ISSN 0975-6299 Vol 2/Issue 2/Apr-Jun 2011

International Journal of Pharma and Bio Sciences

REVIEW ARTICLE

PHARMACEUTICS

# FORMULATION, DEVELOPMENT AND EVALUATION OF METFORMIN HYDROCHLORIDE SUSTAINED RELEASE TABLETS

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## ABSTRACT

There is a continuously growing interest in the pharmaceutical industry for extended release oral drug delivery systems. There is also high interest for design of dosage formulations that allow high drug loading, particularly for actives with high water solubility. The Study was undertaken with an aim to formulation development and evaluation of Metformin sustained release tablets using different polymers as release retarding agent. It is concluded that formulation of sustained release tablet of Metformin containing 13 % HPMC K100 with binder PVP K30 i.e. batch IX can be taken as an ideal or optimized formulation of sustained release tablets for 10 hour release as it fulfills all the requirements for sustained release tablet.

## KEY WORDS

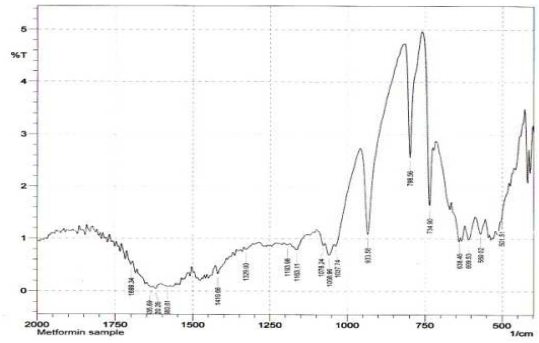
Metformin sustained release diabetes

## INTRODUCTION

Diabetes a global public health problem is a chronic disease and is now growing as an epidemic in both developed and developing countries. Around 150 million people suffer from diabetes in the world out of which above 35 million are Indians. Current drugs used for managing TYPE II Diabetes and its precursor syndromes, such as insulin resistance, fall within five classes of compound such as the biguanides ,thiazolidinediones ,the sulfonylureas,benzoic acid derivatives and alpha glucosidase inhibitors. Metformin is an oral antidiabetic drug from the biguanide class. Metformin is the most popular antidiabetic drug in the united state and one of the most prescribed drug in the country overall with nearly 35 million prescription field in 2006 for generic Metformin alone. The aim of any drug delivery system is to provide therapeutic amount of drug to appropriate site in the body to achieve immediate therapeutic response and to maintain the desired drug concentration. In the recent years sustained release (SR) dosage forms continue to draw attention in the research for improved patient compliance and decreased incidence of adverse drug rections. In general the goal of sustained release dosage form is to maintain therapeutic blood or tissue level of the drug for extended period of time. This is generally accomplished by attempting to obtain "zero order" release from the dosage form. Zero order release constitutes drug release from the dosage form which is independent of the amount of drug in the delivery system. Sustained release system generally do not attain this type of release and usually try to mimic zero order release by providing drug in slow "first order" fashion (i.e. concentration dependent).

## EXPERIMENTAL METHOD

***Identification:*** The procured sample of Metformin was tested for its identification by using FTIR Spectra study .Then bulk characterization of the drug is done .The manufacturer also was confirmed of quality and purity of sample.



***Compatibility study of drug and Excipient***

The drug and excipient compatibility was done at 25$^0$C / 60% ± 5% RH, 30$^0$C / 65% ± 5% RH and 40$^0$C / 75% ± 5% RH. Open and closed vial methods were used. The result does not show any physical change to the mixture after 4 weeks .Chemical compatibility was analyzed by HPLC method as per IP specification. This fact concluded that the drug and excipients are compatible with each other.

***Selection of Excipient:***

The selection of excipient was completely based on article review .The utility of polymer as sustained release profile was already proved.

***Initial Trial:***

Before compression of batches all the polymer were tested with quantity of glidant and lubricant to observe the flow property .The amount was fixed after successive initial trials

| Ingredients | I | II | III | IV | V | VI | VII | VIII | IX | X | XI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Metformin | 500 mg | 500 mg | 500 mg | 500mg | 500mg | 500mg | 500mg | 500mg | 500mg | 500mg | 500mg |
| HPMC K100 | 20 mg | 32mg | 52 mg | 85 mg | 97 mg | 13 mg | 32 mg | 52 mg | 85 mg | 85 mg | 85mg |
| HPMC K4M | ---- | ----- | ---- | ----- | ------ | 7mg | 20 mg | 33mg | ----- | ------ | ------ |
| Avicel | 90 mg | 78mg | 58mg | 25mg | 13 mg | 90mg | 58 mg | 25 mg | 25mg | 25mg | 25mg |
| PVP K30 | 25mg | 25mg | 25mg | 25mg | 25mg | 25mg | 25mg | 25mg | 25mg | ----- | ---- |
| Starch | ---- | ---- | ---- | ---- | ----- | ---- | ------ | ---- | ----- | 25mg | ----- |
| HPC | --- | ---- | ----- | ----- | ----- | ----- | ----- | ----- | ---- | ----- | 25mg |
| IPA | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | ----- | Q.S |
| Water | ---- | ----- | ---- | ---- | --- | ---- | ----- | ----- | ----- | Q.S | ----- |
| Mg Stearate | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg |
| Aerosil | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg | 7.5mg |
| Total | 650mg | 650mg | 650mg | 650mg | 650mg | 650mg | 650mg | 650mg | 650mg | 650mg | 650mg |

***Control of Amount:***

The initial batches were of directly compression method which needs higher amount of excipient to reduce the friability and improve hardness indirectly which affect the release of drug from polymer .The total weight 650 mg was used successfully to meet all criteria.

***DISSOLUTION STUDY***

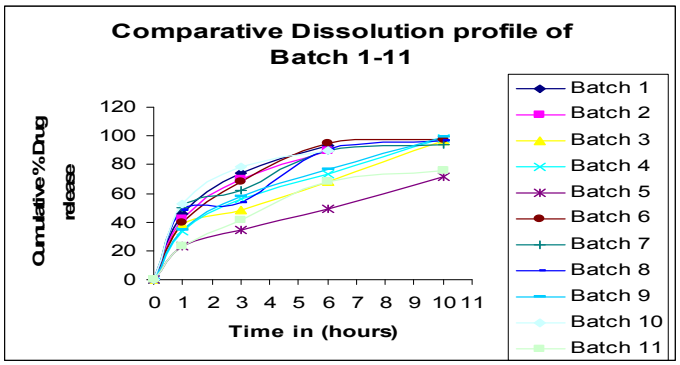
***Dissolution discussion:***

The dissolution was carried out by using dissolution medium water and the release of Metformin from sustained release tablet of various formulations varied according to amount and grade of different polymer. In case of different concentration of polymer such as 5 % HPMC K100 shows release profile 93.57% in VI hour. Then 5% HPMC K100 shows release profile 89.51% in VI hour. Then 8% HPMC K100 shows release profile 96.45 in Xth hour. 13 % HPMC K100 shows release profile 98.69 in Xth hour within specification limit and 15% HPMC K100 shows release profile 71.68% of drug release in Xth hour itself.

The HPMC K100 combined with HPMC K15M taken as three trails in different concentration but the three trials are not showing the drug release in specific time interval. Then the three trials taken as different binder concentration such as PVP K30, Starch, and Hydroxypropylcellulose.

The binder solution starch with water create capping problem during compression. The binder solution HPC with IPA shows hardness is heavy so drug release is less i.e. 75.86 % in Xth hour .so the binder solution

PVP K30 with IPA shows drug release in specific interval of time as per IP Limits




***Compression / Evaluation:***

The sustained release tablets of Metformin were prepared by weight granulation and direct compression. The granules for the matrix tablet were prepared according to the formula given in related table and characterized with respect to angle of repose, moisture content, bulk density and total drug content. Angle of repose was less than $35^0$C for all batches of granules indicating satisfactory floe behavior moisture content of less than 3 % indicates optimum drying of granules. Other parameters for granules were also found to be in acceptable range.

***Stability:***Results of stability studies of batch ix indicate that it is stable at $25^0$C± $2^0$C 60%RH, $30^0$C ± $2^0$C,65%RH, $40^0$C ± $2^0$C,75%RH as there was no significant difference observed for dissolution and other physical parameter of tablet after 3 month.

## RESULT AND DISCUSSION

Identification The procured sample of Metformin was tested for its identification by using FTIR Spectra study. And the Compatibility study of drug and ExcipientThe drug and excipient compatibility was done at $25^0$C / 60% ± 5% RH, $30^0$C / 65% ± 5% RH and $40^0$C / 75% ± 5% RH. Open and closed vial methods were used. Selection of Excipient was completely based on article review .The utility of polymer as sustained release profile was already proved.

Initial Trial**.** Before compression of batches all the polymer were tested with quantity of glidant and lubricant to observe the flow property .The amount was fixed after successive initial trials .

Tablet Parameter**.** In guidance of industrial scientist different parameter of tablet like flow property, dimension hardness, drug content etc. were studied with results in successful trials.

Idea after dissolution study. The amount released in fixed duration was of more importance and were performed with precision and accuracy, the change in amount of polymer was largely dependent of viscosity grade the dissolution study suggested many parameter to control of next batches. Final batch the batch IX immerge as a successful delivery system it was completely dependent of gel swelling and diffusion behavior of HPMC. The different viscosity grades of HPMC were used successfully.Utility of polymer:The use of HPMC in different concentration shows different dissolution study. The drug release in specific time interval is taken as ideal concentration of polymer.

## CONCLUSION

From the above results and discussion it is concluded that formulation of sustained release tablet of Metformin containing 13 % HPMC K100 with binder PVP K30 i.e. Batch IX can be taken as an ideal or optimized formulation of sustained release tablets for 10 hour release as it fulfills all the requirements for sustained release tablet and our study encourages for the further clinical trials and long term stability study on this formulation

## REFERENCE


[1] U.S.P. Convention Krowcyzynski, L., extended release dosage forms, CRS press, Inc. Florida, 1987, 4.

[2] Lachman, L., Liebermann, H.A., Kanig J.L., Eds., In, "The theory and practice of Industrial Pharmacy," III Edn., Lea and Febiger, Philadelphia, 1987, 430–456.

[3] Brahmankar, D.B., Jaiswal, S.B., In: Biopharmaceutics and Pharmacokinetic, A treatise, Vallabh Prakashan, New Delhi, 1st Edn., 1995, 335–357.

[4] Lee, V.H., Robinson, J.R., in "Sustained and controlled release drug delivery systems" Marcel Dekker, New York, 71–121.

[5] Lapidus, J., L'ordi, N.G., J. Pharm. Sci., 57, 1968, 1292–1301.

[6] Columba, P., Bettini, R., Minima, J. Pharm. Sci., 86, 1991-1992, 8–19.

[7] Silvia A. Bravo, Maria C.Lamas , Claudio J.Salomon, (2002) " In – Vitro Studies of Diclofenac Sodium Controlled –Release from biopolymeric hydrophilic matrices" Journal of Pharmaceutical Science 5(3), page no 213-219.

[8] G. Di Colo , S.Falchi , Y.Zambite (2002) " In-Vitro Evaluation of System for pH Controlled peroral delivery of Metformin "Journal of Controlled Release volume 80, issues 1-3 page no. 119-128

[9] Yi- Hung Tsai , Pao –Chu Wu, Yaw-Bin Huang 2003 " "Preparation and Evaluation of Sustained Release microspheres of potassium chloride prepared with ethyl cellulose". **International Journal of Pharmaceutics edition** 260 page no.115 – 121**.**

[10] K**.** Raghuram Reddy , Mutalik S, Reddy S , 2003 " Once daily Sustained release matrix tablets of Nicorandil , formulation and In-Vitro Evaluation" **AAPS Pharm Sci Tech** 4(4),61.

[11] Ebube K. Nkere, Alan B.Jones ., (2004) Sustained release of acetaminophen from a heterogeneous mixture of hydrophilic non ionic cellulose coated tablet " **International Journal of Pharmaceutics**" , 272, 19-27.

[12] Manthena, V.S. Varma., Gargs. (2004) , " Factor 's affecting mechanism and kinetic of drug release from matrix based oral controlled drug delivery system" **American Journal of drug delivery** , 2(1), 43-57.

[13] Owen .I Corrigan , (2004) "Swelling and erosion properties of HPMC matrices" **International Journal of Pharmaceutics** edition 279 year page no .141- 152.

[14] Marina Levina, Fiona Palmer, Alirajabi – Siaboomi(2005), " Investigation of a directly compressible Metformin Hcl 500mg extended release formulation based on hypromellose" **Colorcon Poster representation controlled release society annual meeting** June 2005.

[15] Ouyang D, Nie S, Li W, Guo H(2005) , " Design and evaluation of compound Metformin/glipizide elementary osmotic

pump tablets". **The Journal of Pharmacy and Pharmacology** Article 57(7) page no. 817-820.

[16] Mohammed Reza siahi, (2005), "Design and evaluation of 1 and 3 layer matrics of Verapamil for sustained release" **AAPS Pharma Sci Tech**; 6(4) Article (7).

[17] Ash Patel , Subha Brata Ray RamShrnagat Thakur , "In-Vitro Evaluation and optimization of Controlled release floating drug delivery system of Metformin hydrochloride " **DARU** volume 14 page no. 57-64.

[18] Rachel H (2006) "Metformin extended release is a novel gastric-retentive formulation of ant hyperglycemic agent" **International Journal of Pharmaceutics**

[19] Lian-Dong Hu,Tang x , Zhanq (2006), " Preparation and in vitro / in vivo evaluation of SR release Metformin Hcl pellets ". **Eur. J. Pharmaceutics and Biopharmaceutics** edition 64(2) pages no 185-192.