

A Review on Esomeprazole Microsponges for GERD: A Novel Approach

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Abstract : GERD (Gastro Esophageal Reflux Disease) is a very common disease. People suffering in all age but more common after age of 40 Year. In India around 250 Million of people suffer from GERD. Proton pump inhibitors (PPI) are potent acid-suppressive agents which be can provide relief from symptoms of gastro esophageal reflux disease (GERD) and maintenance of health-related quality of life. Esomeprazole is good highly effective and used in monotherapy in GERD.esomeprazole having shorter half-life So, for the good therapeutic effect and improve bio availability need to be prolong drug release. Microsponges drug delivery system is highly cross link porous in nature and drug release in control manner from pores present on the surface of microsponges and release of drug without dose dumping.

Keyword: GERD, Esomeprazole, Microsponges Drug Delivery, Quassi Emulsion Solvent Diffusion.

❖ INTRODUCTION

1.1 INTRODUCTION TO GERD (1-8)

- Gastroesophageal reflux disease (GERD) is a condition in which the stomach contents (food or liquid) come back into the esophagus. (the tube from the mouth to the stomach).

SYMPTOMS OF GERD

- In the condition of GERD Symptoms like,
Difficulty or pain when swallowing of food or any drinks, Chronic sore throat, Laryngitis, Chest pain, Heart burn, excess of saliva, Inflammation of the gums.

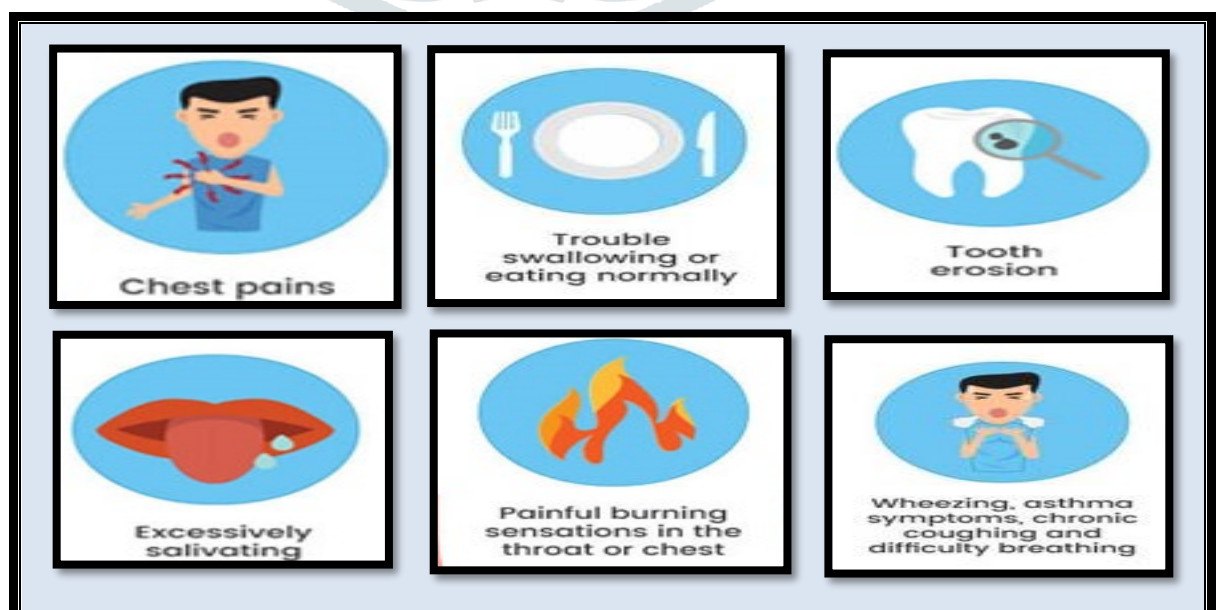


Figure No.1 Symptoms of GERD

Causes

- The main cause of GERD is valve Connected between esophagus and stomach is weaker than the normal condition.
- Another reason like, Excessive Pressure on the stomach from tight clothing or extra body fat.

Other factors may Cause acid reflux:

• Alcohol use
• Pregnancy
• Smoking
• Certain Foods
• Routine Habits

➤ **Pregnancy:**

- Pregnant women experience acid reflux during the first trimester around 90% case found.
- The higher levels of hormones and the pressure applied by the growing fetus.

➤ **Smoking:**

Smoke from cigarettes causes acid reflux by:

- Damaging the mucus membranes
- Reducing the amount of saliva Due to acid from the stomach which causes irritation and pain that can travel.
- Troubling the function of sphincter muscles Damaging the mucus membranes.

➤ **Certain Foods:**

There is a long list of certain food which cause acid reflux example:

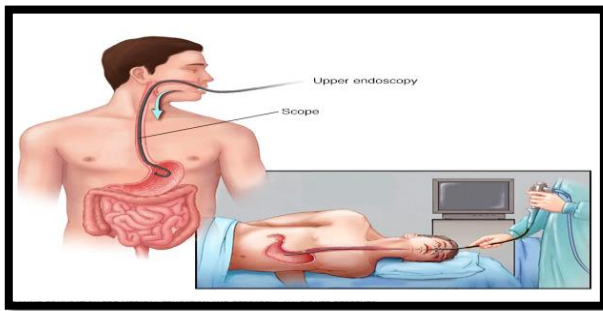
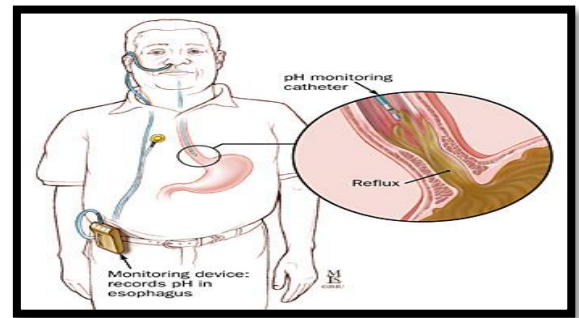
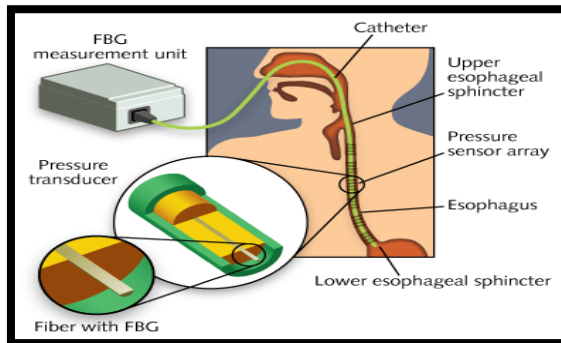
- Carbonated drinks, Fried foods, Spicy food and sauces, Citrus fruits such as oranges, grapefruit, or lemons, Chocolates, Tea, coffee, Alcohol, Onions and garlic, Fatty food or snacks.

➤ **Routine Habits:** Certain lifestyle habits which cause acid reflux problems like:

- overweight can add to the problems of the stomach
- Take high quantity of food at a time which leads to digestion problems
- Habit of eating a heavy food close to the bedtime may also produce stomach problems

Diagnosis

• Upper Endoscopy
• Esophageal pH Monitoring
• Esophageal Manometry
• Barium Radiograph

**Upper Endoscopy****Esophageal pH Monitoring****Esophageal Manometry****Barium Radiograph****Figures No.2 Diagnosis of GERD****Upper Endoscopy**

Upper endoscopy done by Inserts a thin, flexible tube equipped with a light and camera that down into throat. In which examine the inside region of esophagus and stomach. Upper Endoscopy detection inflammation of the esophagus (esophagitis) or any other complications.

Esophageal pH Monitoring

A thin tube is passed through nose or mouth to stomach. The tube is then pulled back into your esophagus. A monitor attached to the tube measures the acid level in esophagus. The monitor record symptoms and activity over the next 24 hours.

Esophageal Manometry

This test for examine the rhythmic muscle contractions of esophagus when swallow. It also measures the coordination and force utilized by the muscles of your esophagus.

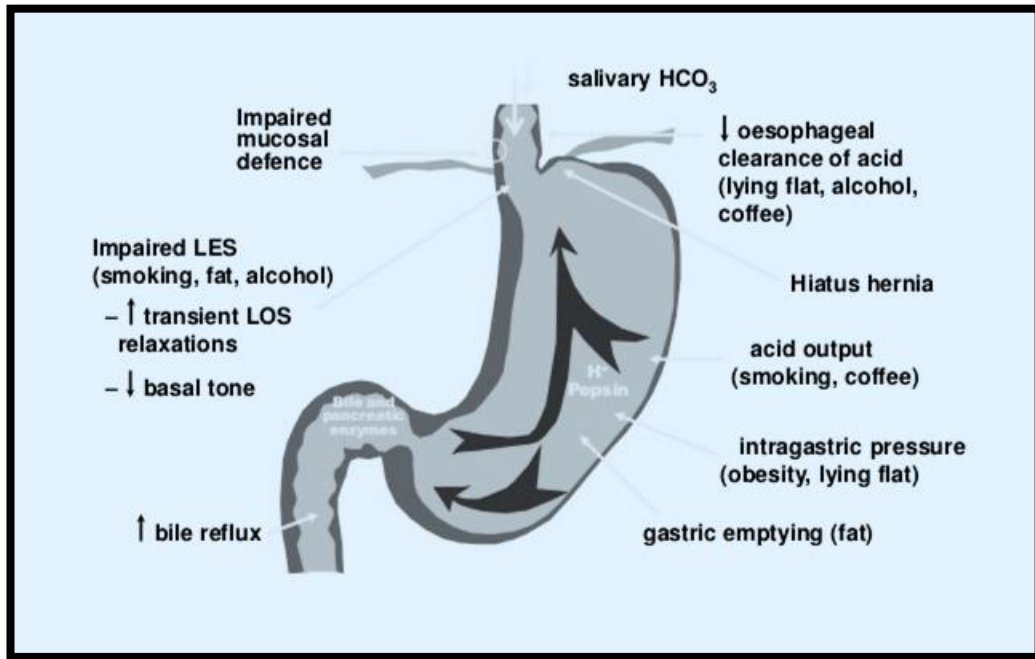
Barium Radiograph

To Swallow barium and x-ray of esophagus and evaluate anatomy of structural problems in esophagus.

Epidemiology:

GERD occurs in all ages but, most common in those older than 40 years of age. About 250 Million of people in India suffer from GERD. Between 20 and 40 percent of those experiencing common heartburn are predicted to actually have a diagnosis of GERD

Pathophysiology:



Figures No.3 Pathophysiology of GERD

Available Management:

1. Non-Pharmacological
2. Pharmacological

Non-Pharmacological management

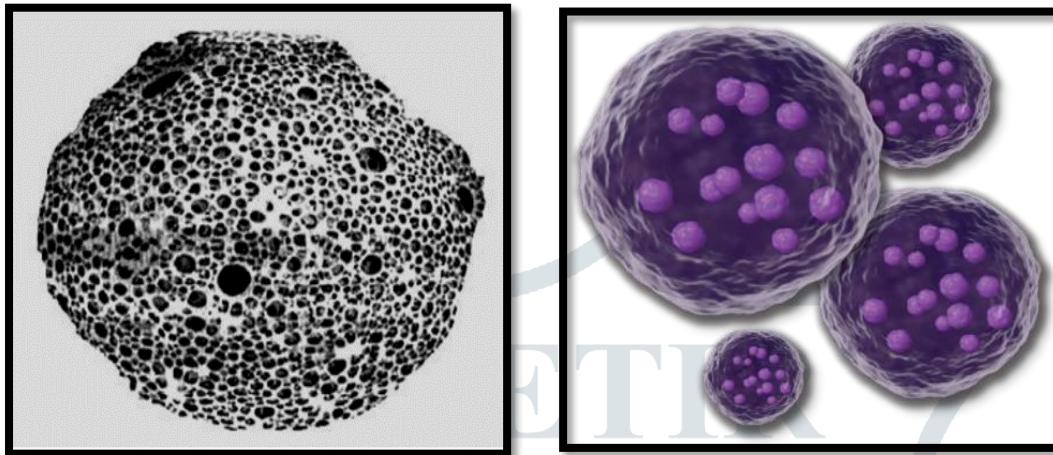
- Lose weight
- Stop smoking & reduce alcohol intake
- Limit meal size and avoid heavy evening meals
- Do not lie down within two to three hours of eating
- Decrease caffeine intake because caffeine cause GERD

Pharmacological Management

Class of drug	Example
H2 antihistamines	Cimetidine, Ranitidine, Famotidine, Roxatidine
Anticholinergics	Pirenzepine, Propantheline, Oxyphenonium
Prostaglandin analogue	Misoprostol
Proton Pump Inhibitors	Omeprazole, Lansoprazole, Pantoprazole, Rabeprazole, Dexlansoprazole, Esomeprazole

1.2 INTRODUCTION TO MICROSPONGES (9-17)

- Microsponges are defined as porous, inert units which are made up of synthetic polymers and act as a shield to the ensnared means capture drug which can be easily entrapped in the form of creams, lotions, and powders.
- A Microsponge Drug Delivery System is, Non collapsible structure with Highly cross linked Structure which can Entrap wide range of drug.
- A Typical Size of the microsponges Between “5-300 μm ” in diameter.



Figures No.4 Structure of Porous Microsponges

1.2.1 Need of Microsponges Drug Delivery System for GERD

Microsponges contains numbers of pores present on the surface that provides Prolong drug release. Due to because of small pores present on the surface of microsponges that release of drug without dose dumping. So that its improve bioavailability and improve therapeutic effect. In the case of GERD Continuous acid reflux to the esophagus from stomach.so its necessary to provided good therapeutic effect for prolong time of period so that microsponges drug delivery good approach for prolong drug release and treatment of continues acid reflux. Also esomeprazole provides good therapeutic effect and also half-life of 1-1.5 Hr. So, need to be Prolong drug release. Esomeprazole is Desired candidate for monotherapy in GERD. Esomeprazole having high potency and Efficacy for treatment of GERD.

1.2.2 Ingredients used in the Formulation of Microsponges

Microsponges formulation composed of internal phase and external phase. Internal phase contain drug + polymer dissolved in desired solvent. And external phase contain water and PVA (Poly vinyl Alcohol) or Aqueous solution of PVA.

1.Polymers: Polymer are responsible for releasing Patten of drug. Used in internal phase as well as External phase.

- Eudragit RS100
- Eudragit RL100
- HPMC K4M
- Ethyl Cellulose
- PVA (Poly vinyl alcohol)

2.Solvent: Solvents are used in internal phase as well as External phase.

- Di chloromethane
- Ethanol
- Acetone
- water

3.Plasticizer: which stabilised the structure of microsponges which provide plasticity to structure of microsponges.

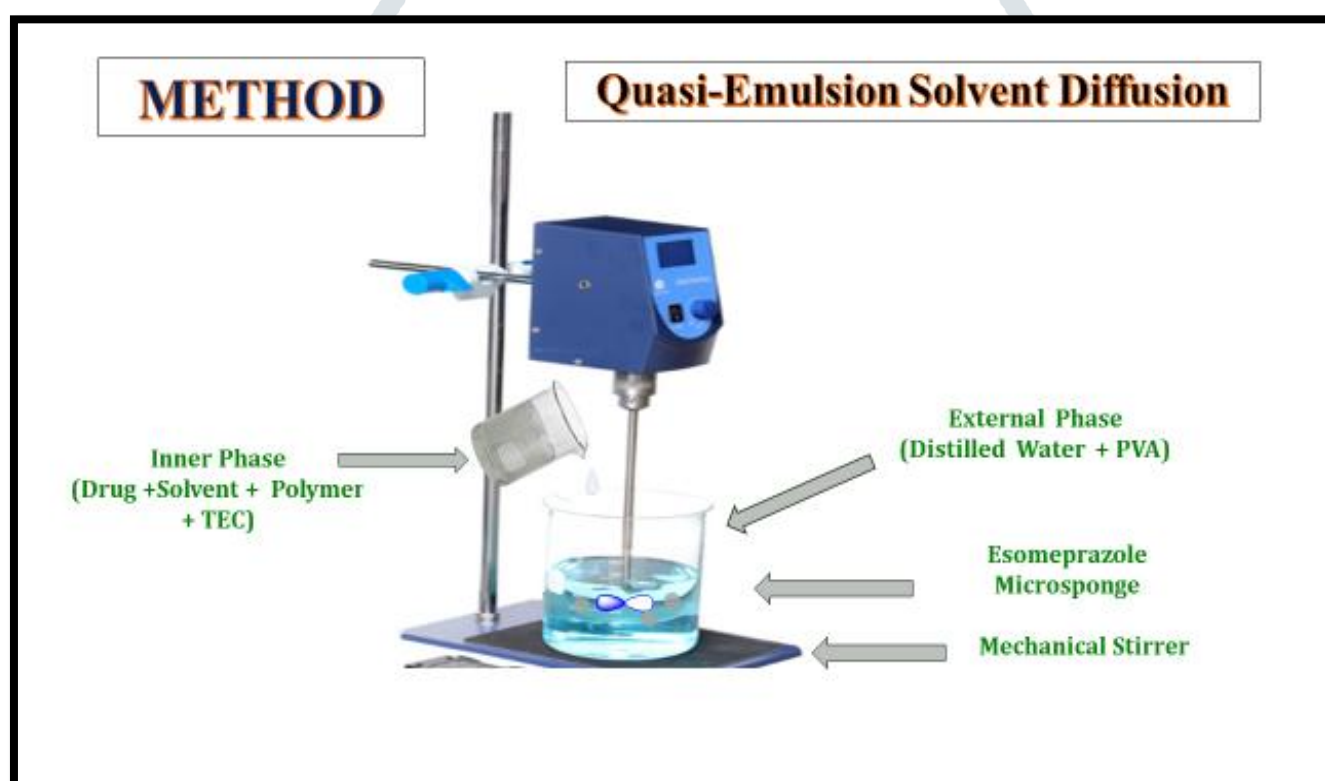
- TEC (Tri Ethyl Citrate)
- Diethyl phthalate
- Tributyl citrate

1.2.3Method of preparation:

Quasi-emulsion solvent diffusion:

In quasi emulsion solvent diffusion technique prepare two phase

1.Internal phase	Drug, polymer and organic solvent
2.External phase	Aqueous solution of PVA



Figures No.5 Method of preparation

Internal phase solution of drug and polymer by adding inorganic solvent i.e. ethanol Acetone dichloromethane



External phase contains the Aqueous solution of PVA with Plasticizer.



Add drop by drop in to the external phase with continuous stirring.



Filter & collect the microsponges at drying at 40°C in Hot air oven



1.2.5 Comparison Between Microsphere, Microcapsule Microsponge

PARAMETER	MICROSPHERE	MICROSPONGES	MICROCAPSULE
Shell	complete	Sponge	complete
Release mechanism	Rupture or burst of cell	Pressure, partition coefficient, Temperature, pH	Rupture or burst of cell
Stability	Potential problems	Stable even change in pH and Temperature.	Potential problems
Loading capacity	Good	More than Microsphere and Microcapsule	Good

1.2.6 Evaluations Parameters of Microsponge:

✓ Particle size

Particle size are calculated using optical microscope or an electron microscope. This is an extremely crucial step, as the size of the particles greatly affects the texture of the formulation and its stability.

✓ Morphology and Surface topography

Morphology and surface topography, various techniques have been used Scanning electron microscopy (SEM), transmission electron microscopy (TEM) etc.

✓ Determination of % Entrapment Efficiency & % yield

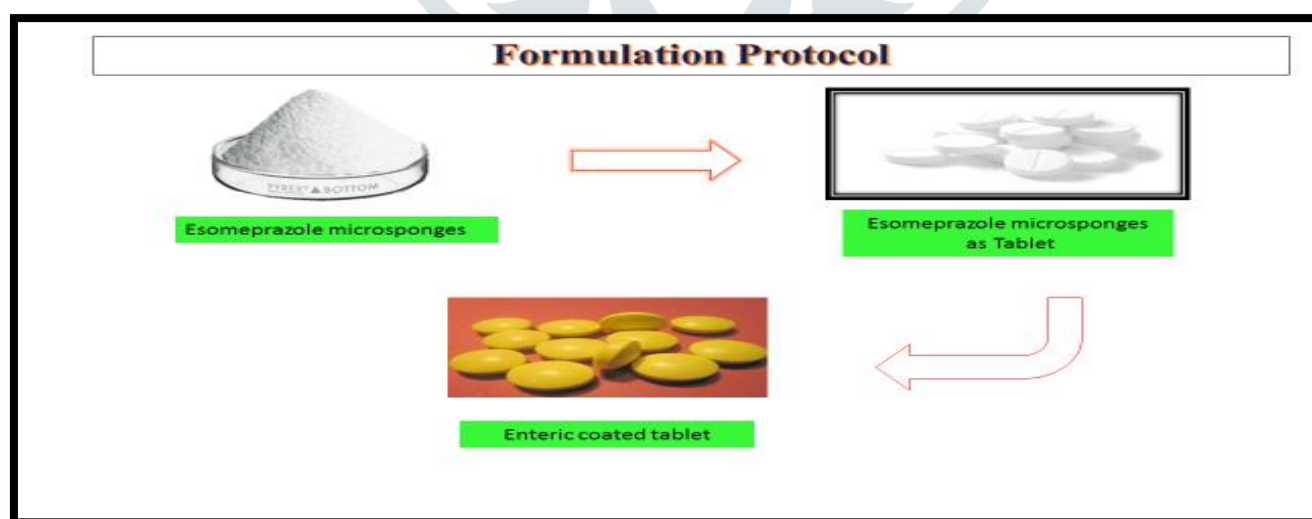
The % Entrapment Efficiency & Production yield of the Microsponges can be calculated according to the following equation:

- **% Entrapment Efficiency** = actual drug content in microsponges / Theoretical drug content x 100

- **% Yield** = Practical Yield / Theoretical Yield x 100

✓ **Dissolution Test:** Dissolution profile of Microsponges can be studied by use of dissolution apparatus USP-II Type dissolution apparatus The dissolution test will be done in 900 ml Phosphate buffer (PH6.8) at the 37±.5 °C, 150 RPM.

1.2.7 Formulation Protocol:



Figures No.6 Formulation Protocol

First prepared Esomeprazole microsponges by quasi emulsion solvent diffusion method after that take equivalent to dose. And add diluent, lubricant and compress the tablet. Esomeprazole is acid labile drug so coating of tablet with the help of enteric coated polymer.

1.2.8. Stability Studies (18)

To measure the drug and formulation stability, stability studies were done according to ICH and WHO guidelines. Optimized formulation Tablet of Esomeprazole Microsponges were kept in the humidity chamber maintained at 40°C and 75% RH for 1 months. The sample were analysed for the physical changes and % drug content, in vitro release profile and other stability indicating parameters after 15 days and 1 month.

Conclusion: Oral delivery of microsponges is novel approach. esomeprazole having shorter half-life So, for the continuous or chronic acid reflux condition requirement for prolong drug release. Microsponges drug delivery system provide prolong drug release due to presence of small pores on surface of microsponges which provides good therapeutic effect against continuous acid reflux without dose dumping. Microsponges drug delivery have number of advantages that will provide the big scope in future for the delivery of drug topically as well as orally with more efficacy and less production cost.

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