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Formulation and Evaluation of Immediate Release Tablet of Metformin Hydrochloride

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Abstract: ***The purpose of this research is to prepare metformin hydrochloride immediate release tablets by wet granulation technique. In order to obtain the best, optimized product ten different formulations were developed. Different binder, disintegrants and lubricants taken as variables. Weight variation, thickness, hardness, friability, disintegration time, in-vitro release and pharmaceutical assay were studied as response variables. The tablet were prepared by direct compression method & later evaluated for parameters. F1-F6 formulation were developed using different combination of Cross carmesllose sodium & Sodium starch glycolate (super disintegrants). Formulations F1 & F2 was compared within formulations shown a release of 90-99%. Formulation F1 (Metformin = 250mg, Cross carmellose sodium = 30mg, Sodium starch glycolate = 14mg, Microcrstalline cellulose = 70mg, Cross Povidone = 16, Magnesium sterate = 20mg) & Formulation F2 (Metformin = 250mg, Cross carmellose sodium = 30mg, Sodium starch glycolate = 10mg, Microcrstalline cellulose = 70mg, Cross Povidone = 20, Magnesium sterate = 20mg) has shown better drug release than other formulations. F1 & F2 has 95.8% & 99.9% drug release respectively.***

Keywords: Metformin hydrochloride, optimization, anti-diabetic drug

1.Review of Literature

1. **R. Margret Chandira *et al*.** Diabetes is a chronic metabolic disease characterized by high glucose levels in the blood. Sustained release gastro retentive dosage forms enable prolonged and continuous input of the drug to the upper parts of gastrointestinal tract and improve the bioavailability of medication that is characterized by narrow absorption window. Gastro retentive floating drug delivery systems (GFDDS) of Metformin HCl, an antidiabetic drug with an oral bioavailability of only 50% (because of its poor absorption from lower gastrointestinal tract) have been designed to increase its residence time in the stomach without contact with the mucosa was achieved through the preparation of floating bilayer matrix tablet by direct compression technique, by using HPMC as release retardant, and NaHCO3 as gas generating agent to reduce floating lag time. Bilayer Floating tablets were evaluated for Hardness, Friability, Weight Variation, Drug content, Floating properties and In-vitro release pattern. The Invitro drug release followed Zero order Kinetics and drug release was found to be diffusion controlled.[6]

2. **Margret Chandira *et al*.** has studied on extended release dosage forms cover a wide range of prolonged action preparations that provide continuous release of their active ingredients for a specific period of time.Metformin Hcl is antihyperglycemic agent used in the treatment of type 2 Non Insulin Dependent Diabetes Mellitus. The extended release formulation of Metformin Hcl (MER), prolongs drug absorption in the upper gastrointestinal tract and permits once daily dosing in patient with Type 2 Diabetes Mellitus .This newer formulation may enhance patient compliance with oral therapy compared to conventional immediate release (MIR) Metformin Hcl in Type 2 Diabetes Mellitus Extended release formulation of Metformin Hcl presents significant challenges due to its poor inherent compressibility, high dose and high water solubility. Extended release matrix tablet of Metformin Hcl were formulated different combinations of polymers in Hydroxyl propyl methyl cellulose (HPMC K 100M CR) and Carbopol 71 G by wet granulation method.[7]

3. **Manoj Shrawan Charde *et al.*** has research on how to prepare metformin hydrochloride immediate release tablets by wet granulation technique. In order to obtain the best, optimized product ten different formulations were developed. Different binder, disintegrants and lubricants taken as variables. Weight variation, thickness, hardness, friability, disintegration time, in-vitro release and pharmaceutical assay were studied as response variables. Capping was observed in formulation containing PVP K-30. However, in the remaining formulation containing PVP K-90, no capping was observed. The formulation A7 was selected as optimized formulation. The different physical properties and in-vitro release profile showed best comparable with the reference product. Optimization has proven an effective tool in product development.[8]

4. **Arcot Ravindran Chandrasekaran *et al.*** studied on the topic of study in-vivo equivalency evaluation of metformin tablets. Dissolution testing is the method for evaluation of physiological availability that depends upon having the drug in dissolved state. They developed an in-vivo test method that fully model the physiological condition in GIT.[9]

5. **Patil S.A. *et al.*** the purpose of this research was to formulate and characterize solid dispersion (SD) of metformin hydrochloride using methocel K100M as the carrier by the solvent evaporation and cogrinding method. The influence of drug polymer ratio on drug release was studied by dissolution tests. SD with 1:4 and 1:5 ratio of

drug to polymer obtained by solvent evaporation and cogrinding were selected as the best candidates suitable for prolonged-release oral dosage form of metformin. [10]

6. **S.C. Baskar *et al.*** has studied the metformin hydrochloride which is better absorbed in the upper intestine. The formulation has optimized on the basis of floating ability and in-vitro drug release. In-vitro drug release test of these tablets indicated controlled sustained release of metformin hydrochloride.[11]

7. **Aedrian A. Abrilla *et al.*** has given review on how to compare the efficacy and tolerability of metformin extended-release (MXR) and the conventional metformin immediate-release (MIR) formulations in adults with type 2 diabetes mellitus (T2DM). MXR was associated with statistically worse but likely clinically similar HbA1c lowering and minimal improvement of GI intolerance compared to MIR.[12]

8. **Giovanna Corti *et al.*** has studied the low bioavailability and short half-life of metformin hydrochloride make the development of sustained release forms desirable. Drug absorption is limited to the upper gastrointestinal (GI) tract, thus requiring suitable delivery systems providing complete release during stomach to jejunum transit. The strategy proposed is based on direct compressed matrix tablets consisting of combination of MH with the hydrophobic triacetyl-β-cyclodextrin, dispersed is polymeric material.[13]

9. **G. Mubeen *et al.*** had studied a simple and sensitive spectrophotometric method which has been developed and validated for estimation of metformin hydrochloride in bulk and in tablet formulation. The primary amino group of metformin hydrochloride reacts with ninhydrin in alkaline medium to form a violet colour ehromogen which is determined spectrophotometrically at 570nm.[14]

10. **Mousumi Kar *et al.*** has given review on metformin hydrochloride chemically, N,N-dimethylimidocarbonimidic, diamine hydrochloride is an antidiabetic agent. A simple, accurate, economical and reproducible HPLC method has been developed for quantitative estimation of metformin hydrochloride from tablet dosage form with formulated microspheres.[15]

11. **Siripong Palee *et al.*** has studied on the diabetic patients taking metformin have been shown to have a lower risk of myocardial infraction. The efficacy of the cardioprotection conferred by metformin regarding the mitochondrial function and dynamic in cardiac I/R injury are still inconclusive. Metformin exerted the highest level of cardioprotection through the reduction in arrhythmia, infrant size, mitochondrial fissionand apoptosis in addition to preservation of mitochondrial function. Dose of metformin also improved mitochondrial and cardiac function. They indicate the potential clinical benefits of acute metformin treatment in acute myocardial infraction.[16]

12. **Victor Cunha *et al.*** has evaluate the use of metformin as a protective factor of HCC in diabetic patients. In these they address data about the use of metformin on the risk of HCC development. All studies have observed that the therapy with metformin was associated with lower risk of HCC compared with non-metformin therapy. Patients treated with insulin or insulin secretagogues, presented increased risk of HCC compared to those treated with metformin.[17]

13. **Famila Takhwifa *et al.*** has given review on the primary therapy for brain tumors, a combination radiotherapy, chemotherapy and corticosteroid but it associated with many adverse effect so there is an urgent need for new compound which could improve brain tumor patient prognosis. Metformin used for type 2 diabetes medication has been examined foe its protective action in cancer reducing cancer risk and cancer related mortality.[18]

14. **Alaba Toluope Agbele *et al.*** had studied the effect of metformin on therapeutic outcomes in cancer patients undergoing radiotherapy. A literature search of the electronic data-base was conducted to retrieve article that investigated the effect of Metformin on radiotherapy. The clinical showed promising therapeutic effect of the combination of metformin with radiotherapy.[19]

15. **Maria Molina-Vega *et al.*** has given review on Metformin, which is known to produce profound changes in gut microbiota, is being increasingly used in gestational diabetes mellitus (GDM). The aim of this study was to elucidate the differences in gut microbiota composition and function in women with GDM treated with metformin compared to those treated with insulin. Metformin in GDM affects the composition and metabolic profile of gut microbiota. These changes could mediate, at least in part, its clinical effects. Studies designed to assess how these changes influence metabolic control during and after pregnancy are necessary.[20]

16. **Wenxing Yang *et al.*** has studied metformin action in Covid-19 and found that metformin was associated with significantly decreased mortality and severity in Covid-19 patients with diabetes. Meta-analysis indicated that following metformin treatment might benefit the patient with type 2 diabetes mellitus both the mortality and severity.[21]

17. **Zemene Demelash Kifle, *et al.*** has studied maintaining proper blood glucose levels using oral antidiabetic drugs like Metformin reduced the detrimental effects of COVID-19 by different possible mechanisms such as Metformin-mediated anti-inflammatory and immunomodulatory activities; effect on viral entry and ACE2 stability; inhibition of virus infection; alters virus survival and endosomal pH; mTOR inhibition; and influence on gut microbiota. Fascinatingly, in diabetic patients with COVID-19, treatment with Metformin was associated with a noticeable reduction in mortality rates

and disease severity among infected patients. Metformin was comprehensively investigated for its anti-inflammatory, antiviral capabilities, immunomodulatory, and antioxidant, which would elucidate its capability to confer vascular and cardiopulmonary protection in COVID-19.[22]

References

[1] G.S. Banker and N.R. Anderson, Tablets. In: L. Lachman, H.A. Lieberman and J.L. Kanig, Theory and Practice of Industrial Pharmacy, 3rd ed., Lea & Febiger, Philadelphia, PA, 1986, pp 293-345.
[2] G.S. Banker and C.T. Rhodes, Modern pharmaceutics, Marcel dekker Inc., New York, pp 287-334.
[3] Clinical Guidelines Task Force, International Diabetes Federation (2005). "Glucose control: oral therapy". In: Global Guideline for Type-II Diabetes. Brussels: International Diabetes Federation, 2007.
[4] National Institute for Health and Clinical Excellence, Clinical guideline 66: Diabetes – Type II (update). London, 2008.
[5] ICH Harmonized Tripartite Guideline Stability Testing of New Drug Substances and Products Q1a (R2), Current step 4 version, (2003).
[6] R. Margret Chandira, A.A. Mohamed Yasir Arafath, Debjit Bhowmik, B. Jayakarl, K.P. Sampath Kumar. "Formulation and Evaluation of Bilayered Floating Tablets of Metformin Hydrochloride". (2012) Vol1/No.6 Page No. 26-39
[7] Margret Chandira, B.S. Venkateshwarlu, Jadhav Anup Shankarran, Debjit Bhowmik, B. Jayakar, T.V. Narayana. "Formulation and Evaluation of External Release Tablets containing Metformin HCl". International Journal of Chem Tech Research Vol 2, No. 2, 2010, pp 1320-1329
[8] Manoj Shrawan Charde, Dhirendra Pandey, S. Jayani. "Formulation and Evaluation of immediate release tablets of Metformin Hydrochloride on laboratory scale". International Journal of Advances in Pharmaceutical Analysis IJAPA Vol. 2 Issue 2 (2012) 30-33
[9] Arcot Ravindra Chandrasekaran, Chan Yoke Jia, Choong Sheau Theug, Teeba Muniady, Selvadurai Muralidharan, Sakkalingam Arumugam Dhanraj. "Metformin: In-vitro Studies and Evaluation". Journal of Applied Pharmaceutical Science. 2011; 1 (5): 214-217
[10] Patil S.A, Kuchekar B.S, Cbabukswar A.R, Jagdale S.C. "Formulation and Evaluation of Extended – Release solid dispersion of Metformin Hydrochloride". (2010) J. Young Pharm Vol 2 / No 2 pp 121-129 doi: 10.410310975 – 1483.63147
[11] S.C. Basak, J. Rahman, M. Rachalingam. "Metformin: Design & In-vitro testing of Floatable gastroretentive tablet of Metformin Hydrochloride". Pharmazie 2007; 62: 145-148
[12] Aedrian A. Abrilla, A. Nico Nahar, I. Pajes, Cecilin A. Jimeno. "Metformin extended – Release versus Metformin immediate release for adults with type 2 diabetes mellitus". A systematic review and meta-analysis of randomized controlled trials. Diabetes Research and Clinical Practice I 78 (2021) Io 8824
[13] Giovanna Croti, Marzia Cirri, Francesca Maestrelli, Natascia Mennini, Paola Mura. "Metformin: Sustained released tablet of Mertformin Hydrochloride in combination with triacetyl-β-cyclodextrin". European Journal of Pharmaceutics & Biopharmaceutics. 2008; 68: 303-309
[14] G. Mubeen, Khalikha Noor. "Metformin: Spectrometric Method for Analysis of Metformin Hydrochloride". Indian Journal. Pharm Sci. 2009; 71 (1): 100-102
[15] Mousumi Kar, P.K. Choudury. "Metformin: HPLC Method for Estimation of Metformin Hydrochloride in Formulated Microsphere and Tablet Dosage Form". 2009 May-Jun; 71 (3): 318-320
[16] Siripong Palee, Louis Higgins, Tom Leech, Siriporn C. Chattiparkorn, Nipon Chattipakorn. "Metformin: Biomedical & Pharmacotherapy. S.Palee". et.al. 2020; 130: 1-10
[17] Victor Cunha, Helma Pinchemel, Cotrim, Raqual Rocha, Kellyanc Carvalho, Lilianc Lins – Kusterer. "Metformin: Annal of Hepatology". V.Cunha et.al. 2020; 19: 232-237
[18] Famila Takhwifa, Tiara Aninditha, Heri Setiawan, Rani Sauriasari. "Metformin: Heliyon. F. Takhwifa" et.al. 2021; 7: 1-7
[19] Alaba Tolulope Agbele, Oluwayomi Peace Faromika, Olufisayo Olalekan Awe, Funke Roseline Amody, Goodness Oreoluwa Edaogbogun, Kalid Abayomi Bello. "Metformin: Radiation Medicine & Protection". A. T. Agbele et.al. 2021; 2: 17-22
[20] Maria Molina – Vega, Marfa J. Picon – Cesar, Corolina Gutierrez – Repiso, Andrea Fernandez – Valera, Fuensanta Lima – Rubia, Stella Gonzalez – Romero, Isabel Moreno – Indias, Francisco J. Tinahones. "Metformin action over gut microbiota is related to weight and glycemic control in gastational diabetes mellitus: A randomized trial". Biomedicine and Pharmacotherapy 145 (2021)
[21] Wenxing Yang, Yuechong Sun, Junzhang, Kui Zhang. "Metformin: Diabetes Research and Clinical Practice". 2021; 178: 1-8
[22] Zemene Demelash Kifle, Alem Endeshaw Woldeyohanis, Chilot Abiyu Demeke. "A review on protective roles and potential mechanisms of Metformin in diabetic patients diagnosed with Covid-19". Metabolism open 12 (2021)
[23] S.M. Dinh, P. Liu, Advances in Controlled Drug Delivery-Science, Technology, and Products, American chemical society, Washington DC, 2003, pp103.
[24] S.V. Sastry, J.R. Nyshadham and J. A. Fix, Pharmaceutical Science and Technology Today, Vol. 3, pp138.
[25] Gilbert, G.S. Banker., and C.T. Rhodes, Modern Pharmaceutics, 4th ed., (2002). Marcel Dekker Inc., New York.
[26] https://pubchemncbi.nlm.nih.gov