International Journal of Pharma Professional's Research
Volume 9, Issue 2, Page No: 1-5
ISSN (Online):0976-6723
ISSN (Print):2249-3948

Available Online at: ijppronline.com

FORMULATION AND EVALUATION OF MICROSPHAERS OF METFORMIN HYDROCHLORIDE

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Abstract
The objective of the present study was to develop sustained release microspheres of Metformin hydrochloride in order to achieve an extended retention in the GIT which may result in enhanced absorption and there by improved bioavailability. The present worker prepared microspheres of Metformin hydrochloride in nine batches using ethyl cellulose (EC) and Poly Vinyl Alcohol (PVA) in different drug polymer ratios taking into account solvent evaporation method. Infrared Spectrophotometric analysis revealed that there was no known chemical/physical interaction between drug & polymer and/or excipients used. The formulations of different batches were subjected to various physicochemical studies such as % yield, particle size, drug entrapment efficiency, in-vitro drug release and stability studies. The results showed that the method was reproducible and easy for the formulation of microspheres. Effect of polymer concentration was also evaluated with respect to their size & drug entrapment parameter studies. The in-vitro release studies indicated that the Metformin hydrochloride loaded microspheres provided sustained drug release over a period of 12 hrs. The optimized batch (B2) showed percentage yield: 57.9, particle size: 200 µm, EE (entrapment efficiency): 60.41% and drug release in 0.1N HCl: 92.853±1.429%. None other than the present worker has reported microsphere formulation with this particular drug using Ethyl cellulose, poly vinyl alcohol and dichloromethane. Therefore, the research, in reference, comprised of quite novel aspects of investigations.

Keywords: Metformin hydrochloride, microspheres, ethyl cellulose, solvent evaporation method.

HOW TO CITE THIS ARTICLE: FORMULATION AND EVALUATION OF MICROSPHAERS OF METFORMIN HYDROCHLORIDE, International Journal of Pharma Professional's Research, 2018, 9 (2).

Introduction
Diabetescharacterized by a gathering of metabolic issue, represented by a high blood glucose level of a person (glycemia), either pertainingto lack of generation of insulin or the body's tissuesare not responding appropriately to insulin or both. Glucose originates from the meals we eat. The body become unable to produce insulin With type 1 diabetes while it does not deliver or utilize the same with type 2 diabetes. Consequently,sugarretained in the blood. On the off chance that there is excessively glucose in the blood it causes major issues. It can harm eyes, kidneys and nerves, so it is likewise called metabolic confusion.There are four types of diabetes,viz. type 1or insulin-subordinate diabetes; type 2or non-insulin-subordinate diabetes; type 3 or Gestational diabetesor type 4 or Adult Diabetes of Young People (MODY). Various symptoms arePolydipsia, Polyphagia, Lethargy, Stupor, Blurred vision, Nausea and Vomiting& Abdominal Pain[1]. Most of the types of diabetes are treatable. There is no known cure for type 1 diabetes. Type 2 can be managed through a mix of activity, eating routine and weight control. Patients with type 1 are regarded with normal insulin infusions and additionally an exceptional eating regimen and exercise. On the off chance that diabetes isn't satisfactorily controlled, the patient has an altogether higher danger of creating intricacies [2].

Insulin, a hormone enables the body to utilize sugar (glucose) from starches. Insulin is enable to maintain hyperglycaemia or hypoglycemia[2-4].The main disadvantage of insulin is that it must be given by injection. Antidiabetic drugsreduce blood glucose levels and are effective by mouth. The oral antidiabetic drugs are used in the treatment of type II diabetes, these drugs can also be used with insulin. In some patients with diabetes, the use of insulin with oral medications may reduce the dose of insulin in some patients[2].

Metformin is an antidiabetic medication of the class "biguanide"of oral antiperglicemic specialists. It controls the level of sugar in the blood. Metformin is consumed as a part of eating regimen and exercise to enhance glycemic control in patients with type 2 diabetes. Metformin is also coupled with insulin or different medications, yet isn't utilized to treat compose 1diabetes [5-6].

Earlier patients have been using dosage forms like Tablet, Capsule to treat the acute and chronic diseases, but the problem is that they have to be taken several times in a day for maintaining the peak plasma level concentration. Hence to overcome to these problems controlled release drug delivery system were developed. The microspheres are tinyballs like particles(diameter-1-1000 µm);also called as microparticles. The microspheres act as a controlled and sustained delivery system asthey maintain the desired drug concentration at site of action and deliver the drug to the target site devoid of undesirable effects [7-10]. The objective of this study was to investigate the effect of parameters like polymer & stabilizer concentration on drug release.

2.0 Materials And Method

Various materials i.e. Metformin hydrochloride, ethyl cellulose, dichloromethane, PVA, ethanol procured from different nationally and internationally reputed sources.

2.1 Drug excipient compatibility study:

2.1.1 FTIR technique:

A finely powdered mixture of drug and KBr was compressed in to discs in a hydraulic press at 75 kg/cm^2. Characteristic peaks obtained with pure drug were compared with that obtained with selected excipients.

2.2 Preparation of Microspheres:

The microspheres of Metformin HCl have been prepared individually using a solvent evaporation method. The weighted amount of drug and polymer was dissolved at room temperature in a mixture of ethanol and dichloromethane (2:1% v/V) at ambient temperature with magnetic stirring. This was poured slowly (Drop wise) in the middle of the dispersion consisted of 20 ml of 1% of PVA aqueous (w/V) and 1.5% (w/w) span 80, during the sonication for 2 h in the ice bath. Subsequently, the system was put on magnetic stirrer during the night for the complete evaporation of organic solvents. The prepared suspension was centrifuged at 1,500 rpm in the presence of 5% mannitol (cryoprotectant). The supernatant was eliminated and the sediment was dried for 48 h for further analysis. The particles obtained were kept in dehydrated conditions [11-14].

Table1:FormulationdesignofMicrospheresofMetformin Hydrochloride:

Formulation Code / Ingredients	A1	A2	A3	B1	B2	B3	C1	C2	C3
Drug(mg)	200	200	200	200	200	200	200	200	200
Polymer (Ethyl cellulose)(mg)	200	400	600	200	400	600	200	400	600
PVA (%)	1	1	1	2	2	2	3	3	3
Dichloromethane(ml)	5	5	5	5	5	5	5	5	5
Ethanol(ml)	10	15	20	10	15	20	10	15	20
Span80 (1.5 %,µl)	100	100	100	100	100	100	100	100	100

ISSN (Online):0976-6723
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2.3 Evaluation of Microspheres:

The Microspheres produced with Metformin HCl, were evaluated for various parameters, namely the% yield, entrapment efficiency, particle size and potential Zeta, surface morphology, in-vitro drug release, release kinetics and stability studies.

3.0 Results And Discussion

3.1 Compatibility Study:

3.1.1 FTIR Analysis:

An FTIR spectra obtained with pure drug was compared with that obtained in combination with other excipients. The retention of characteristic peaks of pure drug in combination confirmed the compatibility of drug with chosen excipients.

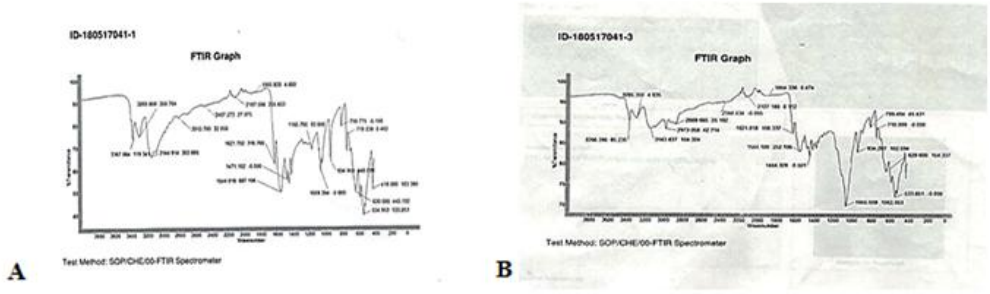

Fig 1: FTIR spectra of Metformin Hydrochloride A: Pure drug; B: Formulation blend

3.2 Evaluation Parameters:

The maximum percentage yield was found to be 57.9% with batch B2 while minimum of 29.7% with batch C3. It may happen due to the fact that the percentage yield decreases with increase in PVA concentration.The % drug entrapment of Metformin hydrochloride microspheres (batches A1-C3) was determined that ranged between 43.45-61.77%.The particle size analysis was performed for all nine batches prepared with drug. The mean diameters of particles for all batches were found in the range of 180-427 µm.The zeta potential of Metformin hydrochloride microspheres (batch A1-C3) was ranged between [(-8.54 & -28.5)])].Surface morphology study showed that microspheres were found to be spherical in shape with rough surfaces. Their size ranged between180-600micron.In–vitro dissolution study of Metformin hydrochloride microspheres (batches A1-C3) revealed that percentage drug release was ranged between 90.954-96.489%in 0.1N HCl at the end of 12 hr.

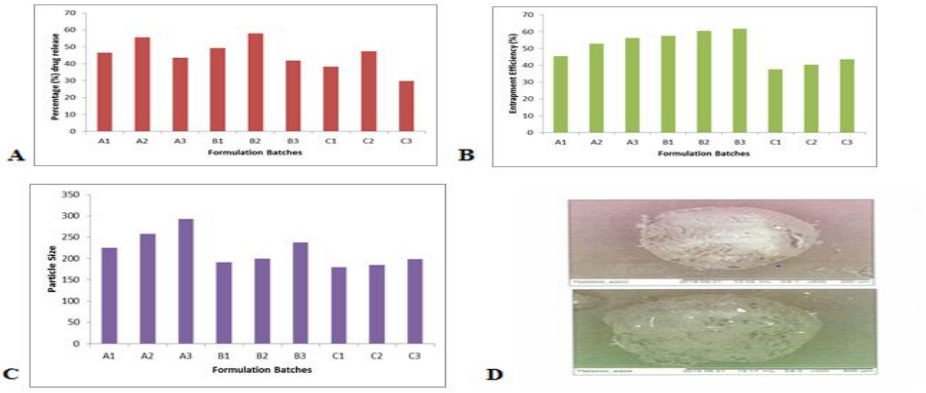

Fig.2: Evaluation parameters of prepared microspheres (batches A1-C3). A: Percentage (%) yield; B: Percentage drug entrapment; C: Mean Particle size; D: SEM of Metformin hydrochloride microspheres at a) 150 X and b) 200X

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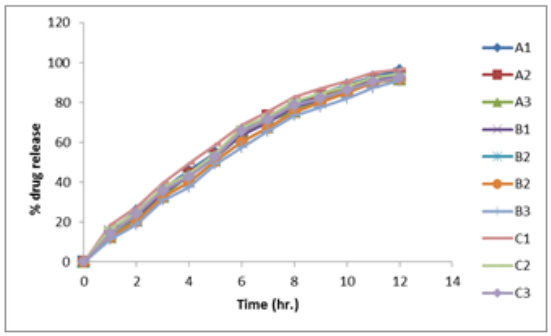

Fig.3: Comparative release profile of Metformin hydrochloride microspheres (batches A1- C3) in 0.1N HCl

Based on above parameters, B2 was considered as best batch among the other batches as it showed satisfactory results. A large quantity of drug particles is entrapped in microspheres and had minimum particle size. Drug release study revealed that this batch showed release in a sustained manner pertaining to small particle size. Hence, this batch was undergone for further studies i.e. release kinetics and accelerated stability testing. The particles belonging to this particular batch had smallest size.The kinetic study performed with Metformin hydrochloride microspheres revealed that drug followed Korsmeyer-peppas release kinetic model.The stability study was performed on the prepared microspheres as per the ICH guidelines at accelerated conditions (40^0±2^0C, 75%±5% RH) for 3 months and the results showed that the formulation was stable.

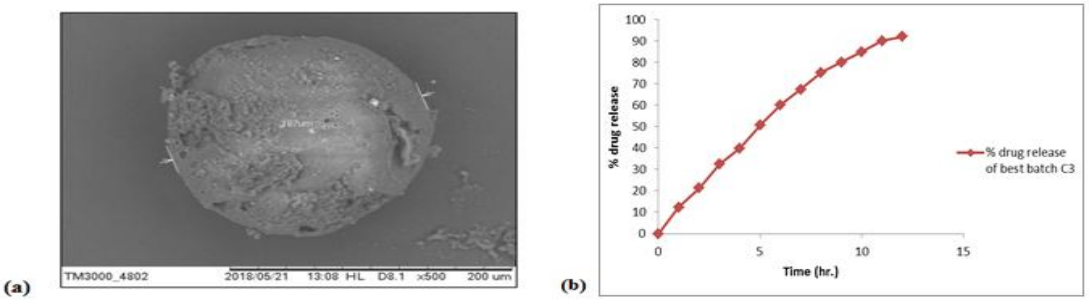

Fig. 4: SEM image (a); and % drug release (b) data of best batch B2 of Metformin HCl microspheres

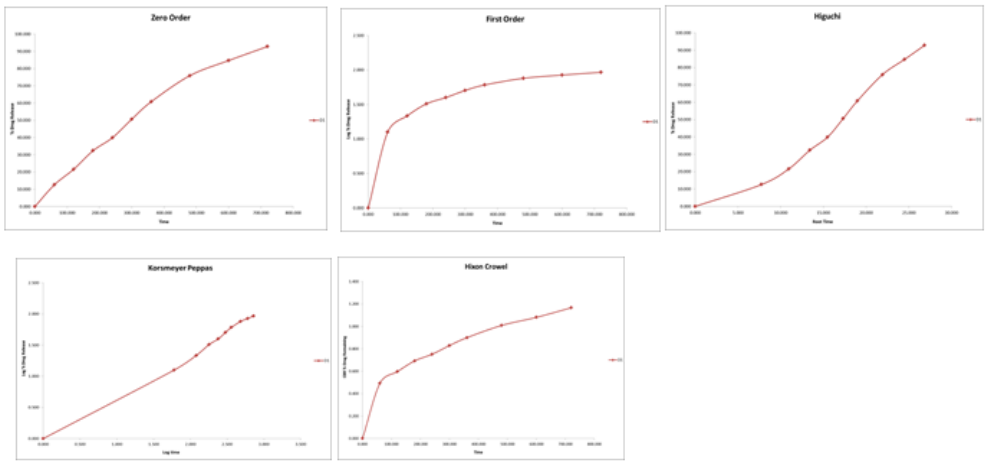

Fig.5: Release kinetic data of best batch (B2) of Metformin hydrochloride microspheres in 0.1N HCl

4.0 Conclusion

The selected drug (Metformin hydrochloride) studied for physicochemical characteristics. FTIR study was carried out for testing the compatibility of the drug with selected polymer and no interaction was observed. Formulation A1, A2, A3, B1, B2, B3 and C1, C2 and C3 (09) were prepared by increasing the polymer, solvent and stabilizer concentration by solvent evaporation method. The concentration of dichloromethane was kept constant. All the prepared formulations evaluated for various parameters. The SEM (Scanning electron microscopy) of microspheres of Metformin hydrochloride revealed that the particles were found spherical in shape.The mean particle size of the microspheres showed that the as the polymer concentration increases, size of the microspheres was also increased. Thus the study clearly indicated a promising potential of sustained release. Result indicated a successful formulation of microspheres of Metformin hydrochloride. It was concluded thatthe drug release from best formulation (B2) was more sustained as compared to others, because of increased diffusional path length and consequent retardation in drug release due to polymer.

5.0 References

1. https://www.medicalnewstoday.com/info/diabetes *Diabetes: Symptoms, causes, and treatments.* Last updated-Thu 5 January 2017.
2. K D Tripathi 2009 *"Essentials of Medical Pharmacology"*, 5thEdition. Jaypee Brothers Medical Publishers Pvt. Ltd., pp. 254-274.
3. Sonksen, P. and Sonksen J. 2000. Insulin: understanding its action in health and disease. *British Journal of Anaesthesia*, doi: 10.1093/bja/85.1.69, published online.
4. https://www.medicalnewstoday.com/info/*diabetes/whatisinsulin.php* Last updated Tue 5 January 2016.
5. PapanasN.andMaltezos E., 2009. Metformin: A Review of Its Use in the Treatment of Type 2 Diabetes Clinical Medicine: *Therapeutics*,Vol-1, pp-1367-1381.
6. https://www.drugs.com/*metformin.html.* Medically reviewed on November 9, 2017.
7. Alagusundaram,M., MadhuSudanaChetty,C., Umashankari K., 2009. Microspheres As A Novel Drug Delivery System - A Review. *International Journal of ChemTech Research* Vol.1, No.3, pp-526-534.
8. Kadam, N. R. and Suvarna, V. 2015. Microspheres: A Brief Review. *Asian Journal of Biomedical and Pharmaceutical Sciences*, vol-5, issue-47, pp-13-19.
9. Kataria, S., Middha, A., Sandhu, P., Bilandi, A. and Kapoor, B. Microsphere: A Review, *International Journal Of Research In Pharmacy And Chemistry*, 2011, 1(4), 1184-1198.
10. Nikam, V.K, Gudsoorkar, VR.,Hiremath S.N., Dolas R.T. and Kashid VA. 2012. Microspheres - A Novel Drug Delivery System: An Overview. *International Journal Of Pharmaceutical And Chemical Sciences*. Vol. 1, issue.1, pp-113-128.
11. Rajput, S., Pathak, A., Shrivastava, N., Baghel R S. 2012 A Review On Microspheres: Methods Of Preparation And Evaluation. *World Journal Of Pharmacy And Pharmaceutical Sciences*, Vol.1, issue.1, pp-422-438.
12. Bansal, H, SimarPreetkaur ,Atul Kumar Gupta. 2011. Microsphere: Methods Of Preparation And Applications; A Comparative Study, *International Journal of Pharmaceutical Sciences Review and Research*, Volume 10, Issue 1, , pp-69-78.
13. Patel N.R., Patel DA., Bharadia P. D., Pandya, V. and Modi D. 2011Microsphere as a novel drug delivery. *International Journal Of Pharmacy & Life Sciences* Vol. 2, Issue 8, pp-992-997.
14. Mishra, S.C., SubhashreeSahoocAjitBeheradBibhukalyan Prasad Nayak. 2016. Development and characterization of ethyl cellulose based microsphere for sustained release of nifedipine. Journal of Pharmaceutical Analysis, Volume 6, Issue 5, pp- 341-344.