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SIMULTANEOUS ESTIMATION OF SITAGLIPTIN PHOSPHATE AND METFORMIN HYDROCHLORIDE IN BULK AND TABLET DOSAGE FORM BY FTIR SPECTROPHOTOMETRIC

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ABSTRACT

Simple, accurate and precise FTIR methods have been developed for the determination of Sitagliptin phosphate monohydrate (STG) and metformin HCL (MET). The simultaneous estimation was carried out at detection wavelength of 206nm using variable wavelength detector. Metformin hydrochloride and Sitagliptin phosphate is an ant diabetic drug. The FTIR spectra of the compound have been recorded. The light absorption activity in the UV-vis region of the drug under different storage conditions has also been analyzed. The characteristic of the drug have been identified and assigned using FTIR spectrum. The proposed methods used to determine each drug in binary mixture with metformin and ternary mixture with metformin and Sitagliptin alkaline degradation product that is obtained after alkaline hydrolysis of Sitagliptin. The methods developed were satisfactorily applied to the analysis of the pharmaceutical formulations and proved to be specific and accurate for the quality control of the cited drugs in pharmaceutical dosage forms.

KEYWORDS: FTIR, UV-Visible spectra, Metformin hydrochloride, Sitagliptin phosphate, Pharmaceutical preparation.

INTRODUCTION

Methods of Drug Analysis are divided into physical, chemical, physiochemical and biological ones. Physiochemical and biological methods are the most commonly used methods for estimation of drug substances present in any dosage form. Physical method of analysis involves the study of the physical properties of a substance. It includes determination of

solubility, colour, density or specific gravity (for liquids), moisture contents, melting, freezing and boiling points. Physiochemical methods are used to study the physical phenomenon that occurs as a result of chemical reactions **[Pathade et al, 2011].**

Among the physiochemical methods the most important are optical methods (refractometry, polarimetry, emission and fluorescence methods of analysis, photometry including photocolorimetry and spectrophotometeric methods covering UV, visible, IR regions, nephalometery or turbidimetery), electrochemical (potentiometry, amperometry, coulometric and polarography) and chromatographic methods**[Shabir et al, 2003].**

Diabetes mellitus

Diabetes Mellitus is commonly referred to as diabetes, is a group of metabolic disorders in which there are high blood sugar levels over a prolonged period. *It* is a condition where people don't produce enough insulin to meet their body's needs and/or their cells don't respond properly to insulin **[Shyamala et al, 2011].**

All types of diabetes mellitus have something in common. Normally, the human body breaks down the sugars and carbohydrates consumed into a special sugar called glucose. Glucose fuels the cells in our body. But the cells need insulin, a hormone, in the bloodstream in order to take in the glucose and use it for energy.

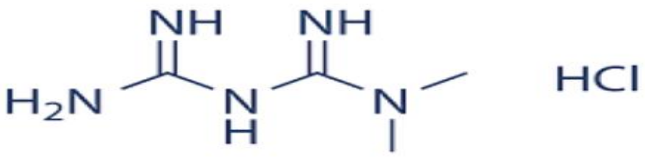
Diabetes is a condition that impairs the body's ability to process blood glucose, the common as blood sugar.

The following table shows the normal and diabetic blood sugar levels.

Table 1: ***Blood sugar level chart.***

Category	Fasting blood sugar(mg/dl)	Just after eating(mg/dl)	3 hours after eating (mg/dl)
Normal	80-100	170-200	120-140
Pre diabetic	101-125	190-230	140-160
Diabetic	126+	220-300	200+

Metformin hydrochloride



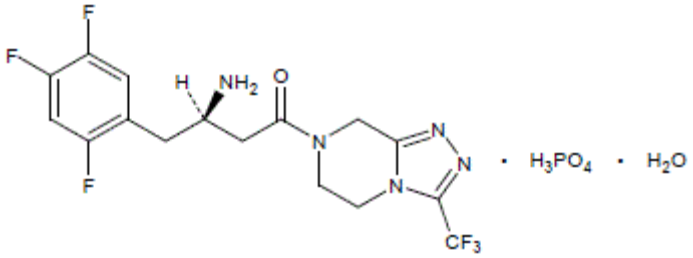
[IUPAC name 3-(diaminomethylidene)-1, 1-dimethylguanidine]

Metformin hydrochloride (1, 1-dimethylbiguanide hydrochloride) is freely-soluble in water, slightly soluble in ethanol, but insoluble in acetone, ether, dichloromethane or chloroform. The pKa of metformin is 12.4.

Medical use

Metformin is primarily used for type 2 diabetes, but is also used in polycystic ovary syndrome. Outcomes appear to be improved even in those with some degree of kidney disease, heart failure**, or** liver problems**.**

Sitagliptin phosphate



[IUPAC name (3R)-3-amino-1-[3-(trifluoromethyl)-6,8-dihydro-5H-[1,2,4]triazolo[4,3-a]pyrazin-7-yl]-4-(2,4,5-trifluorophenyl)butan-1-one]

Sitagliptin is soluble in water, very slightly soluble in ethanol (95 percent), but practically insoluble in heptane. The pKa of metformin is 7.7.

Mechanism of action

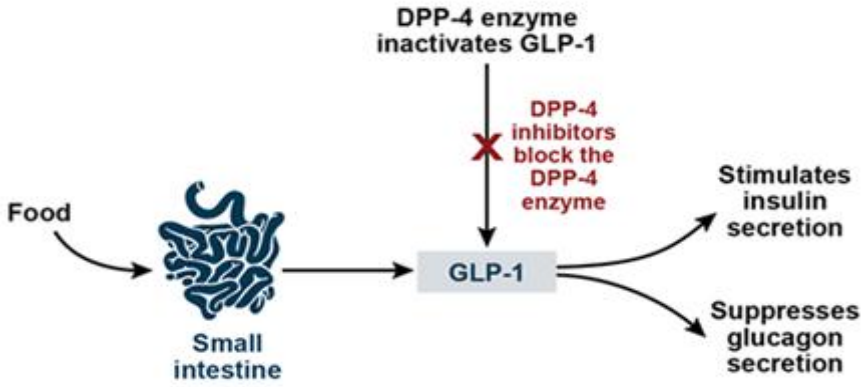


***Fig. 1*: MOA of sitagliptin phosphate.**

Sitagliptin works to competitively inhibit the enzyme dipeptidyl peptidase 4 (DPP-4). This enzyme breaks down the incretions GLP-1 and GIP, gastrointestinal hormones released in response to a meal. By preventing GLP-1 and GIP inactivation, they are able to increase the secretion of insulin and suppress the release of glucagon by the alpha cells of the pancreas. This drives blood glucose levels towards normal. As the blood glucose level approaches normal, the amounts of insulin released and glucagon suppressed diminishes, thus tending to prevent an "overshoot" and subsequent low blood sugar (hypoglycemia) which is seen with some other oral hypoglycemic agents.

Sitagliptin has been shown to lower HbA1c level by about 0.7% points versus placebo. It is slightly less effective than metformin when used as a monotherapy. It does not cause weight gain and has less hypoglycemia compared to sulfonylureas. Sitagliptin is recommended as a second-line drug (in combination with other drugs) after the combination of diet/exercise and metformin fail.

FTIR spectrophotometer (Fourier transform infrared radiation)

Principle

FTIR spectrometry was developed in order to overcome the limitations encountered with dispersive instruments. The main difficulty was the slow scanning process. A method for measuring all of the infrared frequencies simultaneously, rather than individually, was needed. A solution was developed which employed a very simple optical device called an interferometer. The interferometer produces a unique type of signal which has all of the infrared frequencies encoded into it. The signal can be measured very quickly, usually on the order of one second or so. Thus, the time element per sample is reduced to a matter of a few seconds rather than several minutes **[Devika et al, 2013].**

For instance, the molecule can absorb the energy contained in the incident light and the result is a faster rotation or a more pronounced vibration.

MATERIAL AND METHOD

Material – KBr (IR Grade), JANUMET Tablet

- The sufficient amount of Potassium bromide (IRGrade) is weighed and dried at 105° C for 1 hour.
- The sample (JANUMET Tablet) under examination is mixed with dried KBr powder. (Ratio1: 300)

- With the help of small spatula, the sample triturated is transferred to Hydaulic Press (Pressure: 15 KPa)
- Before taking the IR spectra of the sample, the background IR spectrum of the KBr pellet was recorded.
- The IR spectrum of Metformin Hydrochloride and Sitagliptin Phosphate obtained are obtained in figure 2, 3, 4 and 5.

Standard preparation: The standard stock solution of the drug was prepared by weighing accurately about 100 mg metformin HCl and 10 mg sitagliptin phosphate transferred to 100 ml and 10 ml clean dry volumetric flask respectively. Volume was made up to 100 ml with water to prepare 1000 ppm solution respectively.

Sample preparation: Tablet sample equivalent to 7.2 mg was weighed and transferred to 10 ml volumetric flask. Volume was made up to 10 ml with distilled water to prepare 500 ppm solution.

Selection of wavelength: PDA scan of the standard drug dilution showed that the drug absorbs in three regions of UV: 223 nm, 206 nm and 253 nm. It was found that at low concentration the signal to noise ratio at 253 nm and 223 nm was not clear. Hence, 206 nm was selected as the working wavelength so that the method can be used in the lower concentration range.

RESULTS AND DISCUSSION

The spectra obtained with the reference standards under examination are concordant with the spectra given in Indian Pharmacopoeia 2018. Therefore, it is evident that the reference standard taken during the study is a valid standard based on the identification test by FTIR.

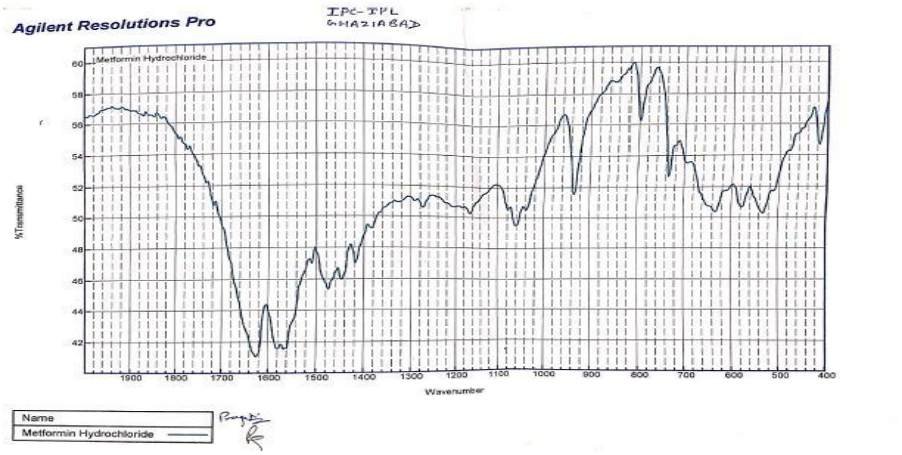


***Fig. 2*: FTIR of the standard (Metformin hydrochloride).**

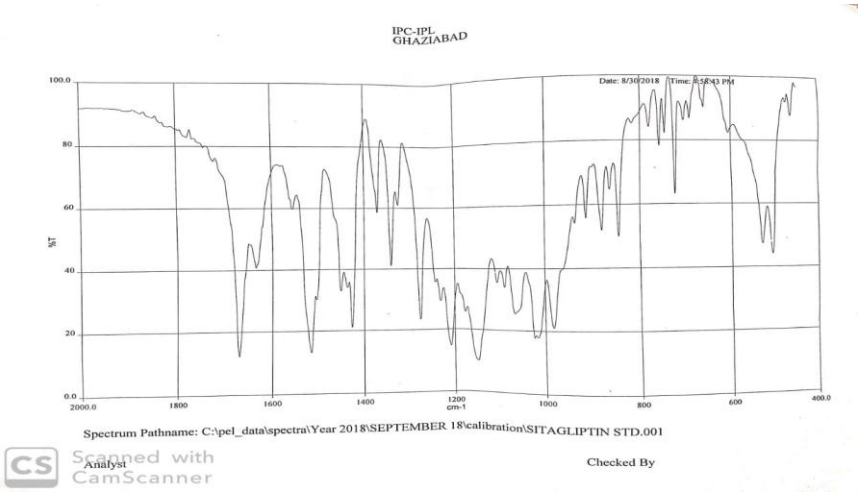


***Fig. 3*: FTIR of the standard (Sitagliptin phosphate).**

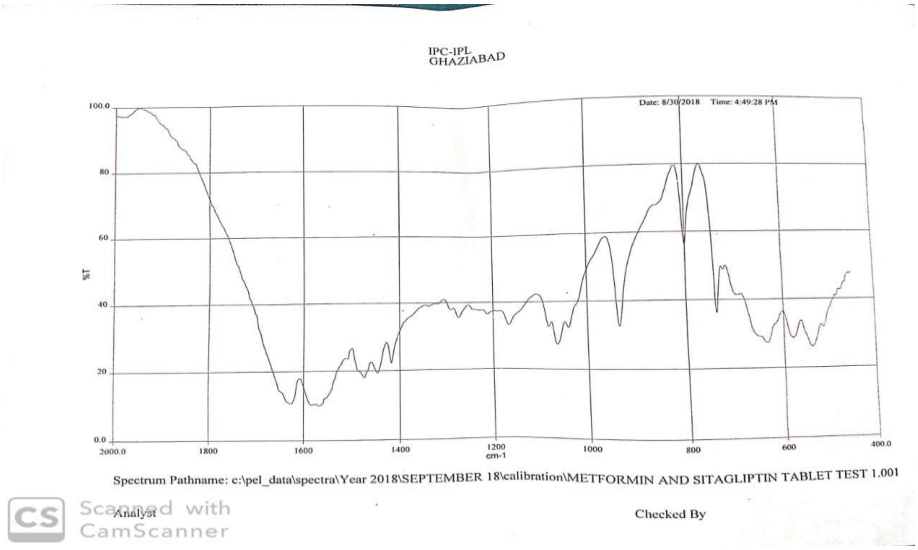


***Fig. 4*: FTIR of the drug sample (JANUMET Tablet).**

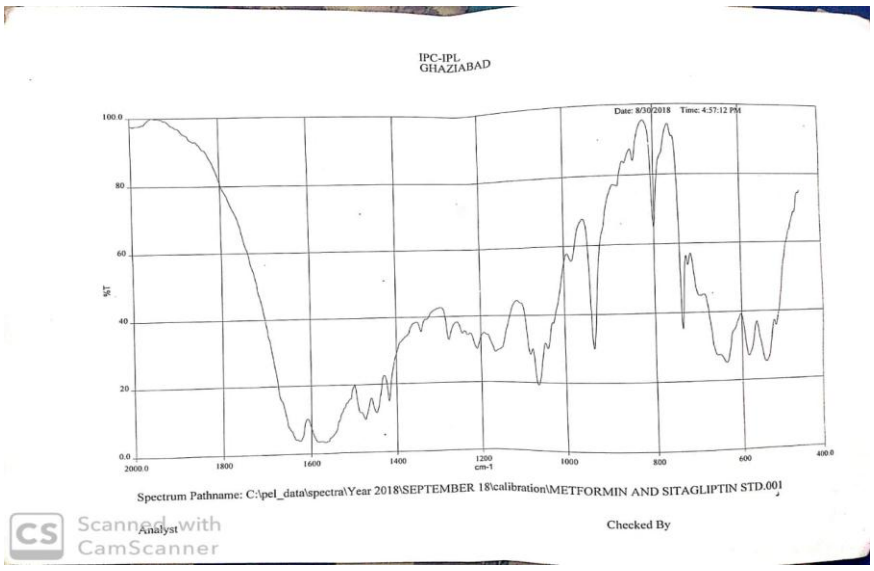


***Fig. 5*: FTIR of the standard (Metformin hydrochloride with sitagliptin phosphate).**

The method was determined at five different concentration levels ranging from 200 ppm to 1000 ppm for Metformin HCl and and 20 ppm to 100 ppm for Sitagliptin phosphate. The calibration curve was constructed by plotting peak area versus concentration of metformin and sitagliptin respectively, and the standard plot and regression equation was determined. Linearity graph at different concentrations % level are shown in figure 6 and 7.

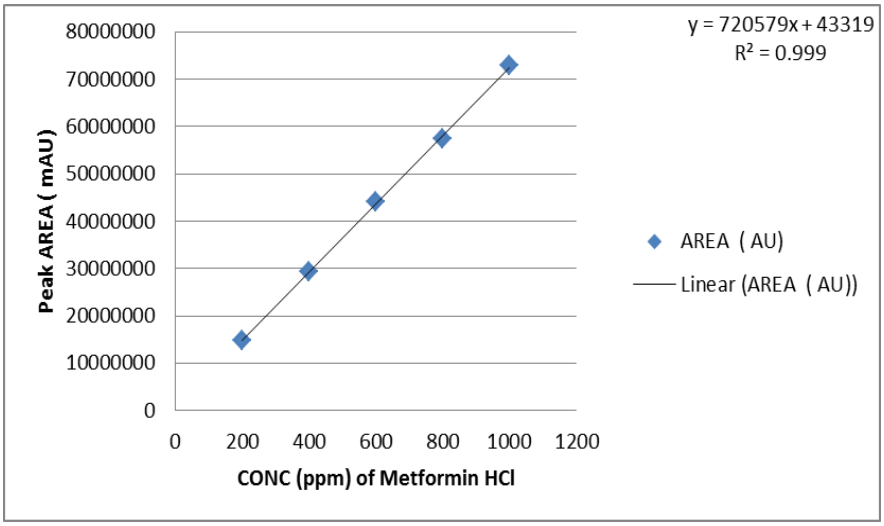


***Fig. 6*: (Linearity data of Metformin Hydrochloride of 5 different concentrations).**

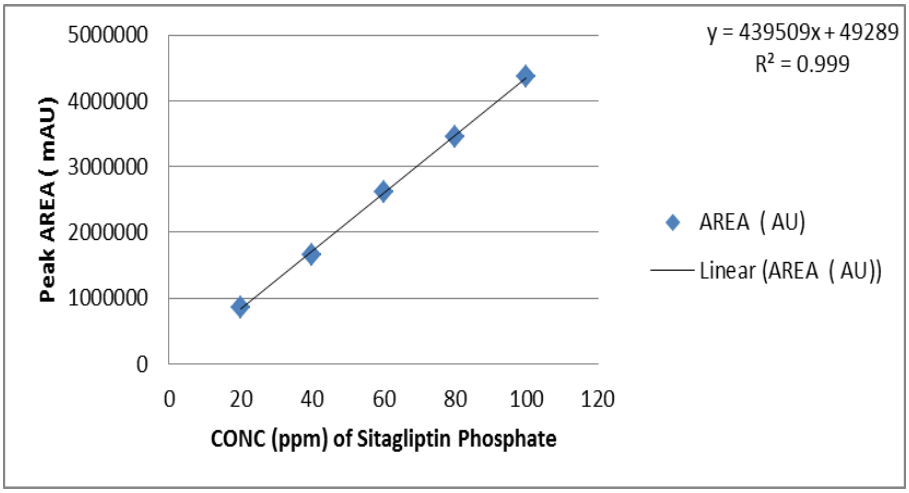


***Fig. 7*: (Linearity data of Sitagliptin phosphate of 5 different concentrations).**

CONCLUSION

FTIR spectroscopy in the clinical analysis of normal samples is clearly demonstrated. The use of the ATR sampling technique provides the FTIR tool as the most convenient diagnostic tool as well as evaluating in diabetes. This can be more conveniently employed in diagnostic procedures, and evaluation of the ant diabetic drug in diabetes.

Metformin hydrochloride and Sitagliptin phosphate is an ant diabetic drug. The FTIR spectra of the compound have been recorded. The light absorption activity in the UV-vis region of the drug under different storage conditions has also been analyzed. The characteristic of the drug have been identified and assigned using FTIR spectrum. A comparison after the sample stored in the ideal conditions and is exposed to environmental hazards is made.

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