MAT JOURNALS

Journal of Pharma and Drug Regulatory Affairs
Volume 2, Issue 1

Controlled Porosity Osmotic Pump Tablets Containing Esomeprazole Double Walled Microspheres-An Overview

Salini C
Assistant Professor, Department of Pharamaceutics, Sanjo College of Pharamceutical Studies, Vellappara, Chithali, Palakkad, Kerala, India

INFO
Corresponding Author:
E-mail Id: *salinialr39@gmail.com*

DOI: *10.5281/zenodo.3477822*

ABSTRACT

Esomeprazole is a BCS 11 compound, proton pump inhibitor used in the treatment of gastric, duodenal ulcer. The half-life of the drug is 4 hour. The drug has poor stability in acidic condition of the stomach. So, it is formulated into small sized and efficient carriers: the microspheres. To improve their residence time, bioadhesive characteristics can be coupled to develop mucoadhesive microspheres. Mucoadhesive microspheres are extensively used in targeted drug delivery due to their advantages like efficient absorption and improved bioavailability of the drugs and a much more intimate contact with the mucus layer, controlled and sustained release of drug from dosage form and exact targeting of drugs to the absorption site. Coating by enteric polymers will help to target the drug action in the intestine, particularly into the ileum region. Microsphere in conventional tablet will have disadvantages like it needs frequency of administration. Osmotic tablet will provide drug release independent of pH, but having the expense of complicated laser drilling. The main advantages of controlled porosity osmotic pump (CPOP) are reduced stomach irritation, no complicated laser-drilling procedures are followed.

Keywords: *Controlled drug delivery, microspheres, muco-adhesion, osmotic system, esomeprazole*

INTRODUCTION

Gastric and duodenal ulcer or peptic ulcer disease (PUD), Zollinger-Ellison Syndrome (ZE) and gastro oesophageal reflux disease (GRD) are upper gastrointestinal disorders sharing a common abnormality: too much acid and pepsin activity for the degree of local tissue resistance. Hydrolytic and proteolytic digestion of the exposed mucosa occurs, followed by inflammation, necrosis and ulceration. The primary class of drugs used for gastric acid suppression is the proton pump inhibitors, omeprazole, lansoprazole, pantoprazole, rabeprazole and esomeprazole [1]. Other class of drugs

like H_2 receptor blockers cimetidine, famotidine, nizatidine, and ranitidine are also used for this purpose, but are now more widely used for maintenance therapy after treatment with the proton pump inhibitors [2-5]. The proton pump inhibitors works by block the secretion of gastric acid by the gastric parietal cells. The extent of inhibition of acid secretion is directly relates to its dose. In some cases, gastric acid secretion is completely blocked for over 24 hours on a single dose. In addition to their role in the treatment of gastric ulcers, they are used to treat syndromes of excessive acid secretion (Zollinger-Ellison Syndrome) and gastroesophageal reflux disease (GERD). Omeprazole is a racemic mixture and esomeprazole is the s-enantiomer of omeprazole [6]. It's having less first pass metabolism than omeprazole so gives higher bioavailability, more effective and longer lasting with blockage over 24hours dosage. Produces increased antimicrobial activity against H.pylori organism than omeprazole. Esomeprazole is irreversibly bound to proton pump inhibitors, less pronounced inter individual variation in gastric pH and might be expected to produce a more consistent clinical response. But it is an acid-liable drug unstable in gastric pH, hence it is incorporated within a polymer matrix to protect drug from low pH of the stomach [7-10].

Microencapsulation

It is the process in which tiny particles or droplets are coated to give small capsules of many useful properties like incorporation of food ingredients, enzymes, cells or other materials of micro metric scale. Microencapsulation can also be used to enclose solids, liquids, or gases inside a micrometric wall made of hard or soft soluble film, so that we can reduce dosing frequency and there by prevents the degradation of pharmaceuticals [11].

Preparation of Microspheres

Different microencapsulation techniques used are as follows:

- Emulsion Solvent Evaporation Technique
- Emulsion Cross Linking Method
- Coacervation Method
- Spray Drying Technique
- Emulsion-Solvent Diffusion Technique
- Multiple Emulsion Method
- Ionic Gelation Method
- Quasi Emulsion Solvent Diffusion

Although all methods offer many significant advantages, it is only for the sake of some drawbacks. Some of the important drawbacks of these techniques include non-uniform coating, non-reproducible release kinetics and more importantly, the use of more or less harsh conditions in the formulation process which limits the many substances such as proteins, enzymes and live cells etc. as core materials for encapsulation. This problem can be overcome by applying a technique is based on principle of Ionotropic gelation (polyelectrolyte complexation). This involves the interaction of a cation (or an anion) with an ionic polymer to generate a highly cross linked structure with the ability to sustain the drug release by holding the drug over a period of time. It is very simple method and it needs only mild laboratory condition for their formation [12].

Double Walled Microspheres

Traditional microsphere formed by a single polymer have drawbacks such as high initial burst, low encapsulation efficiency especially for highly water soluble drugs, inability to lend themselves to pulsatile or zero order release and lack of sustained release for periods during periodic therapy. By exploiting the phenomenon of phase separation between two immiscible polymers dissolved in a mutual solvent, a double-walled microsphere could be manufactured with

the second polymer coating the polymer/drug matrix. The limitation of microspheres made of a single polymer encapsulating drugs includes an initial burst caused by the release of the drug trapped on the surface during the encapsulation process and a progressively slower release rate. Therefore, microspheres made with a two-layered structure may have certain advantages over their counterparts made from single polymers [13].

Formulation of Double Walled Microspheres

Solvent Evaporation Method

Two polymers are dissolved in a volatile organic solvent such as dichloromethane. It is then added into aqueous solution containing surfactant and stirred. As the polymers become more concentrated, they begin to phase separate and form the core shell structure Double walled microspheres [14].

Oil-In-Water (O/W) Method

It can produce Double-wall microspheres (DWMS) with core and shell polymers at their thermodynamically stable configurations according to the spreading coefficient theory [15-18].

Oil -In-Oil Oil-In-Water (O/O/W) Method

It was used for producing double walled microsphere for research purpose.

Layer–by-layer Deposition Method

This method involves the deposition of layer-by-layer film components onto the outer surface of colloidal particles that are removed by physical or chemical means.

For these methods, the control of double walled microsphere and MC dimensions such as outer diameter and shell thickness is typically poor. The emulsion method can produce Double walled microsphere with relatively broad size distribution and the polymer orientation for core and shell may change during fabrication. For layer-by-layer coating, the diameter and shell coating can be very uniform, but these dimensions are controlled by templates. Besides, this method possesses limitations when generating thick layers or encapsulating a liquid core.

Osmotic Drug Delivery System

Most probably the conventional drug delivery system provides an immediate release of drug without any control over the release of the drug and it is difficult to maintain effective drug concentration at the target site for a longer period of time. Hence, to avoid the shortcomings there is the development of various controlled drug delivery systems. Among these, osmotic drug delivery systems (ODDS) utilizes the osmotic pressure created by osmogens is used as driving force for these systems to release the drug in a controlled manner and can be used for both oral and implantation. The drug release is independent of the pH and thermodynamics of dissolution medium. The osmotic drug delivery system offers many advantages over other controlled drug delivery systems, such as easy formulation procedure and simple operation, improved patient compliance by reducing the dosing frequency and prolonged therapeutic effect with uniform blood concentration. Controlled porosity osmotic pump (CPOP) based drug delivery system contains active ingredient, osmogens, semi permeable membrane, channelling agent and water soluble additives. In this system, when water comes in contact with water soluble additives it results in an in situ formation of a Microporous membrane. The main driving force for the release of drug is osmotic pressure. Osmogens maintain concentration gradient across the membrane [19].

CONCLUSION

Since esomeprazole is an acid liable drug encapsulation technique will protect the

drug from an acidic condition of the stomach. Coating by enteric polymers make them as double walled and can target the drug action into the intestine. These microspheres is compressed with osmotic agent and other diluent will forms tablet that release drug by process of osmosis. Finally, coating of the tablet by pore forming agents produces controlled porosity osmotic pump tablet. Controlled delivery of esomeprazole microsphere incorporated in an osmotic tablet progressively deliver a measurable, reproducible amount of drug over a prolonged period could exhibit improved therapeutic effect, quality character of formulation and patient compliance.

REFERENCES

1. Muruganantham V, Jaykar B (2016), "Design & evaluation of buccal tablets of drug loaded microspheres", *JCPS*, Volume 9, Issue 2, pp. 673−678.
2. Naresh Vishal Gupta, Shirodker Natasha et al. (2013), "Bioadhesive Vaginal Tablets Containing Spray dried microspheres loaded with Clotrimazole for treatment of Vaginal Candidiasis", *Acta Pharm*., Volume 63, pp.
3. Supriya Shidhaye, Sheetal Malke et al. (2008), "Taste Masked Orally Disintegrating Tablet Containing Microsphere for Immediate Release", *Journal of Pharmacy Research*., Volume 1, Issue 2.
4. Gamal A Shazly (2013), "Formulation and evaluation of fast dissolving tablets containing taste-masked microspheres of diclofenac sodium for sustained release", *Digest Journal of Nanomaterials and Biostructures.*, Volume 8, Issue 3, pp. 1281–1293.
5. Shivangi Singh (2016), "Formulation and evaluation of metronidazole tableted microspheres for colon drug delivery", *Asian J Pharm Clin Res.*, Volume 9, Issue 3, pp. 398−403.
6. Tiwari S, Verma P (2008), "Microencapsulation technique by solvent evaporation method (Study of effect of process variables)", *Int J Pharm Life Sci*., Volume 8, Issue 2, pp. 998−1005.
7. Redasani V, Jaiswal SB et al. (2012), "Tabletting and coating multiparticulates", *Int J Phar Res Dev.*, Volume 3, Issue 11, pp. 153−159.
8. Das MK, Senapati PC (2007), "Evaluation of furosemide loaded alginate microspheres prepared by ionotropic external gelation technique", *Acta Poloniae Pharm Drug Res.*, Volume 64, Issue 3, pp. 253−262.
9. Priya Shahi et al. (2015), "Microspheres and tablet in capsule system: A novel chronotherapeutic system of ketorolac tromethamine for site and time specific delivery", *International Journal of Pharmaceutical Investigation*., Volume 5, Issue 3, pp. 161−170.
10. Shah N, Patel M et al. (2011), "Design, development and optimization of colon targeted drug delivery system for Crohn'sdisease", *Indian J Pharm Educ Res.*, Volume 2, pp. 42−50.
11. Dharmendra Jain et al. (2016), "Sumatriptan Succinate Loaded Microspheres Containing Compressed Core Tablet", *Bulletin of Pharmaceutical Research*., Volume 6, Issue 2, pp. 56−67.
12. Verma S, Kumar V et al. (2014), "Formulation evaluation and optimization of mucoadhesive microspheres of acyclovir", *Bull. Pharm. Res.*, Volume 4, Issue 1, pp. 14−20.
13. Kannuri R, Challa T et al. (2011), "Taste masking and evaluation methods for orodispersible tablets", *Int. J.Pharm. Ind. Res*., Volume 1, Issue 3, pp. 200−210.
14. Kunal N Patel, Dr. Tejal A Mehta et al., "A review on oral osmotically

driven systems", *Int J Pharm Sci.*, Volume 5, Issue 3, pp. 1005−1013.
15. Rajan K Verma, Sanjay Garg et al. (2004), "Development and evaluation of osmotically controlled oral drug delivery system of glipizide", *Eur J Pharm Bio Pharm.*, Volume 57, pp. 513−525.
16. Xiongkai Cheng, Min Sun (2010), "Design and evaluation of osmotic pump–based controlled release system of Ambroxol hydrochloride", *Pharm Develop Tech.*, Volume 1, pp. 1−8.
17. Ayesha Sultana, VH Sastry (2015), "Controlled porosity osmotic pump (Cpop)-An advanced delivery system for cardio Selective β 1 blockers", *Int J Pharm and Chem Sci.*, Volume 4, Issue 3, pp. 336−350.
18. Arti Banerjee, PRP Verma (2013), "Controlled porosity solubility modulated osmotic pump tablets of Gliclazide", *Int J Pharm Sci.*, Volume 2, pp. 231−242.
19. Sudeesh Edavalath, Shivanad K (2011), "Formulation development and optimization of controlled porosity osmotic pump tablets of diclofenac sodium", *Int J Pharm Sci.*, Volume 3, Issue 1, pp. 80−87.