ABSTRACT
Objective: Nanosponges are tiny sponges with an average diameter below 1μm and consist of cavities filled with drug molecules. Lansoprazole is one of the classes of proton pump inhibitors, it reduces gastric acidity, and used in disorders such as gastric ulcer, duodenal ulcer and reflux oesophagitis.

Methods: In present study for extended delivery of lansoprazole at optimal concentration and to reduce the frequency of dosing and thus to increase patient convenience nanosponges loaded extended release tablets were prepared. Initially four different nanosponges formulations were prepared by solvent evaporation method and evaluated on various parameters. Ethyl cellulose was used as entrapping agent and dichloromethane as cross linking agent in various proportions and evaluated for powder flow properties, % yield, zeta potential, and in-vitro drug release characteristics. All five formulations were evaluated for thickness, hardness, friability, % drug content and in-vitro drug release.

Results: The % drug entrapment efficiency of the nanosponges was found to be best for the formulation NS1 and it was ranged from 68.86±0.10 to 88.66±0.5

Conclusion: From the results, it was found that all the evaluation results are within pharmacopoeial limits. From this study, we concluded feasibility of extended release of Lansoprazole through nanosponge loaded extended release tablets. Formulation of batch NT1, containing HPMC K30 was found to be optimum formulation.

Keywords: Entrapment efficiency, ethyl cellulose, HPMC, in-vitro drug release, lansoprazole, nanosponges.
poor aqueous solubility and bioavailability. Regular usage of lansoprazole causes various adverse effects like abdominal pain, diarrhoea, skin rashes, thrombocytopenia, impotence etc. So, controlled delivery of lansoprazole at optimal concentration may be required. Controlled release of lansoprazole will reduce the frequency of dosing and dose size and may increase patient convenience. Since oral route is preferred than other routes with respect to safety, comfort and reliability.

So the aim of the present study was to develop extended release tablets of lansoprazole nanosponges to deliver at controlled rate to its absorptive site, to reduce the frequency of administration and thus to improve patient compliance.

MATERIALS AND METHODS
Lansoprazole was obtained from Abumec Pharmaceuticals Ltd, Kaduna State. Ethyl cellulose, Polyvinyl alcohol, was obtained from AC Drugs Limited, Enugu State and Dichloromethane, HPMC K30, chitosan were obtained from Afrik Pharmaceuticals Plc, Awo-Omamma. Magnesium stearate, Talc and MCC pH 102 were procured from Avro Pharma Limited, Lagos Nigeria.

Drug-excipient compatibility studies
Fourier transform infrared analysis was conducted to verify the possibility of interaction of chemical bonds between drug and polymers. Samples were scanned in the range from 400-4000 cm⁻¹ and carbon black reference. The detector was purged carefully by clean dry helium gas to increase the signal level and reduce moisture.

Preparation of Lansoprazole nanosponges
Lansoprazole nanosponges were prepared by the emulsion solvent evaporation method by the use of different proportions of polymers and polyvinyl alcohol. Ethyl cellulose was used as entrapping agent and dichloromethane as cross linking agent in various proportions. The disperse phase containing Lansoprazole as a dispersing medium and polymer in 20ml of dichloromethane was added slowly to a definite amount of Poly vinyl alcohol in 100mL of aqueous continuous phase with 1000 rpm stirring speed using magnetic stirrer for 2hrs. The formed nanosponges were collected by filtration and dried in oven at 40°C for 24hrs and packed in vials. The prepared Nanosponges formulations with three different polymers are listed in Table 1.

Table 1: Formulation of Lansoprazole nanosponges.

<table>
<thead>
<tr>
<th>Batch</th>
<th>Drug (mg)</th>
<th>Ethyl cellulose (mg)</th>
<th>Polyvinyl alcohol (gm)</th>
<th>Dichloromethane (ml)</th>
<th>Distilled water (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS1</td>
<td>50</td>
<td>100</td>
<td>2</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td>NS2</td>
<td>100</td>
<td>200</td>
<td>3</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td>NS3</td>
<td>150</td>
<td>300</td>
<td>4</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td>NS4</td>
<td>200</td>
<td>400</td>
<td>3</td>
<td>30</td>
<td>20</td>
</tr>
</tbody>
</table>

Evaluation of nanosponges micrometric properties
Angle of repose, Bulk density, Tapped density, Hausner’s ratio and Carr’s index were determined to assess the flow ability of the prepared nanosponges powder.

Determination of percentage yield
It was calculated accurately by using the weight of final product after drying with respect to the initial total weight of the drug and polymer used for preparation of nanosponges.

\[
\text{% yield} = \frac{\text{Practical weight of nanosponges obtained}}{\text{Theoretical weight (drug + polymers)}} \times 100
\]

Determination of entrapment efficiency
Nanosponges equivalent to 100 mg of the drug were taken and then crushed into powder followed by transferred into a 100 ml volumetric flask consist of 10ml of methanol and the volume was made up with simulated gastric fluid of pH 1.2. After 24 h, the solution was filtered through Whatmann filter paper and the absorbance was measured spectrophotometrically after suitable dilutions.
Zeta Potential determination
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 were mixed thoroughly by batch direct compression method. Five different extended release tablets formulations were prepared with varying concentrations of polymers by direct compression method. HPMC K30 and chitosan were used as polymers, talc as lubricant and magnesium stearate acts as glidant and microcrystalline cellulose was used as a directly compressible binder. Compositions of different formulations were given in Table 3. Lansoprazole nanosponges and all other ingredients were individually passed through sieve number #60 and all the ingredients were mixed thoroughly by triturating up to 15 min followed by lubricated with talc. Finally the lubricated mixture was subjected to direct compression by using RIMEK rotary tablet punching machine.

**Table 3: Formulation of nanosponges loaded extended release tablets of Lansoprazole.**

<table>
<thead>
<tr>
<th>Batch</th>
<th>Nanosponges (mg)</th>
<th>HPMC K30 (mg)</th>
<th>Chitosan (mg)</th>
<th>Magnesium Stearate (mg)</th>
<th>Talc (mg)</th>
<th>Microcrystalline cellulose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT1</td>
<td>200</td>
<td>75</td>
<td>-</td>
<td>5</td>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>NT2</td>
<td>200</td>
<td>50</td>
<td>-</td>
<td>5</td>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>NT3</td>
<td>200</td>
<td>25</td>
<td>20</td>
<td>5</td>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>NT4</td>
<td>200</td>
<td>-</td>
<td>50</td>
<td>5</td>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>NT5</td>
<td>200</td>
<td>-</td>
<td>75</td>
<td>5</td>
<td>3</td>
<td>60</td>
</tr>
</tbody>
</table>

**Table 2: Preformulation parameters of Lansoprazole nanosponges**

<table>
<thead>
<tr>
<th>Batch</th>
<th>Tapped density (gm/cm³)</th>
<th>Carr’s Index</th>
<th>Hausner’s Ratio</th>
<th>Angle of repose (°)</th>
<th>% yield</th>
<th>% Drug entrapment efficiency</th>
<th>Zeta Potential (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS1</td>
<td>0.53±0.12</td>
<td>0.58±0.09</td>
<td>8.61±0.13</td>
<td>1.09±0.06</td>
<td>97.35±0.100</td>
<td>89.43±0.09</td>
<td>-6.1</td>
</tr>
<tr>
<td>NS2</td>
<td>0.49±0.08</td>
<td>0.54±0.11</td>
<td>9.25±0.08</td>
<td>1.04±0.05</td>
<td>81.43±0.120</td>
<td>86.25±0.13</td>
<td>-5.2</td>
</tr>
<tr>
<td>NS3</td>
<td>0.51±0.06</td>
<td>0.56±0.09</td>
<td>8.92±0.06</td>
<td>1.09±0.03</td>
<td>85.41±0.090</td>
<td>81.42±0.08</td>
<td>-5.6</td>
</tr>
<tr>
<td>NS4</td>
<td>0.55±0.04</td>
<td>0.60±0.06</td>
<td>8.33±0.14</td>
<td>1.08±0.04</td>
<td>90.37±0.060</td>
<td>85.43±0.05</td>
<td>-5.9</td>
</tr>
</tbody>
</table>

**EVALUATION OF TABLETS**

**Post compression studies**
The manufactured nanosponges loaded tablets were subjected to weight variation, hardness (Pfizer hardness tester), thickness (Vernier Calipers) and friability (Roche) studies according to the standard procedures.

**Drug content**
Ten tablets were weighed, finely powdered and triturated equivalent to 10 mg of the drug was accurately weighed, dissolved in pH 1.2 buffer and volume was made up to 100 ml with the same buffer. Further dilutions were done to get concentration of 10µg/ml and absorbance was read at 236 nm against blank by UV Visible spectrophotometer.

Figure 2: Dissolution profiles of nanosponges formulations
RESULTS AND DISCUSSION

The present study was aimed for developing Lansoprazole nanosponges loaded extended release tablets using various polymers and excipients. In present study four nanosponges formulations were prepared. Excipients compatibility studies were performed by FT-IR spectroscopy (Figure 1). No significant shifting of the peaks, so polymers used in the study are suitable for the development of Lansoprazole nanosponges formulations.

![Figure 3: In-vitro drug release profiles of nanosponges loaded extended release tablets of Lansoprazole](image)

Percentage yield value of nanosponges was found to be the best for NS1 i.e. 97.35±0.08. It was observed that as the polymer ratio in the formulation increases, the percentage yield also increases. The low percentage yield in some formulations may be due to wastage of the drug-polymer solution.

Table 4: Results of post compression parameters of nanosponges loaded extended release tablets of Lansoprazole

<table>
<thead>
<tr>
<th>Batch</th>
<th>Weight variation (mg)</th>
<th>Hardness (kg/cm²)</th>
<th>Thickness (mm)</th>
<th>Friability</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT1</td>
<td>336±0.38</td>
<td>4.8±0.09</td>
<td>3.49±0.09</td>
<td>0.48±0.09</td>
</tr>
<tr>
<td>NT2</td>
<td>318±0.45</td>
<td>4.7±0.12</td>
<td>3.28±0.11</td>
<td>0.33±0.12</td>
</tr>
<tr>
<td>NT3</td>
<td>310±0.61</td>
<td>4.2±0.13</td>
<td>3.31±0.05</td>
<td>0.46±0.15</td>
</tr>
<tr>
<td>NT4</td>
<td>318±0.28</td>
<td>4.9±0.25</td>
<td>3.48±0.18</td>
<td>0.42±0.08</td>
</tr>
<tr>
<td>NT5</td>
<td>342±0.39</td>
<td>4.1±0.09</td>
<td>3.86±0.08</td>
<td>0.41±0.14</td>
</tr>
</tbody>
</table>

The % drug entrapment efficiency of the nanosponges was found to be best for the formulation NS1 and it was ranged from 68.86±0.10 to 88.66±0.5 and the results indicated that the ethyl cellulose concentration is directly proportional to the entrapment efficiency but polyvinyl alcohol concentration is indirectly proportional to the entrapment efficiency which is due to the low solubility of polymer in aqueous phase (Table 2). The surface charge of nanosponges was determined by zeta potential and it was found to be in the range of 5.2-6.1mv (+30mv). The in-vitro drug release studies of Lansoprazole nanosponges were performed for all the 4 formulations by using USP Type-II i.e. paddle. All the formulations showed drug release for a period of 8h (Figure 2). Among all the formulations NS1 has shown highest percentage of drug release i.e., 98.35% at the end of 8 h. From the results of evaluation parameters, formulation NS1 has shown acceptable results and hence, it was selected for further studies. Five different Lansoprazole nanosponges loaded extended release tablets were prepared using HPMC K30 and chitosan and evaluated for flow properties and in-vitro drug release studies.

The powder blend was subjected to pre-compression studies and obtained results were complied with the pharmacopeial limits (Table 4). The in-vitro drug dissolution studies of nanosponges loaded extended release tablets were performed by taking USP dissolution apparatus-II. In 10 hrs studies, the cumulative percentage drug release was found to be in the range of 42.58±0.09 to 74.81±0.12. Maximum release was shown by the formulations of batch NT1. This may be due hydrophilic nature of HPMC.

CONCLUSION

In present study nanosponges loaded extended release tablets of Lansoprazole showed extended drug release for about 10 h. On the basis of different parameters it is concluded that the nanosponges formulations of batch NS1 and nanosponges loaded extended release tablets of batch NT1 are the optimum formulations. Study concluded that prolonged drug release and nanosponges loaded extended release tablets of Lansoprazole are suitable option for dose reduction, reduced frequency of administration and avoiding related systemic side effects. However further in-vivo study is needed for further estimation of importance of these formulations.

AUTHOR’S CONTRIBUTION

All authors have worked equally for this work.

CONFLICT OF INTEREST

Authors have declared that no conflict of interest is linked with this work.

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