PRONIOSOMES FORMULATION AND EVALUATION BY SLURRY METHOD AS AN EMERGING PROVESICULAR DRUG CARRIER IN NDDS.

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ABSTRACT

The purpose of this research was to formulate and evaluate Gliclazide loaded maltodextrin based proniosomes for oral route administration. For stabilizing niosomal drug delivery system without affecting its properties of merits have resulted in the development of the promising drug carrier “Proniosomes”. Proniosomes is a dry formulation using suitable carrier coated with non-ionic surfactants and can be converted into niosomes immediately before use by hydration. These proniosome-derived niosomes are as good as or even better than conventional niosomes. Gliclazide loaded Maltodextrin, Mannitol and Sorbitol based proniosomes were prepared by slurry method with different surfactant to cholesterol ratio. The proniosome formulations were evaluated for FT-IR study, angle of repose and scanning electron microscopy and other evaluation parametrs. The niosomal suspensions were further evaluated for entrapment efficiency, In-vitro release study, Kinetic data analysis, Stability study. The result from SEM analyses has confirmed the coating of surfactant on the surface of carrier. The formulation based maltodextrin showed higher entrapment efficiency of 82.64 ± 1.25 and In-vitro release of 98% at the end of 24hr was found to be best among the various formulations. The proniosome formulations were evaluated for FT-IR study, angle of repose and scanning electron microscopy and the result showed that the maltodextrin based formulation was best.
suited. Release was best explained by the zero order kinetics. Kinetic analysis shows that the
drug release follows super case II transport diffusion. Maltodextrin based Proniosome
formulation has showed appropriate stability for 90 days when compared with other carriers
reconstituted niosomes by storing the formulation at refrigerator condition.

**KEYWORDS:** Gliclazide, Proniosomes, Maltodextrin, Mannitol, Sorbitol, Span-40, FT-IR,
and SEM.

**INTRODUCTION**
The main aim of this study was to formulate and evaluate the controlled release gliclazide
loaded maltodextrin based proniosomes. The purpose of present work is to made stabilized
proniosome, since these stabilized form proniosome has got various advantages over
conventional dosage form. There is requirements to improve more efficacy with respect to its
Bioavailability, drug release, physical stability, to reduce side effects and toxicity, other reasons
are summarized as following.

- Proniosomal carrier provides sustained release of drug and hence reduces the iv/oral
dosing frequency which in turn results into better patient compliance.
- To maintain the concentration of the release drug within a therapeutic range for extended
period of time.
- Gliclazide is an oral hypoglycaemic drug having short biological half-life and poor
bioavailability make gliclazide an ideal candidate for sustained released, therefore
designing of a proniosomal formulation will result into improved solubility and
bioavailability of drug.
- It can also be given to diabetic patient because maltodextrin is non sweet polysaccharide
i.e. beneficial for the patient of heart and sugar.
- The aim of the present study is to design and develop a oral proniosomal powder i.e. to
develop a vesicular drug carrier technology to an antidiabetic drug Gliclazide, using
maltodextrin as polymer by slurry method.
- The controlled release proniosome formed are so designed that they release the
medicament over a prolong period of time and being a surfactant and cholesterol based
vesicular system it avoids the direct contact of drug with stomach layer and hence reduces
the antidiabetic activity. The main objective of the present study are to protect the
sensitive drug from proteolytic degradation in the stomach and large intestine.
To maintain the concentration of the release drug within a therapeutic range for extended period of time.
After oral administration, it undergoes extensive first pass metabolism in the liver.

**Proniosomes as drug carriers:** The proniosomes are promising drug carriers, because they possess greater chemical stability and lack of many disadvantages associated with liposomes. Niosomes have shown advantages as drug carriers such as low cost, low toxicity due to non ionic nature and chemical stability as compared to liposomes but they are associated with problems related to physical stability, such as fusion, aggregation, sedimentation and leakage and storage.

Proniosomes are dry formulations of surfactant coated carrier vesicles which can be measured out as needed and rehydrated by brief agitation in hot water, the resulting niosomes are very similar to conventional niosomes and more uniform in size. Being dry, free flowing product, Proniosomes minimizes stability problems during storage and sterilization and it has additional merits of ease of transfer, distribution, measuring and storage which makes Proniosomes a pronounced versatile delivery system.

**Advantages of proniosomes over the niosomes**
- Avoiding problem of physical stability like aggregation, fusion, leaking.
- Avoiding hydrolysis of encapsulated drugs which limiting the shelf life of the dispersion.
- Ease on storage and handling.

Proniosomes are recent development in Novel drug delivery system. These are most advanced drug carrier in vesicular system which overcomes demerits of liposomes and niosomes such as:

1. Demerits of liposomes includes:
   - Liposomes require special precautions and conditions for formulation and preparations.
   - Complex method for routine and large scale production.
   - Less chemical stability.
   - High cost.

2. Demerits of niosomes includes physical instability such as:
   - Aggregation.
   - Fusion.
   - Leaking of entrapped drug.
Sedimentation.

Above mentioned demerits of physical instability may lead to hydrolysis of the encapsulated drug which affects the shelf life of the dispersion\(^{[1-4]}\) (Roland Bodmeier et al., 1998; Sung-Ho Kim et al., 2002; Chain Y. W. Et al 1992; Brahmankar D.M. et al 1995).

**ADVANTAGE OF PRONIOSOMES OVER THE OTHER VESICULAR SYSTEMS**

- Minimizes the problems of physical stability of niosomes on storage.
- Required no special conditions during their preparation and storage as in case of liposome.
- In aqueous system, liposome have problems regarding degradation by hydrolysis of phospholipids molecules.
- Convenience of storage, transport, and dosing
- More uniform in size.
- Required relatively low cost materials.
- Better size distribution
- More stable.
- Ease of use.

**MATERIALS AND METHOD**

Commonly used materials for proniosomes preparation are \(^{[5]}\) (Hu et al., 1999).

- Surfactants: Span20, Span40, Span60, Span80, Span85, Tween20, Tween40, Tween80
- Stabilizers: Cholesterol, lecithin
- Carriers: Maltodextrin, mannitol, sorbitol, magnesium aluminum silicate, microcrystalline.
- cellulose, spray dried lactose, glucose monohydrate. Etc.

**Summarized as in tabulated form**

**Table no.1: Commonly used materials for proniosomes formulation.**

<table>
<thead>
<tr>
<th>S.NO.</th>
<th>Class</th>
<th>Examples</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cholesterol</td>
<td>Cholesterol</td>
<td>To prevent leakage of drug formulation. Membrane stabilizer.</td>
</tr>
<tr>
<td>2</td>
<td>Lecithin</td>
<td>Lecithin</td>
<td>Act as Penetration enhancer, membrane stabilizer.</td>
</tr>
<tr>
<td>3</td>
<td>Maltodextrin</td>
<td>Maltodextrin</td>
<td>It provides flexibility in</td>
</tr>
</tbody>
</table>
Sorbitol and other component ratio. It alters or changes the drug distribution.

Surfactants Span 20,40,60,80,85, Tween 20,40,80 etc. For increase drug flux rate across the skin.

**METHODOLOGY**

Method of preparations for proniosomes by following method.

**SLURRY METHOD**

By slurry method: Prepared a 250 μmol stock solution of span 40 and cholesterol.

Prepared in chloroform:methanol/methylene chloride solution(2:1) and 10 mg drug Gliclazide was dissolved in it.

Now it was poured in a 100ml Round Bottom Flask (RBF) containing the maltodextrin carrier.

Additional chloroform:methanol solution was added to for slurry in the case of lower surfactant loading.

The flask was attached to a rotary flask evaporator to evaporate solvent at 60-70 RPM, a temperature of 45±2°C and a reduced pressure of 600 mm Hg until the mass in the flask had became a dry free flowing product.

These materials were further dried overnight in a desiccators under vacuum at room temperature.

This dry preparation is referred to as to as proniosomes and was used for preparation and for further study on powder properties.

These proniosomes were stored in a tightly closed container at a refrigerator temperature until further evaluation.\(^6\)\(^7\) (Srivastava AR et al., 2009; Chauhan et al., 1989).
Table no.2 : Composition of proniosomes formulations or batches.

<table>
<thead>
<tr>
<th>Formulation No.</th>
<th>Formulation code</th>
<th>Ratio(μmol)</th>
<th>Surfactant(mg)</th>
<th>Cholesterol(mg)</th>
<th>Carrier(mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Surfactant</td>
<td></td>
<td>Cholesterol</td>
<td></td>
</tr>
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<td>P1</td>
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<td>10</td>
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</tr>
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<td>3</td>
<td>P3</td>
<td>260</td>
<td>60</td>
<td>130</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>P4</td>
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<td>120</td>
<td>40</td>
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<tr>
<td>5</td>
<td>P5</td>
<td>220</td>
<td>100</td>
<td>110</td>
<td>50</td>
</tr>
<tr>
<td>6</td>
<td>P6</td>
<td>200</td>
<td>120</td>
<td>100</td>
<td>60</td>
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<td>8</td>
<td>P8</td>
<td>160</td>
<td>160</td>
<td>80</td>
<td>80</td>
</tr>
</tbody>
</table>

Table no.3: Solvents ratio

<table>
<thead>
<tr>
<th>S.NO</th>
<th>Chloroform(ml)</th>
<th>Methanol(ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>6</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

IN-VITRO STUDY
Some evaluation parameters are as follows

1. Measurement of Angle of repose
The angle of repose of dry proniosomes powder was measured by a funnel method. The proniosomes powder was poured into a funnel which was fixed at a position so that the 13 mm outlet orifice of the funnel is 5 cm above a level black surface. The powder flows down from the funnel to form a cone on the surface and then the angle of repose was calculated by measuring the height of the cone and the diameter of its base (Chandraprakash et al., 1990).

2. Scanning Electron Microscopy (SEM)
The particle size of proniosomes powder is a very important characteristic. The surface morphology (such as roundness, smoothness, and formation of aggregates) and the size distribution of proniosomes particles were studied by Scanning Electron Microscopy (SEM). Proniosomes were sprinkled on to the double-sided tape that was affixed on aluminium stubs. Now the aluminum stub was placed in the vacuum chamber of a scanning electron microscope (XL 30 ESEM with EDAX, Philips, Netherlands). The samples were observed
for morphological characterization using a gaseous secondary electron detector (working pressure: 0.8 torr, acceleration voltage: 30.00 KV) XL 30, (Philips, Netherlands) (Chandraprakash et al., 1990).

3. Optical Microscopy
The proniosomes or niosomes were mounted on glass slides and viewed under a microscope (Medilux-207RII, Kyowa-Getner, Ambala, India) with a magnification of 1200X for morphological observation analysis after suitable dilution. The photomicrograph of the preparation also obtained from the microscope by using a digital SLR camera (Chandraprakash et al., 1990).

4. Entrapment efficiency
Proniosomes entrapped gliclazide was estimated by dialysis method. The prepared proniosomes derived niosomes were placed in the dialysis bag 50 (presoaked for 24 hrs). Free gliclazide was dialyzed for 30 minutes each time in 100 ml of phosphate buffer saline pH 7.4. The dialysis of free gliclazide always completed after 12-15 changes, when no gliclazide was detectable in the recipient solution. The dialyzed gliclazide was determined by finding out the concentration of bulk of solution by UV spectrophotometer at 228.5 nm. The samples from the bulk of solution diluted appropriately before going for absorbance measurement. The free gliclazide in the bulk of solution gives us the total amount of un-entrapped drug. Encapsulation efficiency is expressed as the percent of drug trapped.

\[
\% \text{ Entrapment} = \frac{\text{Total drug} - \text{Unentrapped drug}}{\text{Total drug}} \times 100
\]

5. Measurement of Vesicle Size
The vesicle dispersions were diluted near about 100 times in the same medium used for their preparation. Vesicle size was measured on a particle size analyzer (Laser diffraction particle size analyzer, Sympatec, Germany). The apparatus consists of a He-Ne laser beam of 632.8 nm focused with a minimum power of 5mW using a Fourier lens [R-5] to a point at the centre of multielement detector and a small volume sample holding cell (Su cell). Hu C. and Rhodes in 1999 reported that the average particle size of proniosomes derived niosomes is approximately 6\(\mu\)m while that of conventional niosomes is about 14\(\mu\)m\(^{8,9}\) (Chandraprakash et al., 1990 & Vora et al., 1998). In-vitro drug release study can be done by Dialysis tubing, Reverse dialysis, Franz diffusion cell method.
6. Dialysis Tubing
According to Muller et al in 2002 studied in-vitro drug release could be achieved by using the dialysis tubing. The proniosomes is placed in prewashed dialysis tubing which can be hermetically sealed. The dialysis sac is then dialyzed against a suitable dissolution medium at room temperature; the samples were withdrawn from the medium at suitable intervals of time, centrifuged and analysed for drug content using suitable method (U.V. spectroscopy, HPLC etc). The maintenance of sink condition is essential\[10,11\] (Puglia et al., 2004 & Muller et al., 2002).

7. Reverse dialysis
In this technique a number of small dialysis as containing 1ml of dissolution medium are placed in proniosomes. The proniosomes are then displaced into the dissolution medium. The direct dilution of the proniosomes is possible with this method; however the rapid release cannot be quantified using this method (Muller et al., 2002).

8. Franz Diffusion Cell
The in-vitro diffusion studies can be performed by using Franz diffusion cell. Proniosomes was placed in the donor chamber of a Franz diffusion cell fitted with a cellophane membrane. The proniosomes was then dialyzed against a suitable dissolution medium at room temperature; the samples were withdrawn from the medium at suitable intervals, and analysed for drug content using suitable method (U.V spectroscopy, HPLC, etc) .the maintenance of sink condition is essential\[10,12\] (Puglia et al., 2004 & Vyas et al., 1982).

9. Drug Release Kinetic Data Analysis
The release data observation obtained from various formulations were studied further for their fitness of data in different kinetic models such as Zero order, Higuchi’s and Peppa’s. In order to understand the kinetic and mechanism of drug release, the result of in-vitro drug release study of proniosomes or niosome were fitted with various kinetic equation like zero order (Equation 1) as cumulative % release vs. time, higuchi’s model (Equation 2) as cumulative % drug release vs. square root of time. r2 and k values were calculated for the linear curve obtained by regression analysis of the above plots.

\[ C = k0t \] \( \ldots \ldots (1) \)
\[ Q = kHt^{1/2} \] \( \ldots \ldots (2) \)
Where k0 is the zero order rate constant expressed in units of concentration / time and t is time in hours.
Q = kHt1/2.....(2)
Where $k_H$ is higuchi’s square root of time kinetic drug release constant. To understand the drug release mechanism \textit{in-vitro} data was analyzed by peppa’s model (Equation 3) as log cumulative % drug release vs. log time and the exponent $n$ was calculated through the slope of the straight line.

$$\frac{M_t}{M_\infty} = bt^n \ldots \ldots(3)$$

Where $M_t$ is amount of drug release at time $t$, $M_\infty$ is the overall amount of the drug, $b$ is constant, and $n$ is the release exponent indicative of the drug release mechanism. If the exponent $n = 0.5$ or near, then the drug release mechanism is Fickian diffusion, and if $n$ have value near 1.0 then it is non-Fickian diffusion\textsuperscript{[13]} (Gibaldi et al., 1982).

\textbf{10. Osmotic Shock}

The change in the vesicle size can be determined by osmotic studies method. Proniosomal formulations are incubated with hypotonic, isotonic, hypertonic solutions for 3 hours. Then the changes in the size of vesicles in the formulations are viewed under optical microscopy\textsuperscript{[14]} (Biju et al., 2006).

\textbf{11. Stability Studies}

To determine the stability of proniosomes, the optimized batches were stored in airtight sealed glass vials at different temperatures. Surface characteristics and percentage drug retained in proniosomes and proniosomes derived niosomes were selected as parameters for evaluation of the stability, since instability of the formulation would reflect in drug leakage and a decrease. In the percentage drug retained (Biju et al., 2006). The proniosomes samples were pick at regular intervals of time (0, 1, 2, and 3 months ), observed for color change, surface characteristics and tested for the percentage drug retained after being hydrated to form niosomes and analysed by suitable analytical methods (UV spectroscopy, HPLC methods etc)\textsuperscript{[15]} (Varaporn et al., 2008).

\textbf{12. Zeta Potential Analysis}

Zeta potential analysis is used for determining the colloidal properties of the prepared formulations. The suitably diluted proniosome derived niosome dispersion was determined using zeta potential analyzer based on electrophoretic light scattering and laser Doppler velocimetry method (Zetaplus\textsuperscript{TM}, Brookhaven Instrument Corporation, New York, USA) (Varaporn et al., 2008).
The temperature was set at 25°C. Charge on vesicles and their mean zeta potential values with standard deviation of 5 measurements were obtained directly from the measurement \(^{[16]}\) (Gregoriadis et al., 1981).

**IN-VIVO STUDY**

**Blood Samples collection from animal rats (rats/mice).**

Orbital bleeding is a procedure used in a rats and mice (though usually not a good choice in rat) to obtain small blood samples.

A glass capillary tube was inserted at the medial canthus to gain access to the mouse orbital venous sinus or rat orbital venous plexus. This area offers a readily accessible site for blood collection. Retro (back/behind). Orbital bleeding may be conducted in a awake mice by a skilled operator. Alternatively, systemic anaesthesia should be consider if compatible with experimental objectives. Due to restraint issues, retro-orbital sampling in the rat should be conducted under general anesthesia. Alternate eyes should be used for sequential bleeds. In the hands of an unskilled operator, retro-orbital sampling has a greater potential than other blood collection routes to result in complications and thus required certification. A traumatized eye will require euthanasia.\(^{[17-19]}\) (Chan YK et al., 2012; Fernandez I et al., 2010; Nyuyki KD et al., 2012).

**IN-VIVO TEST AND STUDY**

**Preparation of animal for studies**

*In-vivo* evaluation studied for Gliclazide loaded proniosomes were performed in diabetes Albino rats of either sex, weighing between 260-330 gm.

↓

After 16 hours overnight fast, the experimental animals were made diabetic by single intraperitoneal administration of cold, freshly prepared solution of Aloxan (Sigma chem., co st: Louis, USA) at a dose of 150 mg/kg dissolved in 2 ml Citrate buffer pH(3.0).

↓

After 1 week animals with fasting blood glucose of 300 mg/dl or more were considered diabetes and were employed in the study.

↓

The rats were divided randomly into 3 groups of 4 rats (animals) each and treated as follow:

Group 1-(Test)=Administration pure drug.

Group 2-(controlled)=Self formulated drug.
Group 3-(Marketed/standard)=Marketed drug.

Group 1- was administered with 2 mg/kg body weight of Gliclazide solution.

Group 2 - were administered with proniosomes loaded gliclazide P7 and P8 at a dose equivalent to 2 mg/kg body weight of gliclazide by using oral feeding needle and

Group 3- was administered with marketed conventional gliclazide tablet.

Blood samples were withdrawn by the retro-orbital puncture at predetermined time at 1 hour intervals upto 24 hours and were analysed for blood glucose by glucose oxidase and peroxidise (GOD/POD) method using commercial glucose kit.[20-23] (S.K. Wangnoo et al.,2005; K.P.R.Chowdary et al.,2003; H.M.Mukhtar et al.,2004; S.Satyanarayana et al.,2006).

Table no.4: Various formulation and evaluation parameters of gliclazide loaded proniosomes dry powder.

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Angle of Repose*</th>
<th>Bulk Density*</th>
<th>Tapped Density*</th>
<th>% Compressibility*</th>
<th>Hausner ratio*</th>
<th>Mean Particle Size* (μm)</th>
<th>Drug Entrapment Efficiency*</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>35.51±2.50</td>
<td>0.55±0.04</td>
<td>0.72±0.02</td>
<td>23.61±2.86</td>
<td>1.30±0.04</td>
<td>4.71±0.51</td>
<td>20.15±1.53</td>
</tr>
<tr>
<td>P2</td>
<td>34.60±1.10</td>
<td>0.52±0.05</td>
<td>0.69±0.03</td>
<td>24.63±2.46</td>
<td>1.32±0.04</td>
<td>3.20±0.24</td>
<td>31.05±2.10</td>
</tr>
<tr>
<td>P3</td>
<td>33.25±0.87</td>
<td>0.54±0.03</td>
<td>0.65±0.04</td>
<td>18.46±4.48</td>
<td>1.20±0.04</td>
<td>2.20±0.10</td>
<td>37.90±1.20</td>
</tr>
<tr>
<td>P4</td>
<td>31.40±0.69</td>
<td>0.54±0.01</td>
<td>0.66±0.05</td>
<td>18.18±6.85</td>
<td>1.22±0.40</td>
<td>2.90±0.15</td>
<td>36.20±1.75</td>
</tr>
<tr>
<td>P5</td>
<td>30.16±0.95</td>
<td>0.58±0.05</td>
<td>0.67±0.02</td>
<td>13.40±3.10</td>
<td>1.15±0.03</td>
<td>2.49±0.50</td>
<td>42.14±2.20</td>
</tr>
<tr>
<td>P6</td>
<td>35.55±1.25</td>
<td>0.57±0.02</td>
<td>0.68±0.04</td>
<td>16.17±3.76</td>
<td>1.19±0.04</td>
<td>2.45±0.24</td>
<td>43.80±1.15</td>
</tr>
<tr>
<td>P7</td>
<td>32.65±2.90</td>
<td>0.53±0.05</td>
<td>0.66±0.02</td>
<td>19.69±1.90</td>
<td>1.24±0.05</td>
<td>1.75±0.10</td>
<td>48.95±2.30</td>
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<tr>
<td>P8</td>
<td>34.26±0.88</td>
<td>0.58±0.01</td>
<td>0.68±0.06</td>
<td>14.70±2.80</td>
<td>1.72±0.02</td>
<td>1.20±0.15</td>
<td>42.80±3.25</td>
</tr>
</tbody>
</table>

*Mean± SD, n=3(All values are the average of three determination)

**IN-VITRO DRUG RELEASE STUDIES**

Table no.5: Comparative cumulative % drug release of formulations R1 to R4

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Time(min)</th>
<th>R1</th>
<th>R2</th>
<th>R3</th>
<th>R4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2.</td>
<td>1</td>
<td>9.20±0.06</td>
<td>7.46±0.73</td>
<td>12.20±0.63</td>
<td>16.50±0.41</td>
</tr>
<tr>
<td>3.</td>
<td>2</td>
<td>16.90±0.17</td>
<td>15.65±0.16</td>
<td>20.57±0.48</td>
<td>25.40±0.13</td>
</tr>
<tr>
<td>4.</td>
<td>4</td>
<td>29.75±0.21</td>
<td>26.53±0.15</td>
<td>33.65±0.34</td>
<td>39.75±0.37</td>
</tr>
<tr>
<td>5.</td>
<td>6</td>
<td>42.46±0.04</td>
<td>42.47±0.30</td>
<td>47.38±0.43</td>
<td>52.40±0.11</td>
</tr>
<tr>
<td>6.</td>
<td>10</td>
<td>55.45±0.15</td>
<td>52.95±0.23</td>
<td>59.50±0.40</td>
<td>67.33±0.86</td>
</tr>
<tr>
<td>7.</td>
<td>15</td>
<td>71.82±0.26</td>
<td>70.20±0.19</td>
<td>76.48±0.13</td>
<td>81.20±0.64</td>
</tr>
<tr>
<td>8.</td>
<td>30</td>
<td>82.68±0.89</td>
<td>81.75±0.26</td>
<td>89.50±1.12</td>
<td>91.56±0.41</td>
</tr>
</tbody>
</table>
Fig.1: *In-vitro* drug release study of R1 to R4

Table no.6: Comparative cumulative % drug release of formulations R5 to R8

<table>
<thead>
<tr>
<th>S.No</th>
<th>Time (min)</th>
<th>Cumulative % Drug Release</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>R5</td>
</tr>
<tr>
<td>1.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2.</td>
<td>1</td>
<td>20.47±0.22</td>
</tr>
<tr>
<td>3.</td>
<td>2</td>
<td>31.30±0.43</td>
</tr>
<tr>
<td>4.</td>
<td>4</td>
<td>43.50±0.71</td>
</tr>
<tr>
<td>5.</td>
<td>6</td>
<td>63.20±0.31</td>
</tr>
<tr>
<td>6.</td>
<td>10</td>
<td>74.84±0.39</td>
</tr>
<tr>
<td>7.</td>
<td>15</td>
<td>83.12±0.41</td>
</tr>
<tr>
<td>8.</td>
<td>30</td>
<td>98.87±0.15</td>
</tr>
</tbody>
</table>

Fig.2: *In-Vitro* drug release study of R5 to R8
Morphological Examination by SEM

![SEM Image]

Fig.3: Scanning electron microphotograph of gliclazide loaded proniosomes formulation. Scale bar indicates 10 mm.

Morphological Examination by TEM

![TEM Image]

Fig.4. Transmission electron micrograph of hydrated proniosomal formulation (at 90 kV with magnification 100,000X)

RESULT AND DISCUSSION

Proniosomes were prepared by the Slurry method using maltodextrin and span 40 as polymer and constant solvent ratio. (Table-2 and 3 Given above)

Proniosomes were prepared using gradually increasing ratio of the ingredients or formulation materials. All Eight formulation were prepared.
The formulation of all batches were evaluated for parameter like angle of repose was found to be between 31.40±0.69 to 35.51±2.50, this indicates satisfactory flowability. Bulk density was found to be between 0.52±0.05 to 0.58±0.05 g/cm³ and tapped density between 0.65±0.05 to 0.72±0.02 g/cm³. Hausner’s ratio was found to be between 1.24±0.05 to 1.32±0.04, lower Hausner’s ratio (<1.25) indicate better flow properties than higher one (>1.25) and Compressibility index was found to be between 13.40±3.10 to 24.63±2.46, Compressibility index (<15%) show better flow properties than (>25%). The mean particle size of the proniosomes significantly decreased with decreasing polymer concentration and was in the range of 4.71±0.51μm to 1.20±0.15 μm.(Table-4).Initially it increases then decreases as amount or concentration of polymers decreases.

In-vitro gliclaizide release studies were performed in simulated gastric fluid (Ph7.4) with 0.02% Phosphate buffer for 10 hrs. (with time intervals of 1 to 30 minutes as given above table no.5).The accumulative release of gliclazide significantly increases with respect to time.

CONCLUSION

In-vitro study data obtained for proniosomes of Gliclazide showed excellent flow property (on basis of angle of repose), good physical stability and prolonged drug release controlled. Proniosomes formulation of different size and drug content could be obtained by varying the formulation variables. Thus, the prepared proniosomes may prove to be better potential for oral route drug delivery.

ACKNOWLEDGEMENT

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REFERENCES


