ORIGINAL RESEARCH

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METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF SOME ANTIHYPERTENSIVE DRUG IN COMBINED DOSAGE FORM USING HYDROTROPIC PHENOMENON

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ABSTRACT-The method development and validation for the estimation of Glimepiride and Pioglitazone using hydrotropic agents provide a reliable and effective means for quantifying these two antidiabetic drugs. The use of hydrotropic solubilization techniques significantly enhances the solubility of the drugs, making them amenable to accurate and precise quantification.

This method holds great promise for pharmaceutical industries and research institutions involved in the analysis and quality control of pharmaceutical formulations containing Glimepiride and Pioglitazone. It offers a viable alternative to traditional solubilization techniques, facilitating the simultaneous estimation of these drugs with improved sensitivity and efficiency.

Overall, the successful development and validation of this method contribute to the advancement of analytical techniques in pharmaceutical research and the enhancement of drug quality control processes. Further applications and adaptations of this method may lead to its broader use in the pharmaceutical industry for the estimation of other poorly soluble drugs.

KEYWORDS:- Glimepiride, Pioglitazone, Validation, Hydrotropic, Analysis, Solubilization

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INTRODUCTION: -Since about 70% of recently discovered drug candidates have poor aqueous solubility, the primary issue facing the pharmaceutical industry at the moment is connected to tactics that increase drug solubility. One of the key characteristics to achieve desired pharmacological response is solubility. The bioavailability of a medicine determines its therapeutic effectiveness, which is ultimately determined by the drug's moiety's solubility Carl A. Neuberg first used the term "hydrotropy" in 1916. The solubility of weakly and sparingly soluble medicines in water can be improved using hydrotropes. It is a chemical phenomenon that makes a medication that dissolves poorly in water more soluble by adding a second solute (hydrotrope). When one solute is present in excess, it makes another solute more soluble.

Through "salt in" or "salt out" effects, hydrotropic agents are ionic organic salts with the ability to alter the solubility of a solute in a particular solvent. The term "hydrotropism" refers to the phenomena of salts that exhibit the "salt in effect" of non-electrolytes. Although they lack colloidal characteristics, they increase solubility by generating weak interactions with the molecules of the solution. A hydrotropic molecule interacts with a less water-soluble molecule through dipole-dipole or weak van der Waals interactions (Pandey*et al.,* 2022; Tripathi *et al.,* 2022).

Mechanism of hydrotropic solubilization

The enhancement of solubility by hydrotrope is based on the self-association of hydrotrope and the association of hydrotropes with solute. Various hypothetical and investigational efforts are being made to clarifying the mechanisms of hydrotrope. The available proposed mechanisms can be abridged according to four designs:

- Hydrotropes self-associate to form aggregates. Another name for it is stacking. Additionally, it attracts the molecules of the solute in the aqueous phase. As a result, solubility increases as hydrotropic agent concentration does.
- The interaction between the hydrotropes and the solute results in a complex with increased aqueous solubility.
- Intermolecular hydrogen bonding modifies the solvent's structure. The solute's solubilityis altered as a result of hydrogen bonding.

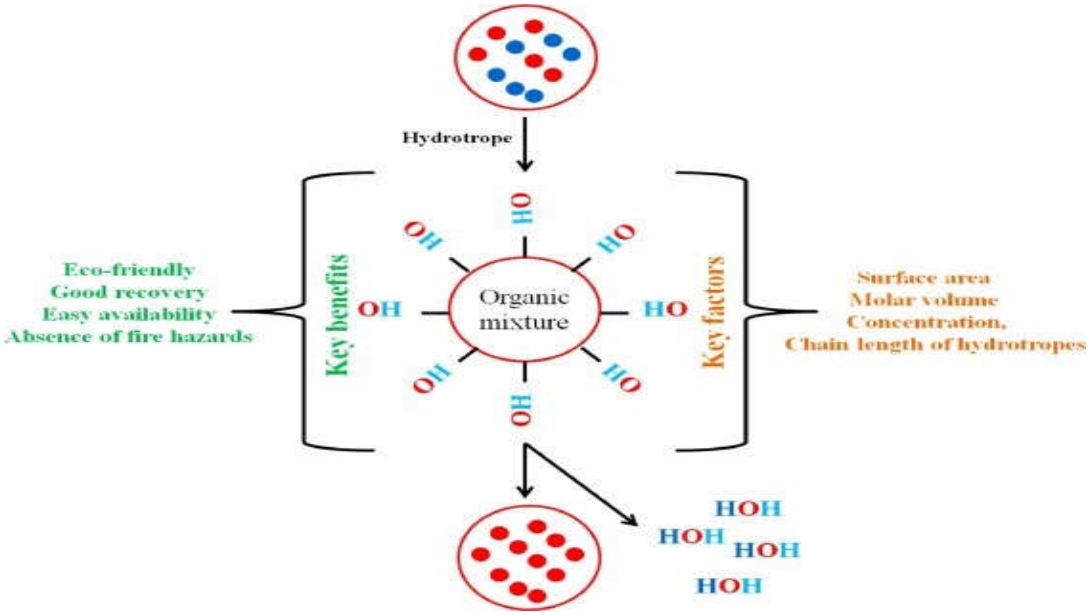

Figure 1: Hydrotropes

Analysis

Analysis is vital in any product or service, and it is also important in drug because it involves life (Hema and Reddy, 2017).Analytical chemistry is the analysis of separation, quantification and chemical additives identification of herbal and synthetic materials constituted with one or more compounds or factors. Analytical chemistry is separated into two predominant classes, a qualitative evaluation that is to say the identification with regardto the chemical additives exists in the sample, whereas quantitative evaluation estimates the amount of positive detail or compound within the

EXPERIMENTAL WORK AND RESULTS:-

FT-IR study carried out by KBr press pellet technique

The concentration of the sample in KBr should be in the range of 0.2% to 1%. The pellet isa lot thicker than a liquid film, consequently a decrease concentration in the sample is required (Beer's Law). For the die set that you'll be the usage of, about 80 mg of the mixtureis wanted. Too excessive of an attention causes typically difficulties to obtain clean pellets. This pellet keeps into the sample cell and scanned between 4000-400 $c.m^{-1}$ and IR spectra are obtained.

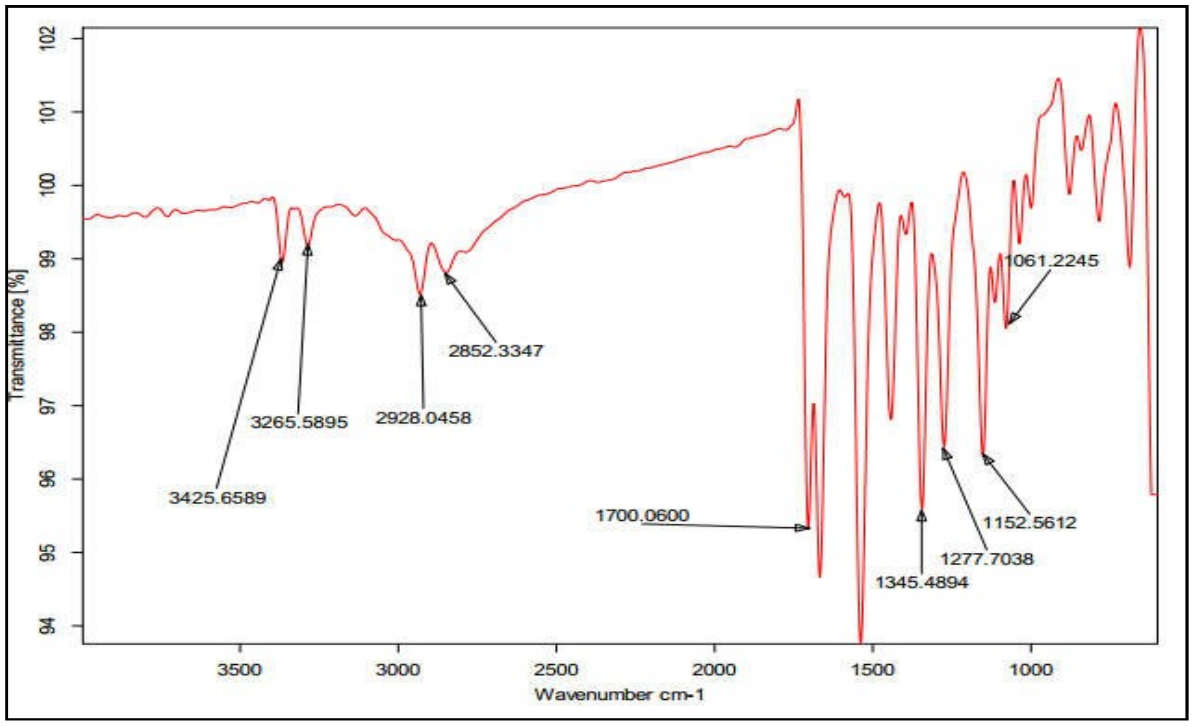

Figure 2: FT-IR spectra of Glimepride

Determination of Solubility Enhancement by UV VIS. Spectroscopy

Solubility studies were performed in distilled water 2M Sodium acetate, 8M Urea, 2M Sodium Citrate,

2M Sodium Benzoate, 2M Ammonium Acetate, 2M Sod. Citrate, 2M Sodium acetate: 2M Sodium Benzoate, 2M Urea: 2M Sodium acetate, 2M Sodium citrate: 8M Urea, 2M Sodium citrate: 8M Urea, 2M Ammonium Acetate: 2M Sod. Citrate at room temperature (25 ± 2^0 C). An excess amount of drug was added to 100ml of solvent in screw- capped glass vials; these were mechanically shaken for 48 hours at 25°C until equilibrium was achieved. Aliquots were withdrawn, filtered through a membrane filter (0.45□) and spectrophotometrically analyzed for solubility.

Selection of wavelength for linearity

Solutions of 2□g/ml of GLP and 20□g/ml PGZ were prepared separately. Both the solutionswere scanned in the spectrum mode from 200 nm to 400 nm. The maximum absorbance ofGLP and PGZ was observed at 216.0 nm and 232.0 nm, respectively. GLP and PGZ showed linearity in the concentration range of 2-10 □g/ml and 10-50□g/ml at their respectivemaxima. Calibration curve was plotted, absorbance versus concentration.

To study the linearity of GLP and PGZ the selected wavelength are:

Table 1: Results of solubility enhancement by UV VIS. Spectroscopy

S. No.	Solvents	Solubility Enhancement (folds)	
		GLP	PGZ
1	2M Sodium acetate	4	7
2	8M Urea	5	8
3	2M Sodium Citrate	6	8
4	2M Sodium Benzoate	4	6
5	2M Ammonium Acetate	7	8
6	2M Sod. Citrate	6	8
7	2M Sodium acetate: 2M Sodium Benzoate (1:1)	7	5
8	2M Urea:2M Sodium acetate (1:1)	6	4
9	2M Sodium citrate:8M Urea (1:1)	7	9
10	2M Sodium citrate:8M Urea (1:1)	8	7
11	2M Ammonium Acetate: 2M Sod. Citrate (1:1)	16	18

Table 2: selected wavelength of GLP and PGZ

1. λ_{max} of GLP	216.0 nm
2. λ_{max} of PGZ	232.0 nm

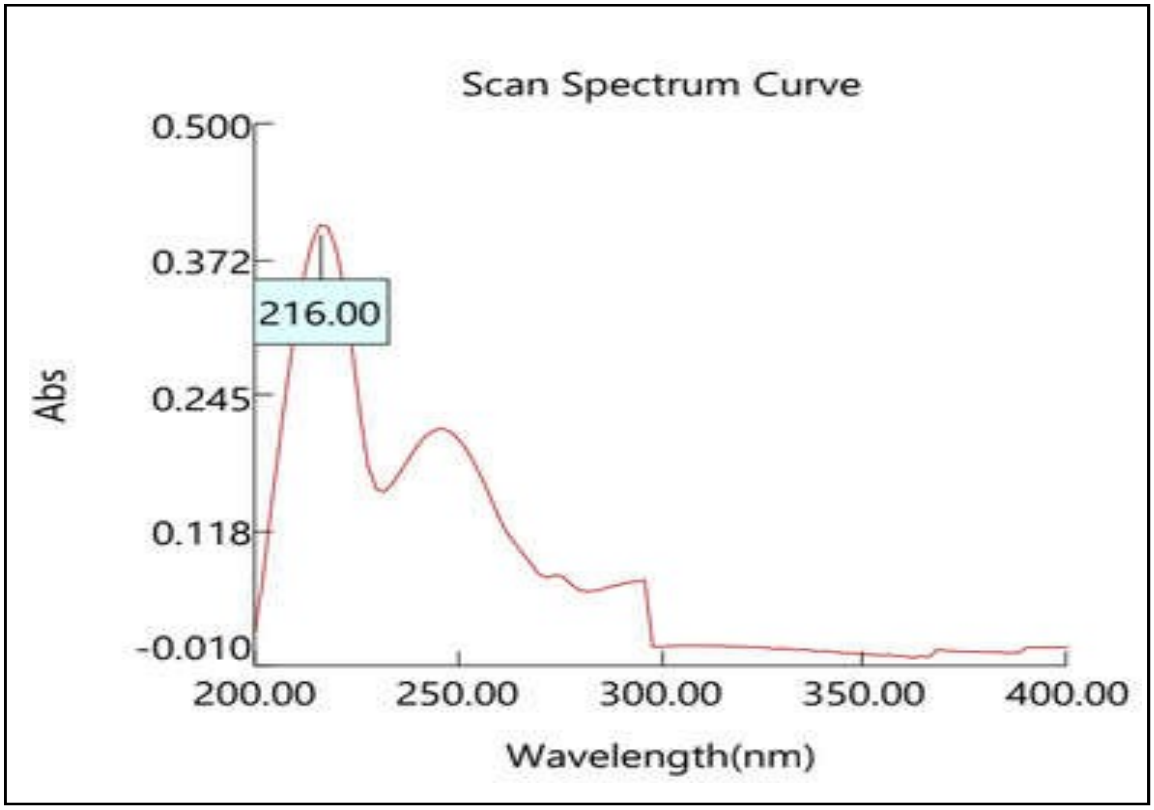

Figure 3: Determination of λ_{max} of GLP

Table 3: Linearity of GLP At λ_{max} = 216.0 nm

StandardConc. (mg/ml)	Rep-1	Rep-2	Rep-3	Rep-4	Rep-5	Mean	S.D.	% RSD
0	0	0	0	0	0	0	0	0
2	0.198	0.197	0.196	0.198	0.197	0.1972	0.001	0.424
4	0.385	0.384	0.385	0.386	0.384	0.3848	0.001	0.217
6	0.599	0.598	0.597	0.597	0.598	0.5978	0.001	0.140
8	0.795	0.794	0.796	0.797	0.798	0.796	0.002	0.199
10	0.995	0.994	0.996	0.997	0.997	0.9958	0.001	0.131

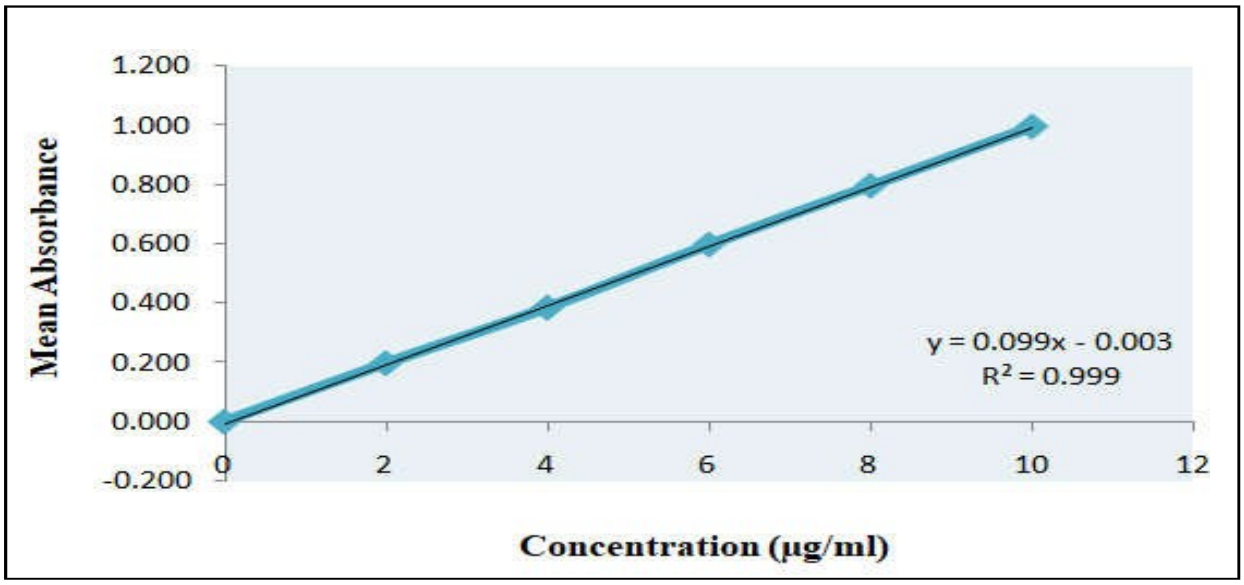

Figure 4: Calibration Curve of GLP

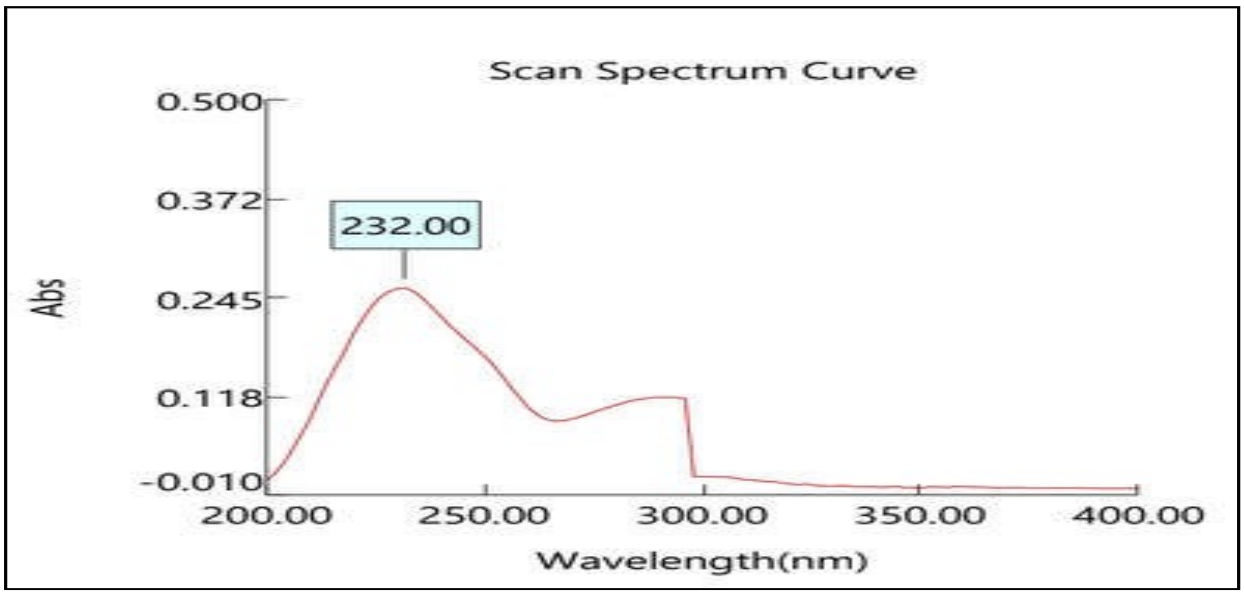

Figure 5: Linearity of PGZ

Table 4: Linearity of PGZ At λ_{max} = 232.0 nm

Standard Conc. (mg/ml)	Rep-1	Rep-2	Rep-3	Rep-4	Rep-5	Mean	S.D.	% RSD
0	0	0	0	0	0	0	0	0
10	0.253	0.254	0.253	0.254	0.255	0.2538	0.001	0.330
20	0.512	0.513	0.512	0.513	0.512	0.511	0.001	0.107
30	0.759	0.758	0.757	0.759	0.758	0.7582	0.001	0.110
40	1.015	1.014	1.015	1.014	1.013	1.0142	0.001	0.082
50	1.229	1.228	1.227	1.228	1.227	1.2278	0.001	0.068

Analysis of tablet sample

Twenty marketed tablets of GLP and PGZ were weighed and ground to a fine powder; amount equal to 2mg of GLP was taken in 10 ml volumetric flask. The PGZ present in this amount of tablet powder was 30mg. Then 8 ml of 2M Ammonium Acetate: 2M Sod. Citrate (1:1) solution was added and the flask was sonicated for about 10 min to solubilize the drug present in tablet powder and the volume was made up to the mark with hydrotropic solution. After sonication filtration was done through Whatman filter paper No. 41. Filtrate was collected and further diluted with RO Water to get the final concentrations of both drugs in the working range. The absorbances of final dilutions were observed at selected wavelengths and the concentrations were obtained from simultaneous equation method. The procedure was repeated for five times.

Table 5: Analysis of tablet formulation of GLP and PGZ

Drug	Label claim(mg)	Amount found(mg)	Label claim(%)	S.D.	% RSD
GLP	2	1.97	98.5	0.152	0.225
PGZ	30	29.58	98.6	0.223	0.263

SUMMARY AND CONCLUSION

The method development and validation for the estimation of Glimepiride and Pioglitazone using hydrotropic agents have been successfully achieved. This study aimed to develop a reliable analytical method for the simultaneous estimation of these two important antidiabetic drugs, which are often co-administered in the treatment of diabetes mellitus.

The use of hydrotropic agents, specifically hydrotropic solubilization techniques, proved to be effective in enhancing the solubility of both Glimepiride and Pioglitazone.

In conclusion, the method development and validation for the estimation of Glimepiride and Pioglitazone using hydrotropic agents provide a reliable and effective means for quantifying these two antidiabetic drugs. The use of hydrotropic solubilization techniques significantly enhances the solubility of the drugs, making them amenable to accurate and precise quantification.

This method holds great promise for pharmaceutical industries and research institutions involved in the analysis and quality control of pharmaceutical formulations containing Glimepiride and Pioglitazone. It offers a viable alternative to traditional solubilization techniques, facilitating the simultaneous estimation of these drugs with improved sensitivity and efficiency.

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CONFLICT OF INTEREST REPORTED: NIL; SOURCE OF FUNDING: NONE REPORTED