www.pharmaerudition.org

ISSN: 2249-3875

International Journal of Pharmaceutical Erudition

Research for Present and Next Generation

FEB 2019

Vol: 08 Issue:04

(1-9)

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

Research Paper

A PREFORMULATION STUDY OF PURE METFORMIN HCl

Tomar A.,*Wadhwani S., Bhadauria R.S.
Shrinathji Institute of Pharmacy, Nathdwara.

Metformin HCl is a first line drug of choice for the treatment of type II diabetes which act by decreasing hepatic glucose output and peripheral insulin resistance.[1] It can be given to obese patients with overweight having normal kidney function. The overall objective of preformulation testing is to generate information useful to the formulator in developing stable and bioavailable dosage forms, to determine kinetics and stability of drug and to establish drug excipients compatibility.Preformulation study was done and all results were in the range of prescribed in Indian Pharmacopoeia, so the drug was found to be of standard prescribed purity and quality. Infra red spectra of the drug reveal that there is no significant interaction between drug polymers. A solution of 10µg/mL of Metformin HCl was scanned in the range of 200 to 400 nm. The drug exhibited the λ_{max} at 234 nm in distilled water has good reproducibility graph. UV method was used for Estimation of Metformin HCl and absorbance values were measured using an ultraviolet–visible (UV-VIS) spectrophotometer at λmax 234 nm.

Key words: Metformin HCl, preformulatio andtype II diabetes

INTRODUCTION

Diabetes is a chronic health problem with devastating, yet preventable consequences. It is characterized by high blood glucose levels resulting from defects in insulin production, insulin action, or both. Globally, rates of type II diabetes were 15.1 million in 2000, the number of people with diabetes worldwide is projected to increase to 36.6 million by 2030. Out of these, 90-95% of these cases were adults with type II diabetes. Type II diabetes impacts men and women proportionately; there are over 12 million men with diabetes and 11.5 women with diabetes. Metformin HCl is a first line drug of choice for the treatment of type II diabetes which act by decreasing hepatic glucose output and peripheral insulin resistance.[1] It can be given to obese patients with overweight having normal kidney function.The overall objective of preformulation testing is to generate information useful to the formulator in developing stable and bioavailable dosage forms, to determine kinetics and stability of drug and to establish drug excipients compatibility.[2]preformualtion studies have a significant impact on manufacturing, storage, and performance of the drug production. Preformulation studies strengthen the scientific foundation of the guidance, provide regulatory relief and conserve resources in the drug development and evaluation process, improve public safety standards, enhance product quality facilitate the implementation of new technologies, and facilitate policy development and regulatory decision making.it also gives directions for development of formulation in choice of drug form, excipients, composition, physical structure, helps in adjustment of pharmacokinetic and biopharmaceutical properties, support for process development of drug substance support for process analytical technology, produce necessary and useful data for development of analytical methods.

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

It not only helps to guide dosage form selection, but also provides insights into how drug products should be processed and stored to ensure their quality.[3]

Material & methods: Pure Metformin HCl is obtained from Intas Pharmaceuticals as a gift sample.

Methods:

1.Organoleptic Properties : The organoleptic studies of Metformin HCl like general appearance like nature, colour, odour etc. were performed and observed.[4]

2. Detection of Melting Point Range: For determination of melting point USP method was followed. Small quantity of Metformin HCl was placed into a sealed capillary tube. The tube was placed in the melting point apparatus. The temperature in the apparatus was gradually increased and the observation of temperature was noted at which Metformin HCl started to melt and the temperature when the entire drug gets melted. This method is also known as open capillary method.[5]

3. Partition coefficient: To determine the partition coefficient of the Metformin HClthe shake flask method was used; it is the classical and the most useful method of determination of partition coefficient. The procedure could be explained as excess amount of API was added in 10 mL mixture of n-Octanoland water (1:1). The system was prepared in triplicate and wash gently in the separating funnel for 24 hours for achieving equilibrium. Then the two phases were separated and centrifuge at 8000 rpm for 20 minutes. After centrifugation, the concentration of Metformin HCl in both phases was determined by UV spectroscopy and partition coefficient was calculated using the equation.[6]

$$\text{LogP} = \log (K_{o/w})$$

4. FT-IR Spectrum of pure drug: FTIR spectroscopy was performed on Fourier transformed infrared spectrophotometer. The pellets of drug and potassium bromide were prepared by compressing the powders at 20 psi for 10 min on KBr-press and the spectra were scanned in the wave number range of 4000- 600 cm^{-1}.Fourier Transform Infrared Spectrophotometry was used for structure analysis of drug (Metformin HCl).[7]

5. Solubility study: An excess amount of the drug was added to 10 mL volumetric flask having different media (i.e. distilled water,simulated gastric fluid pH-1.2, simulated intestinal fluid pH-6.8, and simulated intestinal fluid pH-7.4). Drug was added to this till saturation occurred and shaken at room temperature for 48 h. After that, samples were filtered, appropriately diluted and analyzed at 234nm using UV visible spectrophotometer.[8,9]

6. UV Spectrum Analysis of Metformin HCl: The solution was scanned in the range of 200 to 400 nm to fix the maximum wave length and UV spectrum was obtained.[10,11]

7. Calibration Curve of Metformin HCl: 1mL of the standard stock solution was taken and diluted to 10mL with distilled water (100µg/mL), from the

above solution 0.2, 0.4, 0.6, 0.8 and 1 mL were pipetted out and diluted to 10 mL with distilled water to get the final concentration of 2, 4, 6, 8 and 10µg/mL respectively.[12,13,14]

8. Drug -Excipient Compatibility Study: The primary objective of this investigation was to identify a stable storage condition for Metformin HCl in solid state and identification of compatible excipients for its formulation. In this method, different excipients were selected and mixed separately with drug in proportion generally used in the formulation.[15]

A) Drug - Excipients Interaction by FT-IR: Fourier-transform infrared (FT-IR) spectroscopy was performed on the samples to determine the structure of the organic compounds and to identify the presence of specific functional groups within the sample. Furthermore, drug- polymer 1:1 interactions were examined using the resulting spectra. Spectra are obtained by passing infrared radiation through a sample and determining what fraction of incident radiation is adsorbed at a particular energy. The peak energy in the spectrum correspondence to the frequency of vibrations of the part of sample compound.[16]

B) Physical Stability study: Physical stability studies are done to identify the compatible and stable storage conditions and to identify compatible excipients for the preparation. Sets of mixture of drug and polymers were prepared, for physical compatibility studies (visual observation only), from which –

- 1 set was kept at $2^0 - 8^0$ c
- 1 set was kept at 60^0 c
- 2 set was kept at 25^0/60% RH, in open and closed conditions respectively
- 2 set was kept at 40^0/75% RH, in open and closed conditions respectively.[17]

Result & Discussion:

1. Organoleptic Properties: In organoleptic evaluation, Metformin HCl was found to be White crystalline odourless powder.

2. Detection of Melting Point Range: Melting point of Metformin HCl was found to be in the range of 222ºC to 226ºC which was in the range as prescribed in Indian Pharmacopoeia, so the drug was found to be of standard prescribed purity and quality.

3. Partition Coefficient: The partition coefficient of Metformin HClwas calculated from the ratio between the concentration of Metformin HClin oil (n-octanol) and aqueous phase (water). The ratio between the concentration of Metformin HClin oil (n- octanol) and aqueous phase (water) was determined and the partition coefficient of Metformin HCl(log P) was found to be 0.062 which was in the range as prescribed in Indian pharmacopeia so the drug was found to have hydrophillic character.

4. FTIR Spectrum of Metformin HCl

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

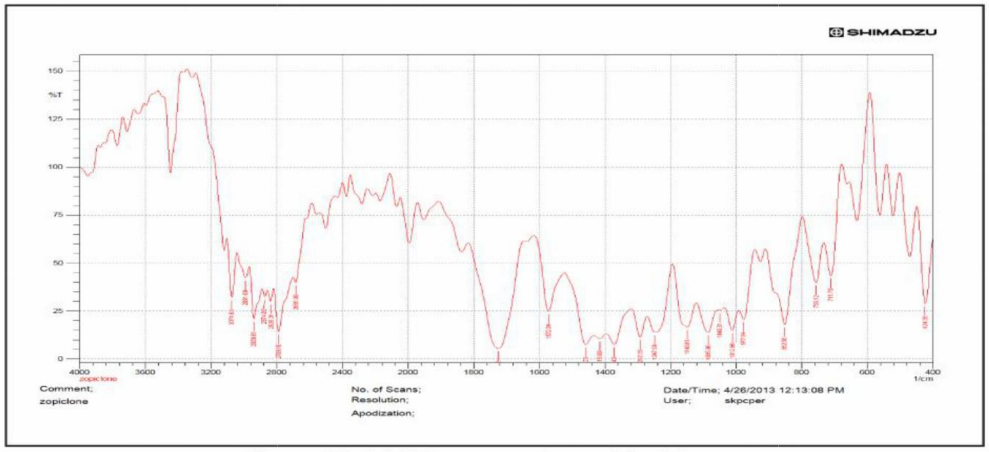

Figure 1: FTIR spectra of pure Metformin HCl

Table 1: Interpretation of IR spectrum of Metformin HCl

Sr. No.	Functional Group	Range	Wave number
1	C-H Stretching	3500-3000 cm^{-1}	3372.5336
2	N-H Stretching	3600-3200 cm^{-1}	3295.7108
3	C–H Stretching	3200-3000 cm^{-1}	3174.0850
4	O–H Stretching	3000-2500 cm^{-1}	2692.4447
5	C≡C Streching	2500-2000 cm^{-1}	2214.0358
6	N–O asymmetric stretching	2000-1500 cm^{-1}	1574.5393
7	C-N Streching	1500-1000 cm^{-1}	1416.8613
8	=C–H bending	1000-500 cm^{-1}	934.9509

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

5. Determination of absorption maxima: A solution of 10µg/mL of Metformin HCl was scanned in the range of 200 to 400 nm. The drug exhibited the λ_{max} at 234 nm in distilled water has good reproducibility graph.

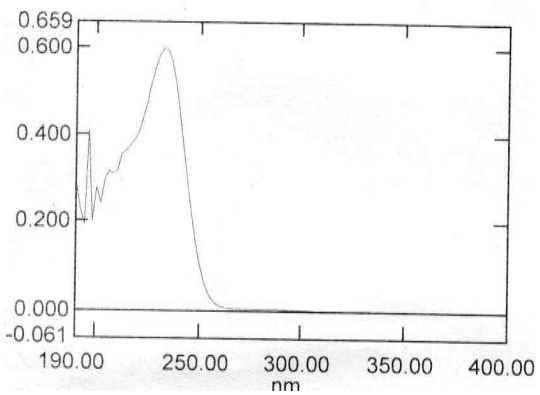

Fig. 2: Absorption maxima of Metformin HCl

6. SolubilityStudy : In solubility studies it was found that Metformin HCl is Freely Soluble in water, SGF pH 1.2,SIF pH 6.8 and SIF pH 7.4.

Table 2: Solubility Studies of Metformin HCl

Solvent	Saturation solubility (µg/mL)
Water	145
SGF pH 1.2	256
SIF pH 6.8	282
SIF pH 7.4	156

7. Calibration Curve: The UV calibration curve of Metformin HCl was constructed as 1mL of the standard stock solution was taken and diluted to 10mL with distilled water. Serial dilutions of the stock solutions were prepared and their absorbance values were measured using an ultraviolet–visible (UV-VIS) spectrophotometer at λmax 234 nm. Linearity was observed over a concentration range of 2-20 µg/mL. The absorbance values of different concentration of Metformin HCl nm wavelength are given in Table 3.

Table 3: Calibration data of Metformin HCl at 234 nm

Concentration (µg/mL)	Absorbance at 234nm
0	0
2	0.1915
4	0.4186
6	0.5465
8	0.7371
10	0.9155

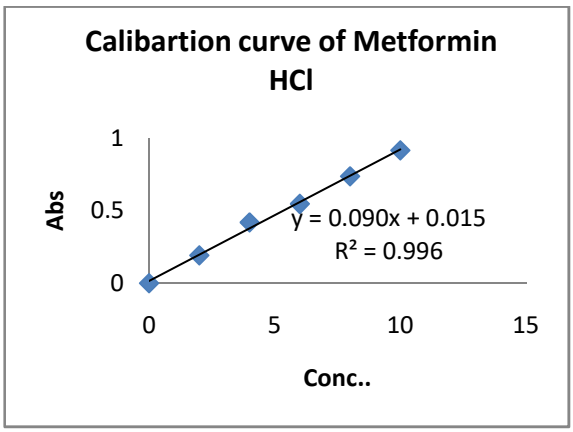

Fig. 3: Calibration curve of Metformin HCl at 234 nm

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

8. Drug –Excipient Compatibility Study

A) Drug –Excipient Interaction By FT-IR: Drug- polymer 1:1 interaction was examined using the resulting spectra. Spectra are obtained by passing infrared radiation through a sample and determining what fraction of incident radiation is adsorbed at a particular energy. The peak energy in the spectrum correspondence to the frequency of vibrations of the part of sample compound.physical mixture of drug and polymer also show same FTIR wave numbers peak as pure Metformin HCl in figure, so these results suggest that there is no any functional group changes of Metformin HCl. So all ingredients are chemically compatible with each others.

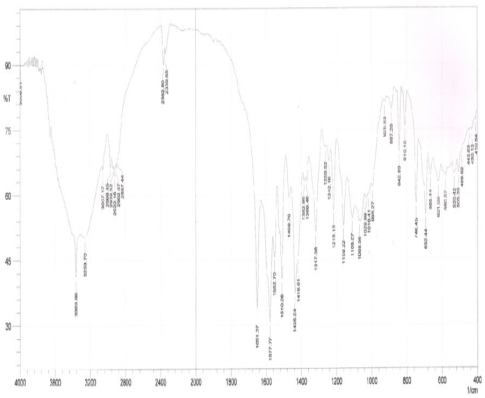

Fig. 4: FTIR spectra of pure Metformin HCl+ HPMC K4M

Physical stability data: Drug polymer compatibility study was performed at different temperatures and humidity conditions were recommended by ICH guidelines.

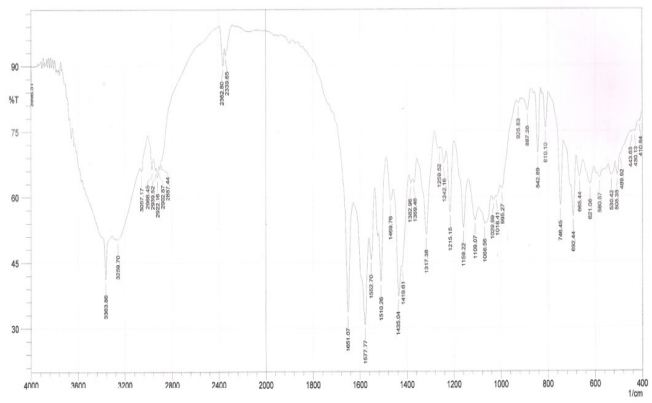

Fig. 5: FTIR spectra of pure Metformin HCl+ HPMC K15M

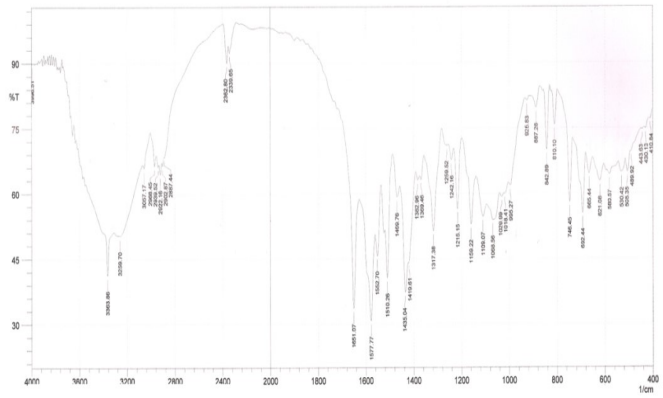

Fig. 6: FTIR spectra of pure Metformin HCl+ HPMC K100M

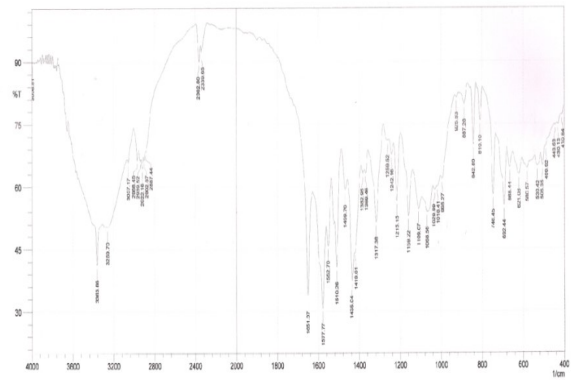

Fig. 7: FTIR spectra of pure Metformin HCl+ CMC

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

The result of drug– polymer compatibility study in shows in table. No change in color was observed when physical mixture of the Metformin HCl with the entire polymer used in the formulation was kept in below mentioned ratio at different temperatures and humidity conditions. So, the polymers to be used were found to be physically compatible with Metformin HCl and hence suitable for use in formulation.

Table 4: Drugs and Excipient Compatibility Study

Ingredients	Initial	40⁰ C/75% RH	
		15 Days	30 Days
Metformin HCl	White powder	White powder	White powder
HPMC K4M			
HPMC K15M			
HPMC K100M			
CMC			
MCC			

Summary & Conclusion: Diabetes is a chronic health problem with devastating, yet preventable consequences. It is characterized by high blood glucose levels resulting from defects in insulin production, insulin action, or both. Globally, rates of type II diabetes were 15.1 million in 2000, the number of people with diabetes worldwide is projected to increase to 36.6 million by 2030. Out of these, 90-95% of these cases were adults with type II diabetes. Type II diabetes impacts men and women proportionately; there are over 12 million men with diabetes and 11.5 women with diabetes. Metformin HCl is a first line drug of choice for the treatment of type II diabetes which act by decreasing hepatic glucose output and peripheral insulin resistance. It can be given to obese patients with overweight having normal kidney function. Preformulation study was done and all results were in the range of prescribed in Indian Pharmacopoeia, so the drug was found to be of standard prescribed purity and quality.Infra red spectra of the drug reveal that there is no significant interaction between drug polymers. A solution of 10µg/mL of Metformin HCl was scanned in the range of 200 to 400 nm. The drug exhibited the λ_{max} at 234 nm in distilled water has good reproducibility graph. UV method was used for Estimation of Metformin HCland absorbance values were measured using an ultraviolet–visible (UV-VIS) spectrophotometer at λmax 234 nm. Linearity was observed over a concentration range of 2-20 µg/mL.

REFERENCE

1. PamuSandhya, FaheemUnnisa Begum, Afreen. Formulation and Evaluation of Bilayer Tablets of Glimepiride and Metformin HCl. IOSR Journal of Pharmacy and Biological Science, 2018; 9(1): 38-45.

2. RenatiDamodar and BabjiMovva. Preparation and In-vitro Evaluation of Metformin HCl Tablets Containing Sustained

Release Beads for Increasing Therapeutic Window. Journal of bioequivalence and bioavailability, 2017; 6(3): 91-95.

3. G Sridhar Babu, D Vijay Kumar, M Aishwarya, P S Malathy. Formulation and in vitro characterisation of sustained release matrix tablets of Metformin HCl. Journal of Global Trends in Pharmaceutical Sciences, 2016; 5(14), 2085-2092.

4. Mohammad RaquibulHasan, Md. AbulHossen, AumitRoy,Tufikul Islam and Md. Saiful Islam Pathan. Preparation of Metformin HCl Extended Release Matrix Tablets by Direct Compression Method and Its in vitro Evaluation. British Journal of Pharmaceutical Research, 2015; 4(24): 2679-2693.

5. DharmendraSolanki, Surendrakumar Jain, SujataMahapatra. Formulation and evaluation of sustained release Metformin HCl tablet using natural polysaccharide. American journal of Pharmtech research, 2014; 4(6): 492-502.

6. A Madhusudhan Reddy, Ayesha Siddika, P Surya BhaskaraRao, P Manasa, J Siddaiah, P SrinivasaBabu. Formulation and evaluation of sustained release matrix tablets of Metformin HCl. Indian journal of research in pharmacy and biotechnology, 2013; 1(2), 197-200.

7. ChandanGarg and Vikrant Saluja. Once-daily sustained-release matrix tablets of Metformin HCl based on an enteric polymer and chitosan. Journal of pharmaceutical educational research, 2013; 4(1), 92-97.

8. KottaKranthi Kumar, M. Narasimha Reddy, R.Naga Kishore. Formulation and evaluation of bilayer matrix tablet of Pioglitazone HCl Metformin HCl USP 15mg & 500mg. Asian journal of pharmaceutical and clinical research, 2013; 6(3), 155-161.

9. ChinmayaKeshariSahoo, A. Amulya Reddy, VandanaKethavath and PrashanthSurabi, Eshwar Mule. Designing of Sustained-Release Metformin HCl Tablets for the Treatment of Type-II Diabetes Mellitus. Asian journal of chemical and pharmaceutical research, 2013; 1(1): 42-46.

10. R Charulatha, et.al. Design and evaluation of acebrophylline sustained release matrix tablets. Scholars Research Library, 2012; 4 (2): 530-535.

11. Mohd Abdul Hadi, et.al. Formulation and Evaluation of Sustained Release Matrix Tablets of Montelukast Sodium. International Journal of Pharmacy, 2012; 2(3): 574-582.

12. Naga RajuPotnuri et al. Effect of binders, lubricants and fillers on drug release from Diltiazem Hydrochloride Bi-Layered matrix tablets obtained by direct compression and wet granulation technique. International Journal of Pharmacy, 2012; 2(1): 117 – 128.

13. Kamlesh J et al. Formulation and evaluation of sustained release matrix tablets of Metformin HCl using pH dependent and pH Independent Methacrylate polymers. British

Journal of Pharmaceutical Research, 2011; 1(2): 29 – 45.Basavaraj K Nanjwade, et.al. Formulation and Extended-Release Metformin HCl matrix tablet. Tropical Journal of Pharmacy, 2011; 10(4): 375 – 383.

14. Bangale G.S, et.al. Formulation and Evaluation of Natural Gum Based Matrix Tablets for Oral Controlled Delivery of Nimodipine. Indian Journal of Pharmaceutical Education and Research, 2011; 45(4): 252-268.

15. T Rajasekharan et al. Formulation and evaluation of Hydroxypropyl methylcellulose based controlled release matrix tablets for Theophylline. Indian Journal of Pharmaceutical Sciences, 2011; 50(4): 205 – 214.

16. Deepak Gupta et.al. Formulation and development of sustained release matrix tablets containing Metformin HCl. Pharmacologyonline, 2011; 2: 879-885.

17. HimansuBhusanSamal, et.al. Formulation and evaluation of sustained release zidovudine matrix tablets. International Journal of Pharmaceutical Sciences, 2011; 3 (2): 32-41.