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FORMULATION AND EVALUATION OF DELAYED RELEASE ESOMEPRAZOLE PELLETS AND STUDY ITS RELEASE PROFILE

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Abstract

This study describes the development of a new Esomeprazole delayed release gastro-resistant formulation with improved storage stability. A three-step:Drug, Sub (seal),Enteric Coating. Coating process was employed using a fluid bed coater. Various formulation factors (namely- size and quantity of starting sugar spheres, binder quantity during drug-layering, sub (seal)-coating polymer type, and quantity and enteric coating quantity) were evaluated and the whole process was modeled with the aid of Fluid bed equipment (FBE). Results showed that the selection of small-sized pellets (45/60 mesh size) can lead to agglomeration, while weight gain due to Sub (seal)-coating increases the dissolution rate of Esomeprazole. The enteric-coating applied showed good gastro-resistant performance in both 0.1 N HCl and pH 4.5 media. The effect of cellulose-based sub(seal)-coating polymers, (namely, hydroxypropyl cellulose and hydroxypropyl methyl cellulose) on formulation's storage stability at 40 ± 2 °C/75 ± 5%RH indicated that only hydroxypropyl methyl cellulose was able to stabilize ESO delayed-release formulations in terms of assay, dissolution, and gastro-resistance performance. Esomeprazole magnesium is formulated as delayed release pellets to provide desired effect at certain time in maintained drug concentration without any unwanted effect with patient compliance also to improve its bioavailability by decreasing its expose to gastric acid.

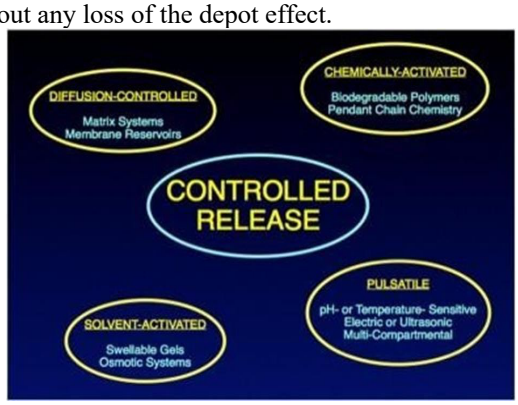
Developing any new drug molecule is pretty pricey and time eating process. Betterment of protection and efficacy ratio of the preceding pills has been tried via one-of-a-kind techniques such as drug therapy, dose titration, and healing drug monitoring. Delivering drug at a regular and managed rate, sluggish and focused transport are different very appealing techniques and were used vigorously. It could be very exciting to notice that the significant paintings and lots of guides from USA, Europe are authored with the aid of using the Indian researchers.[1–3] Controlled drug delivery systems (CDDS) may include the maintenance of the drug levels within a desired range, the need for lesser administrations, appropriate use of the drug in question, and increased patient compliance. While these advantages can be significant, the disadvantages cannot be ignored like the possibility of toxicity or non-biocompatibility of the materials being used, undesirable by-products from degradation, any surgery required to implant or remove the system, the chances of patient discomfort from the delivery device, and the higher cost of controlled-release systems when compared with the traditional pharmaceutical formulations.

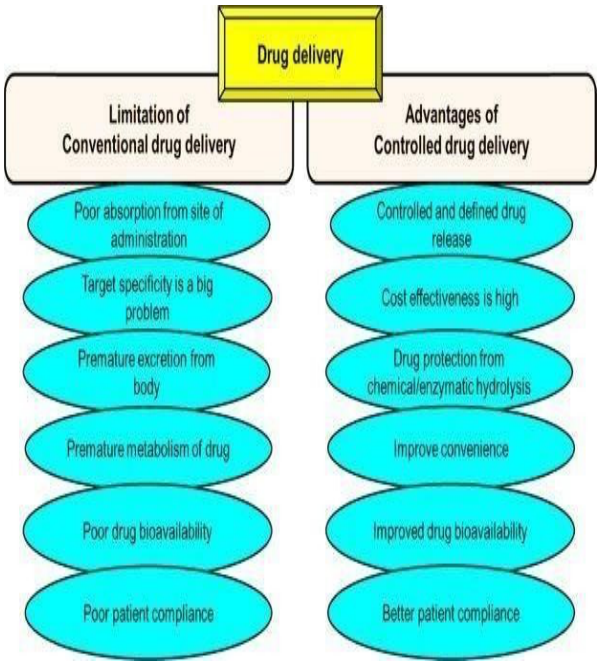
Keyword- CDDS, Esomeprazole, Pellets, fluid bed equipment.

INTRODUCTION

Controlled drug delivery systems can include the maintenance of drug levels within a desired range, the need for fewer administrations, optimal use of the drug in question, and increased patient compliance. While these advantages can be significant, the potential disadvantages cannot be ignored like the possible toxicity or non-biocompatibility of the materials used, undesirable by-products of degradation, any surgery required to implant or remove the system, the chance of patient discomfort from the delivery device, and the Corresponding Author's Contact information: Debjit Bhowmik * Nimra College of Pharmacy, Andhra Pradesh, India E-mail: debjit_cr@yahoo.com higher cost of controlled-release systems compared with traditional pharmaceutical formulations. The ideal drug delivery system should be inert, biocompatible, mechanically strong, comfortable for the patient, capable of achieving high drug loading, safe from accidental release, simple to administer and remove, and easy to fabricate and sterilize.

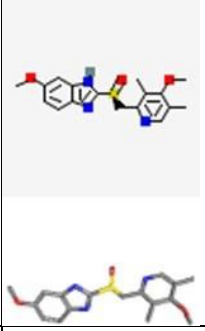
The motive of many of the original controlled-release systems is to achieve a drug delivery profile that would yield a high blood level of the drug for over a long period of time. With various traditional drug delivery systems, the drug level in the blood follows in which the level rises suitably after the administration of the drug and then again decreases until the next administration. The key point with the traditional drug administration is that the blood level of the drug should remain between the maximum value, which may represent a toxic level, and the minimum value, below which the drug does not show its desired impact on the patient. Pellets that are used to administer orally are administered in the form of a hard gelatin capsule or any disintegrating tablets which quickly liberate or release its contents in the stomach and will get distributed throughout the gastrointestinal tract (GI) without any loss of the depot effect.





A future trend will definitely demand strong, thermally stable, and highly abrasion- resistant textiles, where the plasma treatments can make a substantial contribution. The comfort of functional textiles from the user‘s point of view always becomes a priority. For example, integrating electronics into clothing industry is an innovative concept, which opens up new horizons in the form of a host of multifunctional, wearable electro-textiles for sensing and monitoring various body functions, delivering communication facilities, data transfer, individual environmental control, and many other applications. [41]

DRUG AND EXCIPIENTS PROFILE
ESOMEPRAZOLE-

Structure	
Classification	Proton Pump Inhibitor
Molecular Formula	C17H19N3O3S
Synonyms	Esomeprazole (S)-Omeprazole(-)-Omeprazole119141-88-7 (S)-(-)-Omeprazole
Molecular Weight	345.4 g/mol

PHARMACODYNAMICS-

Esomeprazole is a stomach acid secretion inhibitor that is used to treat gastro esophageal reflux disease (GERD), erosive esophagitis healing, and H. pylori eradication to lower the risk of duodenal ulcer recurrence. Esomeprazole belongs to a new class of anti secretary compounds, also called the substituted benzimidazoles, that do not exhibit anticholinergic or H2 histamine antagonistic properties but are responsible in suppressing gastric acid secretion by specific inhibition of the H + /K + ATP ase at the secretary surface of the gastric parietal cell. Acid secretion into the gastric lumen is inhibited as a result. This effect is dose- dependent, and regardless of the stimulus, it inhibits both basal and induced acid secretion. The s-isomer of Omeprazole, which is a racemate of the S- and R- enantiomers, is Esomeprazole. In vitro, Esomeprazole and Omeprazole both limit acid secretion to the same level, with no notable differences between the two substances.

EXPECTED OUTCOMES FROM THE STUDY

The study was performed to eradicate a major problem of medicines being over-priced. The high cost of prescription drugs threatens healthcare budgets, and limits funding available for other areas in which public investment is needed. Drug companies cite high drug prices as being important for sustaining innovation. But the ability to charge high prices for every new drug possibly slows the pace of innovation.

Also, to start up with the study, drug was quite difficult to be selected. But heart burn and acidity are one of the most common problems now-a-days. So drug selection was made upon day-to-day problems.

Esomeprazole (PPI) suppresses the excess acid produced inside the stomach giving relief to the patient.

As per the current formulation which was going on Drug-coat (polymer) [Methyl acrylicacid and ethyl acrylate copolymer dispersion]. It is quite expensive for the formulation thus making the medication costly. So, a new formulation was developed by replacing the currently used polymer by DCPD (Di-calcium phosphate di-hydrate).

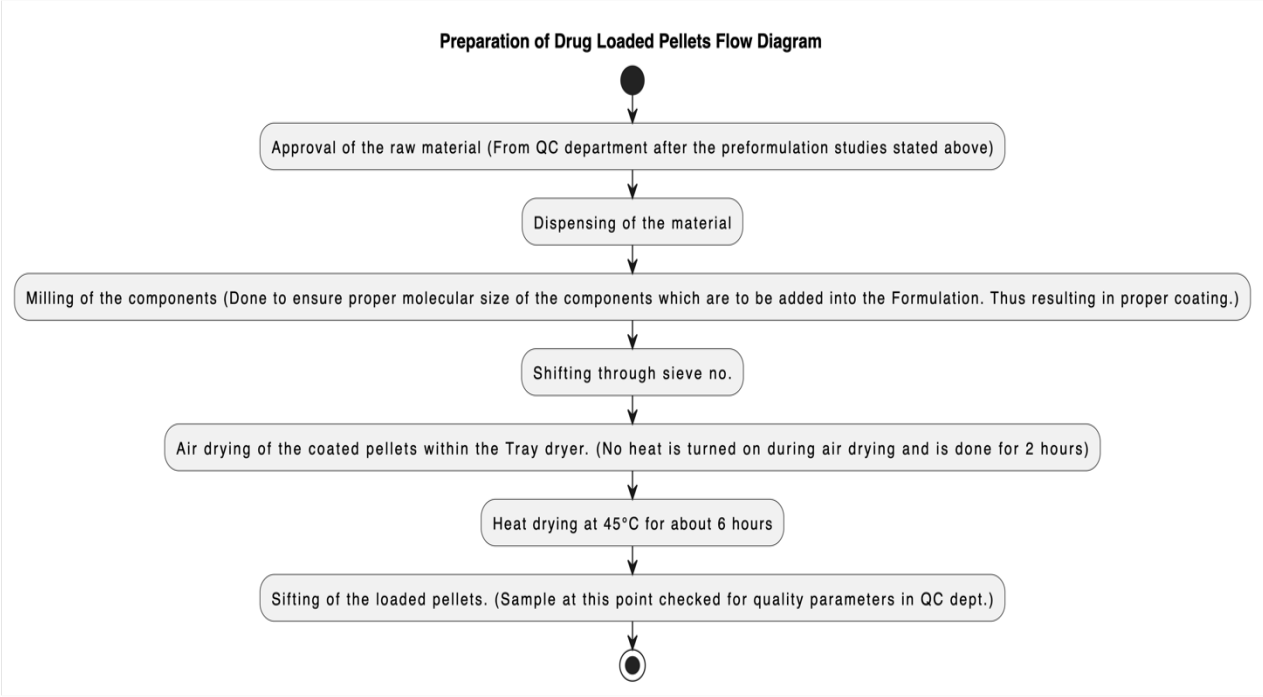
DCPD was analyzed and found a good polymer and filler as well. Also, it was quite cheap when compared to drug-coat. The replacementtook place almost at the end i.e., at the enteric coating stage.

- The outcomes of the new formulation are expected to be within the range. Making a cost effective formulation for people and company as well.
- Increasing the therapeutic effects of the drug.
- To prepare a delayed release enteric coated formulation which is stable in the acidic environment and release the drug under favorable conditions?

RESERCH METHODLOGY

PREPARATION OF DRUG LOADED PELLETS FLOW DIAGRAM:

After the preformulation study was done, pellets were prepared: -



RESULTS AND DISCUSSION

In the existing formulation, Drugcoat (Meth acrylic acid and ethyl acrylate copolymer) is being used extensively for stability purpose. Hence increasing the cost of the formulation.

So, we urge to minimize the cost of the preparation and make it more effective and provide a good therapeutic response. Thus, Drugcoat was replaced by another stabilizer and filler as well DCPD (Di-calcium phosphate di-hydrate).

DCPD is available in the market at much lower prices as compared to Drugcoat. Also, is a great filler and stabilizer which can increase the therapeutic response of the product formulation.

This study is carried out to evaluate the effects of the changed material over the formulation.

Technology(CDDS/SRDDS)

Sustained Release Drug Delivery System (SRDDS) is designed to release a drug at a predetermined rate by maintaining a constant drug level for a specific period of time with minimum side effects. The present review is concerned with the patent study of drug release through controlled or sustained release dosage forms.

1.Solubility: It is freely soluble in water and in anhydrous ethanol, practically insoluble in n-hexane.

2. Melting Point: Melting point was found within the range 150-155°C.

3. FTIR: Fourier transform infrared spectroscopy (FTIR) uses the mathematical process (Fourier transformation) to translate the raw data into the spectrum. FTIR method is used to obtain the infrared spectrum of transmission or absorption of a sample. FTIR identifies the presence of organic and inorganic compounds in the sample. Depending on the IR absorption frequency range 600–4000 cm−1, the specific molecular groups induced in the sample will be determined through spectrum data in the automatic software. FTIR has been used as a novel approach to characterize the variability in fuel stability of various biodiesel/antioxidant samples.

4. HPLC: Liquid chromatography is a technique used for the separation of substances. High performance liquid chromatography (HPLC) is a method for the analysis of a wide range of products. The separation principle of HPLC is based on the distribution of the sample between the mobile phase and a stationary. Depending on the structure of the analyte, the molecules are retarded while passing the stationary phase. Hence, different constituents of a sample are eluted at different times. Thereby, the separation of the sample ingredients is achieved.

Also to study the effectiveness of the new cost effective product formulation.

CONCLUSION

This research aimed to develop and evaluate the delayed release pellets of Esomeprazole drug. Based on various results, it was found that the delayed release formulations are more effective and has patient compliance. Also, a major ascendancy is less dosing frequency. Based on the quantitative and qualitative analysis, the results were found to be complying with the trends. To better understand the implications of these results, future studies could address various prospects. In vivo characterisation demonstrated that the prepared formulation is adequate and appropriate for delayed release impacts. In vitro permeability shows relatively high drug permeation in the prepared formulation when compared to the existing formulations. All the findings support the application of delayed release pellets, as a long term cure for most common problem of hyper acidity and GERD.

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