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An Outline on Various Methods Used in Formulation and Evaluation of Lansoprazole of Liposome & Pro-Liposome.

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Abstract - *The medication lansoprazole is used to treat stomach and intestine ulcers, erosive esophagitis (esophageal damage caused by stomach acid), and other disorders including Zollinger-Ellison syndrome that involve excessive stomach acid. Frequent heartburn that occurs at least twice a week is treated with over-the-counter (OTC) lansoprazole. This medication is not meant to provide immediate relief from heartburn symptoms. A medicine that lowers stomach acid is marketed under the trade names Prevacid and other names. It is used to treat Zollinger-Ellison syndrome, gastroesophageal reflux disease, and peptic ulcer disease. Comparability to other proton pump inhibitors of efficacy (PPIs). It is consumed orally. Pro-liposome applications are highlighted along with various formulation techniques (Film-deposition carrier method, Spray drying method, Fluidized-bed method, and Supercritical anti-solvent method), evaluation criteria (Hydration study, Zeta potential, Flow property, Release study, Particle Size, Entrapment Efficiency), and formulation techniques. This might aid in the development and testing of lansoprazole further. There have also been reports of distinct lansoprazole characteristics connected to its pharmacological profile and mechanism of protection in treating various illnesses. White crystalline powder, lansoprazole is very little soluble in water and easily soluble in ethanol, methanol, and acetone. The goal is to create lansoprazole in a biocompatible and low-toxic form that may be utilised to treat ulcerative colitis, inflammatory bowel syndrome, gastric, duodenal, and peptic ulcers.*

Key Words: Lansoprazole, Liposome, Pro-liposome, method, release study.

1. INTRODUCTION

The medication lansoprazole is used to treat stomach and intestine ulcers, erosive esophagitis (esophageal damage caused by stomach acid), and other disorders including Zollinger-Ellison syndrome that involve excessive stomach acid. Frequent heartburn that occurs at least twice a week is treated with over-the-counter (OTC) lansoprazole. This medication is not meant to provide immediate relief from heartburn symptoms. A medicine that lowers stomach acid is marketed under the trade names Prevacid and other names. [1] It is used to treat Zollinger-Ellison syndrome, gastroesophageal reflux disease, and peptic ulcer disease. [2] Comparability to other proton pump inhibitors of efficacy (PPIs). [3] It is consumed orally. Pro-liposome applications are highlighted along with various formulation techniques (Film-deposition carrier method, Spray drying method, Fluidized-bed method, and Supercritical anti-solvent method), evaluation criteria (Hydration study, Zeta potential, Flow property, Release study, Particle Size, Entrapment Efficiency), and formulation techniques. This might aid in the development and testing of lansoprazole further. There have also been reports of distinct lansoprazole characteristics connected to its pharmacological profile and mechanism of protection in treating various illnesses. White crystalline powder, lansoprazole is very little soluble in water and easily soluble in ethanol, methanol, and acetone. The goal is to create lansoprazole in a form that is low in toxicity and biocompatible and may be used to treat conditions including ulcerative colitis, inflammatory bowel syndrome, gastric, duodenal, and peptic ulcers. [3] Effects may endure for a few days and begin over the course of a few hours. [1]. Constipation, stomach discomfort, and nausea are typical adverse effects. [2] [5] Osteoporosis, low blood magnesium, a Clostridium difficile infection, and pneumonia are examples of serious adverse effects. [4] [5] The safety of use during pregnancy and breast-feeding is questionable. [1] It operates by inhibiting the stomach parietal cells' H+/K+-ATPase. [2] In medical practise since 1992, lansoprazole was first patented in 1984. [6] It is accessible as a generic drug. [7] With more over three million prescriptions written, it was the 188th most frequently prescribed drug in the US in 2017. A lansoprazole is reportedly excreted in the urine in amounts between 14 to 23%, and this range includes both conjugated and unconjugated hydroxylated metabolites. A Drugs of the proton pump inhibitor family are typically recommended for conditions where there is an excess of acid in the body. CYP2C19 and CYP3A4 often metabolise them. It is not shown that P-glycoprotein activity is likewise inhibited by proton pump inhibitors. Therefore, the purpose of our work was to describe lansoprazole as substrates and inhibitors of P-glycoprotein. In Caco-2 and L-MDR1 cells that express the P-glycoprotein, polarised transport of the drugs was evaluated. Using digoxin as a P-glycoprotein substrate, lansoprazole's ability to inhibit efflux transport was evaluated. In conclusion, our findings show that proton

pump inhibitors are P-glycoprotein substrates and inhibitors.

Pro-liposomes are a flexible system since they are accessible in dry form, which makes them simple to distribute, measure, transport, and store. The liposomes produced during reconstitution are more homogeneous in size and resemble traditional liposomes[15]. The pro-liposomes' solid form attests to their improved stability and practicality.

1.1. Merits of Pro-Liposome:

1. High hydrophilic material trapping.

2. Improved bioavailability is one of pro-liposomes' therapeutic advantages.

3. Preventing medication deterioration in the GIT

4. Fairly inexpensive.

5. Pro-liposomes, which are employed for controlled medication release and targeted drug delivery.

6. Proton pump inhibitor targeting.

Table 1 Comparison between liposome's and pro-liposome's

Liposome	Pro-liposome
Liposomes are Unilamellar or multilamellar spheroid structures.	PLs are used as alternatives for liposomes.
Composed of phospholipid and cholesterol.	Composed of water soluble porous powder as carrier phospholipids
The solubility of liposomes increases with oxidation and they have a propensity to clump together or fuse during hydrolysis.	In order to create free-flowing granular material that exhibits superior stability, increased solubility, and controlled release, drug and phospholipid material is coated on carrier material.

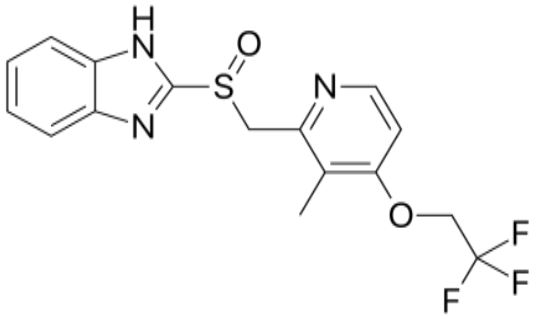

Figure 1 Structure of Lansoprazole

Table 2.Morphological characters of Lansoprazole.

IUPAC name	RS)-2-([3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl]methylsulfinyl)-1H-benzo[d]imidazole.
Molecular formula	$C_{16}H_{14}F_3N_3O_2S$
Route of administration	*By mouth, Intravenous*
Elimination	1.0 – 1.5 hr.
Excretion	Kidney and fecal
Melting point	The melting point is approx **166 °C**
Molecular weight	369.36g.mol-1
Solubility	freely soluble in ethanol and methanol slightly soluble in acetone and very less soluble in water.
Colour	white crystalline powder

2. METABOLISM AND MECHANISM OF ACTION OF LANSOPRAZOLE

It works by specifically inhibiting the membrane enzyme H+/K+ ATPase in the parietal cells of the stomach. In clinical studies, the treatment of reflux oesophagitis with lansoprazole was superior to placebo or histamine (H2)-receptor antagonists. Lansoprazole is a protodrug that must undergo protonation in an acidic environment in order to be activated as a PPI. When lansoprazole is protonated, it may interact with the cysteine residues Cys813 and Cys321 on the parietal H+, K+-ATPase to produce stable disulfides. PPIs in general have the capacity to bind covalently to their targets, which allows them to offer persistent suppression of acid secretion.

CYP3A4 and CYP2C19 metabolise lansoprazole mostly in the liver. The two main metabolites that are produced are the lansoprazole sulfone derivative and 5-hydroxy lansoprazole.

3. MATERIALS AND METHODS

3.1. Chemicals and Reagents.

Two kinds of food-grade soybeanlecithins from Lipoid GmbH (Ludwigshafen, Germany) were used to make proliposomes: phosphatidylcholine from hydrogenated, purified soy Phospholipon 90H (P90H), which contains a minimum of 90% weight-for-weight phosphatidylcholine (PC), a maximum of 4% weight-for-weight lysophosphatidylcholine (LPC), and 2% weight-for-weight triglycerides (TG), and fat-free powder lecithin Lipoid S40 (LS40), which contains a minimum of 40% weight-for-weight phosphatid (PI).

Curcumin that was crystallised and purified was purchased from Sigma-Aldrich (St. Louis, MO, USA). Guar gum (GG) was purchased from xodoCientifica (Hortolândia, SP, Brazil) and xanthan gum (XG) (Grindsted Xanthan 80) was provided courtesy of DuPont (Cotia, SP, Brazil). From Synth, we obtained sucrose, dimethyl sulfoxide (DMSO), and sodium benzoate (Diadema, SP, Brazil). The compounds utilised in this investigation were all of the reagent grade kind. Throughout the studies, deionized water (from a Direct Q3 system, Millipore, Billerica, MA, USA) was utilised.

4. METHODS OF PREPARATION

Pro-liposomes (PLs) are prepared by two methods -

- Film-deposition carrier method.
- Hand shaking method

4.1.Film Deposition Carrier Method

Pro-liposomes are created using the film deposition carrier technique. This procedure involves discharging a coating of pharmaceuticals and phospholipids onto a permeable, water-soluble carrier material. As shown in Figure 1, a feed tube injects an evaporative solution drop by drop onto a core of carrier material that is stored in a vessel of a rotary flashevaporator under vacuum. The evaporative solution contains a solution of medication and phospholipids. When a free-flowing powder matrix is obtained, overwetting of the matrix is prevented at any time and a subsequent aliquot of organic mixture is fed[9]. To control the amount of carrier that is required to help the lipids, chosen carriers should have high surface area and permeability. Additionally, it permits a high surfactant to carrier mass proportion for the generation of pro-liposomes. Due to their water solubility, they may produce liposomal dispersion quickly after hydration, and by properly regulating the size of the previous powder, a relatively small range of reconstituted liposomes can be obtained. Maltodextrin, sorbitol, microcrystalline cellulose, magnesium aluminium silicates, mannitol, and others are the most often utilised carriers[16]. Sluggish solvent inclusion and evaporation steps[17]. Modify the process by spreading the carrier component in an organic medicine and phospholipid combination in the rotary evaporator vessel before managing the vacuum evaporation to eliminate this problem. In contrast to the real technique, this results in a stable and less time-consuming lipid dispersion that is very consistent and well-organized.

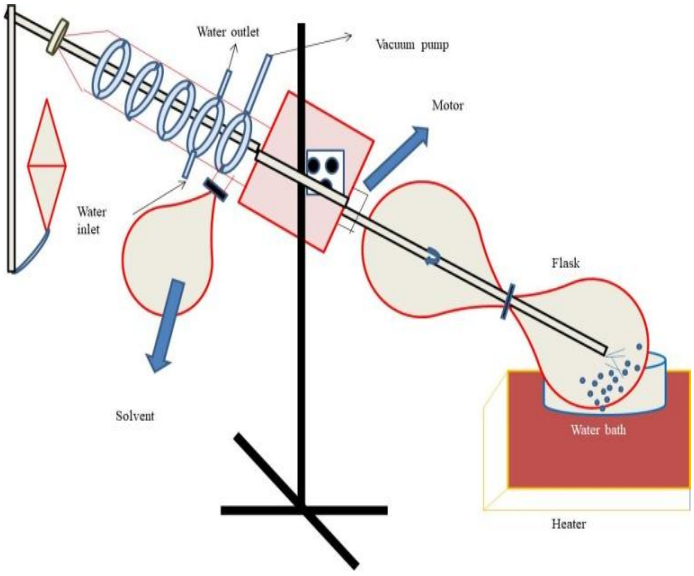

Figure 2 Apparatus for preparing PLs film deposition carrier

5. EVALUATION OF PRO-LIPOSOME

5.1. Scanning Electron Microscopy(SEM):

Basically, it's utilised to study the PL powder's surface structure. Additionally, it is utilised to compare the appearance of liposomes and pure carrier material. Pro-liposome formulation confirms after carrier material in the formulation approves the disposition of phospholipids on the carrier.

5.2. Transmission electron microscopy(TEM):

This technique is often used to examine the liposome's structure after PL powder hydration. In this procedure, the pro-liposome powder is hydrated with distilled water before being examined under a microscope to determine its lamellarity and form.

5.3. Hydration Study:

Studies on hydration are based on the fact that liposomes are created when they come into contact with an aqueous environment. This method involves adding a small amount of dry pro-liposome powder to a glass slide, gradually adding water, and using a microscope to observe vesicle formation. As soon as hydration starts, dissolution and disintegration start happening quickly. When water comes into contact with the lipid surface of pro-liposomes, liposomes are created. This procedure continues until the carrier and lipid layer have completely dissolved.

5.4.Zeta Potential:

Surface charge of the particle may be used to calculate zeta potential. It is the potential difference between the solution's electro-neutral zone and its densely bonded layer's surface (shear place).

5.5. Flow Property:

The flow feature of a powder formulation may be used to describe satisfied homogeneity and handling processing operations. It is necessary to examine the pro-properties liposome's for formulations based on solid powder. The parameters Angle of repose, Carr's Index, and Hausner's ratio may be used to evaluate it.

6. CONCLUSION

The use of liposomes and pro-liposomes has been a significant contributor to the resolution of issues with the stability, bioavailability, and solvability of medications that are only partially soluble. There has been tremendous progress made toward the creation of pro-liposomes as viable oral dosage forms; nevertheless, there are currently no medicines that are available on the market.

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