogliptin in Their Combined dose form. Validation concludes that developed uv methodology is linear, accurate, precise, specific and sturdy. It may be successfully acquired for routine quality control analysis of metformin and Alogliptin in Combined dose form. This methodology can currently transfer to utilize for routine laboratory analysis and assay of metformin and Alogliptin in their combined dose form.

V. ACKNOWLEDGEMENTS

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VI. CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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