PREPARATION AND EVALUATION OF LANSOPRAZOLE NANOSPONGES

R. NAZEMOON
Associate Professor
Department Of Pharmaceutics
Vijaya College Of Pharmacy Hyderabad
9866108709
nazemoonr@gmail.com

A. VIJAYA RANI
B Pharmacy
Vijaya College Of PharmacyHyderabad
8978901498
angothvijayarani20012gmail.com

Abstract

Drug delivery technology has created renewed interest in pharmaceuticals by giving them a fresh term of life through therapeutic objectives. Targeting medicine delivery has become a key issue in recent years. Which the researchers are dealing with. Drug with a specific target administration resulting in increased therapeutic effectiveness, Side effects will be reduced, and the dosing schedule will be adjusted.be the most recent developments in the field of medicines. Because of its potential for controlled drug delivery, nanosponges have emerged as one of science's most promising technologies.

Introduction

The nanosponge delivery method can accurately adjust release rates or target pharmaceuticals to a specific anatomical spot, which might have a huge influence on the health-care system. Because of its great stability, large carrier capacity, and ability to incorporate both hydrophilic and hydrophobic molecules, this nanosized delivery system has clear benefits for drug delivery. By adjusting the amount of cross linker to polymer, nanosponges can be produced to be a specific size and release drugs over time[1]. When these nanosponges are synthesized in the application of magnetic substances, they can become magnetized. Because of their small size, nanosponges can distribute drugs to the lungs and veins in a controlled manner. Drugs encapsulated within nanosponge pores are protected from premature degradation and their stability is improved[2].

This little sponge circulates around the tumor cell until it reaches the surface, where it releases its drug cargo in a steady stream.

Nanosponge is three to five times more effective than direct injection at slowing tumor growth. The drug is released at the tumor rather than circulating broadly throughout the body, and it is more effective for a given dosage, according to nanosponges targeted delivery systems. Nanosponges have a number of advantages, including fewer adverse side effects due to the fact that lower amounts of the drug will come into touch with healthy tissue[3].

Nanoparticles vs. Nanosponges: What's the Difference?

The difference in porosity and size is the fine line that separates nanoparticles from nanosponges. Nanoparticles are measured in nanometers, while nanosponges have pores measured in nanometers. Their overall size can range from micrometers to micrometers, but they are usually less than 5m. Nanosponges have been described as nonporous nanoparticles / microparticles onnumerous occasions.

Because they contain both hydrophobic and hydrophilic groups, nanosponges have a variety of domains in their structure.

NANOSPONGES HAVE MANY

BENEFITS

1. As nanosponges are amphiphilic, they can transport both hydrophobic molecules in the hydrophobic cavity and hydrophilic molecules in the gaps between the hydrophobic moieties at the same time. Drugs that are hydrophobic can be loaded into the nanosponge structure to boost their solubility.
2. Nanosponges have the ability to deliver controlled and predictable drug release.
3. Nanosponges can be identified with specific linkers to target diseased cells, resulting in improved efficacy while lowering adverse effects, lowering dose and dosing frequency, and increasing patient compliance.
4. Nanosponges can dramatically reduce medication irritation while maintaining efficacy.
5. Natural biodegradability and adaptability for commercialmanufacturing
6. They are employed as a transport fluid when mixed with water. They can be used to cover up bad tastes.
7. The main disadvantage is the ability of these nanosponges to include just tiny molecules is their only drawback.

NANOSPONGE CHARACTERISTIC FEATURES

- By altering the crosslinker topolymer ratio, nanosponges of a certain size can be created.
- They are nontoxic, porous particles that are insoluble in most organic solvents and can withstand temperatures of up to 3000°C. They are stable at pH levels ranging from 1 to 11.
- They float in water in a clear, opalescentsuspension.
- They can be recreated using simple thermal desorption, solvent extraction, microwaves, and ultrasounds.
- Their three-dimensional structure allows them to catch, transport, and release a variety of chemicals selectively.
- Chemical linkers allow nanosponges to bind to the target location moreeffectively.
- Nanosponges can produce inclusion and non-inclusion complexes by combining with certain drugs.
- Magnetic properties can be imparted to nanosponges by introducing magnetic particles to the reactionmixture.

POLYMERS USED IN THE MAKING OF NANOSPONGES:

In order to make nanosponges, a variety of polymers and cross linkers are used.

Hyper cross-linked polystyrenes, cyclodextrins, and their derivatives such as Alkyloxy carbonyl Cyclodextrins, Methyl- Cyclodextrin, and Hydroxy Propyl- Cyclodextrins are examples of polymers.

Poly(valerolactoneallylvalerolacton e), Poly (valerolactoneallylvalero- lactone oxepanedione), Ethyl Cellulose, Poly vinyl alcohol are copolymers.

Carbonyl diimidazoles, Carboxylic acid dianhydrides, Diarylcarbonates, Dichloromethane, Diisocyanates, Diphenyl Carbonate, Epichloridine, Glutaraldehyde, Pyromellitic anhydride, 2,2-bis (acrylamido)Acetic acid, Epichloridine, Gluteraldehyde, Pyromellitic anhydride, Pyromellitic anhydride, Pyromellitic[8,9].

METHODOLOGY

Lansoprazole nanospongespreparation

Different methods were used to make lansoprazole nanosponges.

Pluronic, ethyl cellulose, and polyvinyl alcohol proportions. Using the emulsion solvent diffusion technique, F68 was created. The scattered phase containing 100 mg lansoprazole and a series of steps 30 mL of ethyl cellulose dissolved in a quantity of ethyl cellulose (Table 1). A specific amount of dichloromethane was gently added to a specific amount of water. In 100 mL of aqueous continuous phase, dissolve PVA. The combination. A magnetic stirrer was used to agitate the mixture for two hours at 1000 rpm. The lansoprazole nanosponges that had developed were collected. Vacuum filtering and drying in a 400°C oven for 24 hours[5,10].

Percentage Yield:

After drying, the lansoprazole nanosponges were weighed. The following formula was used to determine the percentage yieldvalue: Weight ofnanosponges/Total solids weightEquals percent yield

Efficiency of entrapment:

The entrapment effectiveness of lansoprazole nanosponges was calculated using a UV spectrophotometric technique.

	F1	F2	F3	F4	F5	F6
Lansoprazole (mg)	100	100	100	100	100	100
Polyvinyl alcohol (mg)	600	800	900	1000	1100	1200
Ethyl cellulose (mg)	400	600	800	1000	800	600
Pluronic F68 (mg)	200	200	200	200	200	200
Dichloromethane (mL)	30	30	30	30	30	30
Distilled water (mL)	100	100	100	100	100	100

At 293 nm, a calibration curve for lansoprazole in methanolic HCl was plotted in the range of 3-18 g/mL (Beer's Lambert's range). The concentration of lansoprazole and its absorbance had an excellent linear relationship[11]

(r2=0.9993, m=0.0469, n=3). Each batch was given 100 mg of lansoprazole nanosponges, which were powdered in a mortar and dissolved in 100 mL of methanolic HCl. After centrifuging at 1000 rpm for 30 minutes, lansoprazole was extracted, filtered, and the concentration was calculated using calibration curve data. Percentage entrapment was calculated as follows: % Entrapment efficiency= Actual drug contentin the nanosponge×100/Theoretical drug content.

Particle size measurement

The average particle size of lansoprazole nanosponges were determined by photon correlation spectroscopy (PCS) using a Nano ZS-90 (Malvern Instruments limited, UK) at a fixed angle at 25° . Sample was diluted 10 times with distilled water and then it was analysed for particle size[5,11].

Zeta potential:

The zeta potential was measured for the determination of the movement velocity of the particles in an electric field and the particle charge. In the present work, the nanosponges was diluted 10 times with distilled water and analysed by Zetasizer using Laser Doppler Micro electrophoresis (Zetasizer nano ZS, Malvern instruments Ltd., UK)[5,11.]

Table 1. Composition of lansoprazole nanosponges

Table 2. formulation of lansoprazole tablets

Ingredient	Quantity (mg)
Nanosponges (F2)	35 (equivalent to 30 mg of lansoprazole)
Microcrystalline cellulose	60
Magnesium stearate	5

Table 3. Evaluation parameters of lansoprazole nanosponges

	Percentage Yield	Entrapment efficiency	Particle size (nm)	Zeta Potential (mV)
F1	38.35±1.27	50.71±0.73	190.69	-4.9
F2	59.57±1.09	86.93±0.65	83.4	-5.2
F3	34.68±1.17	79.57±1.01	103.26	-5.6
F4	28.24±0.97	78.04±1.62	114.91	-6.1
F5	33.31±2.1	70.31±0.94	135.33	-5.3
F6	24.8±1.73	69.47±1.2	173.27	-5.2

(Mean ± SD, n=3)

Table 4. Evolution of lansoprazole tablets

Formulation	Weight variation	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Assay (%)
F1	Complies	3.18±0.14	5.66±0.29	0.886	99.93±1.16
F2	Complies	3.23±0.11	5.65±0.2	0.752	99.47±1.81
F3	Complies	3.09±0.17	5.72±0.15	0.892	98.18±1.43
F4	Complies	3.21±0.09	5.81±0.1	0.836	99.97±1.97
F5	Complies	3.27±0.21	5.9±0.21	0.811	99.01±2.13
F6	Complies	3.15±0.12	5.83±0.07	0.798	98.43±1.73

Particle shape and morphology:

Scanning electron microscopy was used to analyse the morphology and form of nanosponges (LEO 440I). a sample of was held in a vacuum and was deposited on a glass slide. The Using a thin gold/palladium coating, samples were coated. A coater for sputtering. SEM stands for scanning electron microscope. Operated with a 15 kV acceleration voltage[12].

Fourier transform infrared spectroscopy studies:

The Perkin Elmer Model 1600 was used to perform the FTIR spectrum observations at room temperature (USA). Samples were dissolved in KBr powder, and then pellets were formed under pressure of 5 tonnes. Powder diffuse reflectance on an FTIR spectrophotometer was used to obtain FTIRspectra[12].

Differential scanning calorimetric studies:

Studies using the differential scanning calorimeter (DSC-60; Shimadzu Corporation, Japan) were done to determine whether a medicine will work with certain types of polymers. Samples (3-5 mg) were heated (range 50-400 0C, 10 0C/min) in crimped aluminium pans in a nitrogen environment using a DSC after calibration with Indium and lead standards. Automatic results were calculated for the melting point and enthalpy of fusion[12].

Preparation of lansoprazole tablets:

Lansoprazole tablets were prepared by direct compression method. The prescribed quantity of lansoprazole nanosponges, polymers and excipients (Table 2) were mixed homogeneously and the mixture was then compressed into tablets (100 mg) using an 8 mm, biconcave punches on a 'Rimek mini press 16 station rotary compression machine[13].

Evaluation of lansoprazole tablets: Weight

variation:

The weight variation test was performed according to specifications given in the Indian Pharmacopoeia on 20 tablets. The maximum acceptable limit is ±7.5% deviation of an individual weight from average weight.

Thickness:

The thickness of 20 randomly selected tablets from each formulation was determined in mm using a vernier calliper (Pico India).

Hardness:

Twenty tablets were randomly selected from each formulation and measured hardness in kg/cm2 using Monsanto type hardness tester.

Friability:

Tablet friability was measured using the Roche Friabilator. Randomly selected twenty pre-weighed tablets were placed in the apparatus and operated for 100 revolutions and then the tablets were reweighed. The friability was determined as the mass loss in percent according to following to Equation F= (WA-WB/WA) ×100 Where F: Friability, WA: Initial weight (gm), WB: Final weight (gm); the acceptable limits of the weight loss should not be more than 1%.

Assay:

Ten tablets were randomly selected from each formulation and crushed to a fine powder in mortar with pestle. Weigh accurately equivalent to 10 mg of lansoprazole from fine powder then transfer in 100 mL volumetric flask, 100 mL of methanolic HCL was added to dissolve and sonicated for 20 minutes. Lansoprazole was extracted by centrifuging at 1000 rpm for 30 min. The samples were filtered, diluted and analysed UV spectrophotometrically at 239 nm.

Enteric coating of lansoprazole tablets:

Enteric coating of optimized lansoprazole tablets was done to protect the drug in acidic environment. Coating solution was prepared by dissolving 5% w/v of cellulose acetate phthalate and 1.5% w/v of propylene glycol 400 in acetone. Coating solution was applied by dip coating technique using pipette (10 mL) attached to vacuum pump. Vacuum pump produced suction force that allowed tablet to adhere to pipette mouth. This adhered tablet was then partially dipped in coating solution to allow coat formation at one side of tablet[14].

The other side was coated when other side dried.

In vitro release studies (15,16):

A calibration curve was plotted for lansoprazole in pH 1.2 and pH 6.8 buffers in the range of 3-18 µg/mL (Beer's Lambert's range) at 306 nm and 285 nm respectively. A good linear relationship was observed between the concentration of lansoprazole and its absorbance in pH 1.2 buffer (r2=0.9987, m=0.0089, n=3) and pH 6.8 buffer (r2=0.9979, m=0.0189, n=3).

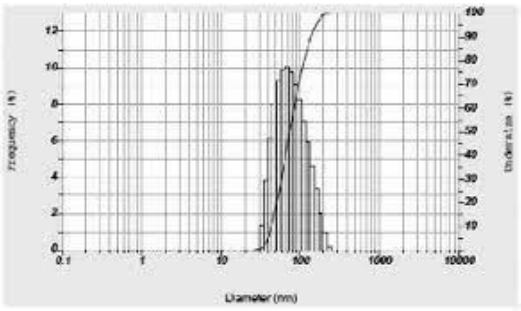

Fig1.Particle size of lansoprazole nanosponges(F2)

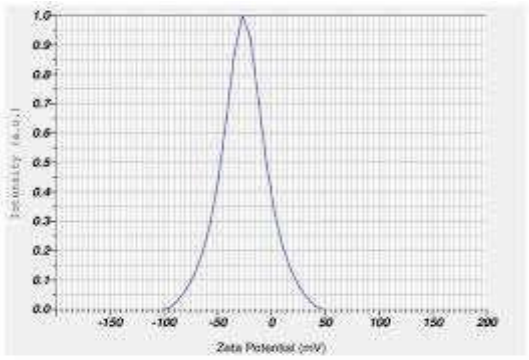

Figure 2. zeta potential of lansoprazole nanosponges(F2)

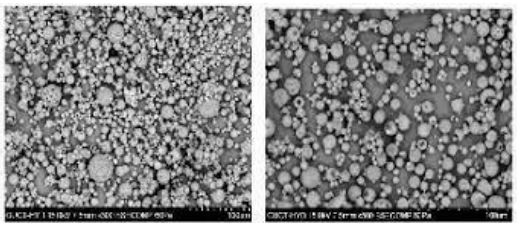

Fig 3. scanning electron micro graph of lansoprazole nanosponges

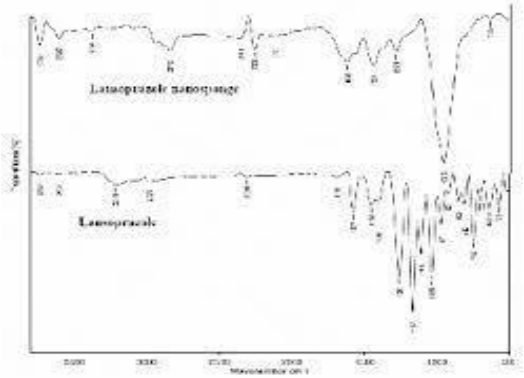

Fig 4. FTIR spectra of lansoprazole and lansoprazole nanosponges

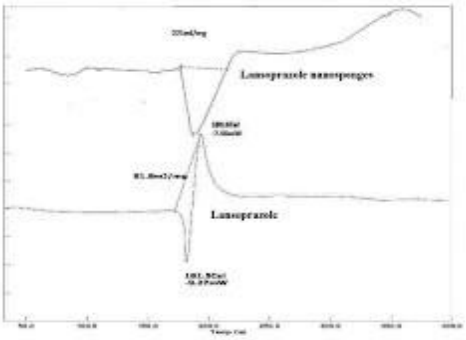

Fig 5. DDSC thermograms of lansoprazole and lansoprazole nanosponges

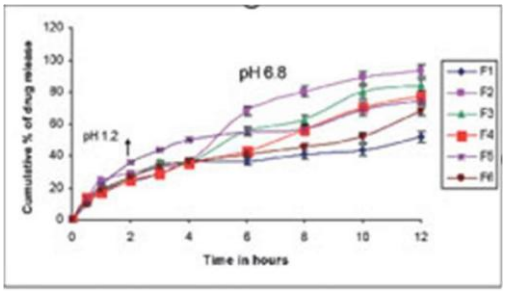

Fig 6. Invitro release profiles of lansoprazole nanosponges

Evaluation of release kinetics (17-20):

To investigate the mechanism of lansoprazole release from nanosponges and enteric coated tablets, the release data was analysed for zero order, first order, Higuchi model and Korsmeyer-Peppas model. The data was presented in the following graphical representation and regression analysis was performed.

Mt versus t (zero order)

Log cumulative % of drug remained versust (first order)

Mt versus square root of t (Higuchi)

Log Mt versus log t (Korsmeyer-Peppas) Mt is the cumulative % of drug released/permeated at time t. Korsmeyer et al (20) derived a simple relationship which described drug release from a polymeric system.

$Mt/M\infty = kt^n$

Where, $Mt/M\infty$ is the fraction of drug released at time t, k is the rate constant and n are the release exponent. Release curve where $Mt/M\infty < 0.6$ was used to determine the exponent 'n' value. The n value was used to characterize different release mechanisms. For example, n = 0.45 for Case I or Fickian diffusion, $0.45 < n < 0.89$ for anomalous behaviour or non-Fickian transport, n=0.89 for Case II transport, and $n > 0.89$ for Super Case II transport. Fickian diffusional release occurs by the usual molecular diffusion of the drug due to a chemical potential gradient. Case II relaxational release is the drug transport mechanism associated with stresses and state-transition in hydrophilic glassy polymers, which swell in water or biological fluids. This term also includes polymer disentanglement and erosion. The rate constant 'k', coefficients of correlation (r2) and 'n' of each model

were calculated by linear regression analysis.

Results and discussion

Table 2 displays the percentage yield value, drug entrapment effectiveness, particle size, and zeta potential of lansoprazole nanosponges.

Percentage yield value of nanosponges was found to be best for F2. Further increasing the concentration of polymer, the % yield was found to be decreased due to the sticky nature of the product which cannot be filtered. The entrapment efficiency of nanosponges was found to be best for formulation F2. Further increasing the concentration of the polymer, entrapment efficiency was found to be decreased due to low solubility of polymer in aqueous phase (22,23). The size of the nanosponges was found to be in the range 83.4 nm to 190.69 nm (Table 3 and Figure 1). The zeta potential of the nanosponges was found to be in the range -4.9 mV to -5.6 mV (Table 3 and Figure 2). The negative sign indicates the stability of nanosponges.

The lansoprazole nanosponges' SEM pictures were seen in Figure 3. SEM investigation showed that the particles were small, round, and had many pores on their surface. (Nanosponges of lansoprazole). The pores are internally tunnelled. This could result from the dichloromethane's migration from the of the nanosponges' surface (5).

Figure 4 displays the FTIR spectra of both pure lansoprazole and lansoprazole nanosponges. The distinctive absorption peaks of pure lansoprazole were seen in the FTIR spectra at 3608 cm for N-H stretching, 2976 cm for aromatic C-H stretching, 2308 cm for aromatic C-N stretching, 1577 cm for C=C stretching, and 1261 cm for S=O stretching. Additionally, lansoprazole nanosponges displayed nearly identical absorption peaks, demonstrating their high compatibility with polymers.

Pure lansoprazole's DSC thermogram displays a prominent peak at 181.50C, which corresponds to its melting point (Figure 5). Lansoprazole nanosponge demonstrated a comparable endothermic peak at 180.80C, indicating there was no drug-polymer interaction.

Weight variation, hardness, friability, thickness, and in vitro dissolving investigations were performed on the enteric coated tablets. All of the tablets had an average weight of 101.272.78. All tablets' deviations were discovered to be within the acceptable range. Therefore, all formulas met the official requirements for weight uniformity and passed the test. The tablets' thickness was determined to be 3.37 mm plus 0.21 mm. The tablets' hardness was determined to be 5.7 0.10 kg/cm2. The percentage of tablets that were friable was 0.89, or less than 1 percent, showing that the friability was within the allowed range. All of the tablets had favourable characteristics and met the I.P. requirements for weight fluctuation, hardness, and friability. No medication was released from a lansoprazole enteric-coated tablet into an acidic media. which is desirable and, after 24 hours, 94.243.02 percent (Figure 7). The profile of the release of the plot indicated that the zero-order kinetic model may best describe the kinetics of lansoprazole enteric coated tablets. (r2=0.981) Linearity 0.071 is the release exponent (n) value The release

from coated pills, as seen in (Table 5) Fickian release, which is a release that is always accompanied with diffusion process (20)

CONCLUSION

The lansoprazole-containing nanosponges displayed the majority of the optimal qualities needed for an oral controlled release dosage form. It has become possible to create nanosponges with a smaller particle size of 83.4 nm thanks to a negatively charged surface charge. Continuous regulated release up to 12 hours was suggested by the release profile. For a period of 24 hours, lansoprazole enteric coated tablet demonstrated controlled release behaviour by not releasing the medicine into an acidic milieu, which is desirable. It has been discovered that the nanosponge systems have good potential for sustained medication release, which can consequently be advantageous, such as dose reduction, decreased administration frequency, and avoiding systemic adverse effects related to. Therefore, it might be said the oral enteric coated tablet—nanosponges—was developed is considered to be perfect and efficient in the treatment of gonorrhoea and associateddiseases.

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