Nanosponge is a modern category of material and it is made up of tiny particles with a narrow cavity of few nanometers. These narrow cavities can be filled with various types of substances; these tiny particles are having capability due to which it is able to carry both hydrophilic and lipophilic drug substances [1]. Release the drug at specific target site instead of circulate through the body it will more effective for particular given dosage [2, 3]. The invention of nanosponges has become significant step towards overcoming the complexity associated with the newly developing systems. The small size and porous nature of nanosponges can bind poorly water-soluble drugs within the matrix and improve their solubility and bioavailability [4]. Nanosponges are able to entrap both hydrophilic as well as lipophilic drug molecules because of their inner hydrophobic cavities and external hydrophilic branching, thereby offering unparalleled flexibility. Nanosponge obtained by using suitable cross-linking agent also by different organic and inorganic materials [5]. The stability of these formulations over a wide range of pH in GI fluids and stable over 130 °C compatible with most patient compliance and comfort. This drug delivery system having entrap wide variety of ingredients and reducing side effects, improve stability, increased elegance and formulation flexibility [6].

The effort to improve dissolution and solubility of poorly and practically water insoluble drugs remains one of the most challenging tasks in drug development. Several methods have been introduced to increase dissolution rate and thereby oral absorption and bioavailability of such drugs. Among various approaches, Nanosponges has shown promising results in improving solubility, wettability, dissolution rate of drug and subsequently its bioavailability [7]. The nanosponges can overcome some of the shortcomings of the conventional dosage forms. GLZ is one of the second-generation sulphonylurea, anti diabetic drug which stimulates insulin release. It is used for the treatment of non-insulin dependent diabetes mellitus. GLZ is classified under class II according to biopharmaceutical classification system (BCS). The drug shows low, pH dependent solubility. In acidic and neutral aqueous media, GLZ exhibits very poor solubility. This poor solubility may cause poor dissolution and unpredicted bioavailability. Preparation of nanosponges of GLZ to improve the dissolution rate of GLZ and subsequently its bioavailability. The main objective of the study was to increase the amount of dissolved drug molecules at the absorption site by increasing the dissolution rate, since for class II drugs like GLZ, in vivo dissolution rate is rate-limiting step in drug absorption. nanosponges were selected as the method of choice since it would be easier in subsequent formulating. The nanosponges were prepared at various drug-to-carrier weight ratios by emulsion solvent diffusion method.
Production yield (PY) can be determined by calculating the initial weight of raw materials and final weight of nanosponges.

Production yield = \( \frac{\text{Practical mass of nanosponges}}{\text{Theoretical mass(polymer+ drug)}} \times 100 \)

The percentage yield of different batches was determined by weighing the nanosponges after drying [9].

Drug entrapment efficiency

To calculate the entrapment efficiency accurately weighted the quantity of nanosponges (10 mg) with 5 ml of methanol in a volumetric flask was shaken for 1 min using vortex mixer. Then the solution was filtered and diluted and the concentration of G LZ was determined spectrophotometrically at 229 nm [9].

Loading efficiency = \( \frac{\text{Actual drug content in nanosponge}}{\text{Theoretical drug content}} \times 100 \)

Determination of drug content

To study the amount of drug incorporated in the nanosponges, GLZ was extracted from the nanosponges by dissolving them in 25 ml Methanol. The resulting solution was filtered through a 0.45-micron membrane filter. The GLZ content in the methanolic extracts was analyzed spectrophotometrically by using a UV-Visibl

**Table 1: Formulation of GLZ loaded nanosponges**

| Materials                  | F1       | F2       | F3       | F4       | F5       |
|---------------------------|----------|----------|----------|----------|----------|
| Drug: polymer(mg)         | 100:100  | 100:200  | 100:300  | 100:400  | 100:500  |
| PVA(96w/v)                | 0.5      | 0.5      | 0.5      | 0.5      | 0.5      |
| Dichloromethane (ml)      | 20       | 20       | 20       | 20       | 20       |
| Triethyl citrate (ml)     | 0.5      | 0.5      | 0.5      | 0.5      | 0.5      |
| Distilled water (ml)      | 100      | 100      | 100      | 100      | 100      |

% drug content = \( \frac{\text{Wa}}{\text{Wt}} \times 100 \)

Where, Wa = Actual drug content and Wt = Theoretical drug content

Determination of particle size

The size of particles is maintained during polymerization for the formation of free-following powders having fine aesthetic attributes. Particle size analysis of loaded and unloaded nanosponges performed by laser light diffraction or Malvern zeta sizer. The cumulative graph is maintained or plotted as particle size against time to study effect of particle size on drug release [11].

**In vitro drug release studies**

In vitro drug release studies were performed in triplicate using USP Paddle method at 50 rpm and 37±0.2°C in 90 ml of phosphate buffer (pH 6.8) [12]. 100 mg of the formulated nanosponges is used for each experiment. Samples were taken at appropriate time intervals for 1 h interval for 10 h. The samples were measured spectrophotometrically at 229 nm. Fresh dissolution medium was replenished each time when sample is withdrawn to compensate the volume.

Fourier-transform infrared analysis

Fourier-transform infrared (FTIR) spectra of pure G LZ and pure polymer (Eudragit), and nanosponges of drug G LZ was taken to access interaction if any interaction between drug and polymer in mixtures. The scanned mixture by using an FTIR (Jasco-460 plus). The FTIR spectra of mixtures were compared with that of the pure drug and Polymer to assess any change in the principle peaks of spectra of pure drug and polymer [13].

Differential scanning calorimetry

Differential scanning calorimetric (DSC) studies of pure GLZ, pure polymer (Eudragit S100) and nanosponges of drug GLZ with Eudragit S100 was performed to assess what changes happen during the heat change and thermal behavior of the drug is also determine. The pure drug sample shows sharp endothermic peak at melting point of drug. The samples were kept on DSC reference pan and DSC curves were obtained by differential scanning calorimeter (DSC 60; Shimadzu) at a heating rate of 10 °C/min from 0 to 300 °C in nitrogen atmosphere [14].

Scanning electron microscopy studies

Scanning electron microscopy (JSM-5200, Tokyo Japan) was used to analyze particle size and surface topography was operated at 15kV acceleration voltage. A concentrated aqueous suspension was spread over a slab and dried under vacuum. The sample was shadowed in a cathodic evaporator with a gold layer 20 nm thick. Photographs were elaborated by an image processing program and individual NP diameters were measured to obtain mean particle size.

Nanosponges that showed the best results in the solubility and dissolution studies were subjected to scanning electron microscopy (SEM) studies to confirm the changes mounting made during the formation of nanosponges. Samples were prepared by powder onto a brass stub using graphite glue and coated with gold under vacuum before use. Images were recorded at the required magnification at an acceleration voltage of 10 KV using a scanning electron microscope [15].
Stability studies

Accelerated stability studies: -40 °C±2 °C/75%RH±5%RH. As per ICH guidelines, the samples for stability analysis must be exposed to an environment of 40°C ±2°C/75%RH±5%RH for a period of 6 mo. As per the standard protocol, the samples must be analysed at 0, 1, 2, 3- and 6-months’ time points. Accelerated stability studies were performed for the final optimized formulation. Samples were analysed at 1, 2 mo’ time points [16].

RESULTS

Preformulation studies

Calibration curve of GLZ

Evaluation of nanosponges

Production yield

The production yield (PY) can be determined by calculating the initial weight of raw materials and final weight of nanosponges.

The percentage yield of different batches was determined by weighing the nanosponges after drying. The percentage yields of different formulations were found to be in the range of 73.8±0.30%–85.6±0.32% as shown in below table 2.

Drug entrapment efficiency

The drug entrapment efficiency found in the range of 62.8±0.22 to 73.1±0.39. The increases concentration of polymer the drug entrapment efficiency also increases.

Table 2: Percentage yield of different batches of nanosponges

| S. No. | Batch | Yield (%) |
|-------|-------|-----------|
| 1     | F1    | 73.8±0.30 |
| 2     | F2    | 75.2±0.25 |
| 3     | F3    | 85.6±0.32 |
| 4     | F4    | 78.9±0.18 |
| 5     | F5    | 80.1±0.16 |

Average of three values±SD n=3

Table 3: Drug entrapment efficiency of different batches of nanosponges

| S. No. | Batch | Entrapment efficiency (%) |
|-------|-------|---------------------------|
| 1     | F1    | 62.8±0.22                 |
| 2     | F2    | 66.2±0.25                 |
| 3     | F3    | 70.6±0.77                 |
| 4     | F4    | 71.8±0.36                 |
| 5     | F5    | 73.1±0.39                 |

Average of three values±SD n=3

Determination of drug content

The various batches of the nanosponges were subjected for drug content analysis. The powdered nanosponges (30 mg) were dissolved in adequate quantity (100 ml) of phosphate buffer pH 6.8 then filter. The UV absorbance of the filtrate was measured using a UV spectrophotometer at 229 nm.

The drug content of different formulation was found to be in the range of 77.21±0.17 to 90.62±0.25 as shown in below table 4.

Table 4: Drug content values of different batches of nanosponges

| S. No. | Batch | Drug content (%) |
|-------|-------|------------------|
| 1     | F1    | 77.21±0.17       |
| 2     | F2    | 83.36±0.11       |
| 3     | F3    | 90.62±0.25       |
| 4     | F4    | 85.32±0.13       |
| 5     | F5    | 86.92±0.09       |

Average of three values±SD n=3
Particle size analysis

The average particle size was obtained in range of 303±2.36 nm to 680±2.50 nm. The change in the concentration of polymer results in variation of particle size of nanosponges.

The average particle size of formulation batch F3 showed minimum particle size i.e. 418±2.23 nm while formulation batch F5 showed maximum particle size i.e. 680±2.50 nm. An increase in the concentration of polymer leads to increase in the particle size of nanosponges.

Table 5: Particle size of different batches of nanosponges

| S. No. | Formulation code | Particle size (nm) |
|--------|------------------|--------------------|
| 1      | F1               | 303±2.36           |
| 2      | F2               | 380±2.59           |
| 3      | F3               | 418±2.23           |
| 4      | F4               | 519±2.66           |
| 5      | F5               | 680±2.50           |

Average of three values±SD n=3

In vitro drug release study

In vitro drug release for GLZ loaded nanosponges for a period of 10 h, was carried out by using Phosphate buffer (pH 6.8) at 37±0.5 °C using cellophane membrane of 0.22 nm. From the dissolution profile of formulations F1 to F5, it is concluded that formulation batch F3 shows a better drug release profile than other formulations. Cumulative % release has been shown for average of three preparations. Cumulative % drug release for all the formulations are depicted in the table 6.

Table 6: In vitro drug release studies

| Time in (h) | 1:1 | 1:2 | 1:3 | 1:4 | 1:5 |
|-------------|-----|-----|-----|-----|-----|
| 1           | 10.07±0.90 | 11.99±1.12 | 15.25±0.78 | 13.56±1.42 | 10.04±0.92 |
| 2           | 15.32±0.85 | 23.68±0.80 | 19.48±0.82 | 20.2±1.36 | 20.53±1.00 |
| 3           | 25.36±0.92 | 32.72±0.99 | 33.79±1.02 | 31.94±0.96 | 31.76±1.14 |
| 4           | 39.98±0.65 | 40.34±1.12 | 51.93±0.98 | 42.4±1.22 | 40.29±1.50 |
| 5           | 49.92±1.12 | 50.38±1.50 | 65.03±1.14 | 56.3±1.33 | 44.4±1.04 |
| 6           | 55.23±1.01 | 58.3±0.98 | 69.3±1.32 | 65.7±1.18 | 50.97±1.22 |
| 7           | 63.74±0.58 | 64.71±1.11 | 77.7±1.26 | 71.1±1.08 | 61.3±1.16 |
| 8           | 70.96±1.20 | 75.95±0.96 | 82.15±1.08 | 77.9±1.12 | 76.3±1.32 |
| 9           | 75.26±0.74 | 81.52±1.25 | 85.78±0.98 | 86.2±0.90 | 84.28±1.24 |
| 10          | 84.32±0.62 | 87.36±1.32 | 94.40±1.12 | 91.4±0.88 | 90.3±1.20 |

Average of three values±SD n=3

Fig. 2: Graphical presentation of % drug release of F1 to F5 batches

Modeling of dissolution profile

In the present study, different release kinetic equations (zero order, first order, Higuchi equation and Korsmeyer-peppas equation) were applied to interpret the release rate of drug from nanosponges. The data of in vitro release were fitted to these models and equations to explain the release kinetics of GLZ from nanosponges [17].
Fig. 3: Zero order release kinetics

Fig. 4: First order release kinetics

Fig. 5: Higuchi model

Fig. 6: Korsmeyer-peppas model
The in vitro release profile of the formulations indicates that the rate of drug release was higher for formulations, among all the formulations F3 shows more amount of drug release with the medium amount of polymer ratio. The plot of time vs cumulative % drug release in the zero-order kinetic model the regression coefficient value shows linearity as shown in (fig 3). The slopes and regression coefficient values ($R^2$) of various mathematical models for optimized batch F3, 0.9927, 0.9711, 0.9475, 0.7425 for zero order, first order, Higuchi and Peppas model respectively. The good linearity observed with the zero-order and regression coefficient value is higher. Hence this formulation is best fitted into zero-order release model.

FT-IR studies

Table 7: $R^2$ values of different release kinetic models

| Formulation | Zero order kinetics | First order kinetics | Higuchi model | Korsmeyer-Peppas model |
|-------------|---------------------|----------------------|---------------|-----------------------|
|             | $R^2$               | $R^2$                | $R^2$         | $R^2$                 |
| F1          | 0.9823              | 0.9529               | 0.9326        | 0.8079                |
| F2          | 0.9612              | 0.9462               | 0.9524        | 0.7541                |
| F3          | 0.9927              | 0.9711               | 0.9475        | 0.7425                |
| F4          | 0.9865              | 0.9576               | 0.9462        | 0.7608                |
| F5          | 0.9923              | 0.9021               | 0.9205        | 0.7878                |

**Fig. 7: FT-IR spectra of pure GLZ**

**Fig. 8: FT-IR spectra of Eudragit S100**

**Fig. 9: FT-IR spectra of the physical mixture (drug+polymer)**
DSC studies

Fig. 10: FT-IR spectra of prepared nanosponges

Fig. 11: DSC thermogram of Pure GLZ

Fig. 12: DSC thermogram of polymer

Fig. 13: DSC thermogram of the physical mixture (drug+polymer)
Stability studies

Optimized formulation was subjected to stability studies as per ICH guidelines. Various parameters such as drug content, and *in vitro* drug release were measured before and after 30, 60, days of stability. Results of stability studies are shown in below table 8.

Results of stability studies showed there is no significant change in the above mentioned parameter after elevated temperature and humidity conditions during stability studies. Thus, it can be proved from the stability studies that the prepared formulation is stable and not much affected by elevated humidity and temperature conditions.

| Time (day) | Drug content (%) | *In vitro* drug release (%) |
|------------|------------------|-----------------------------|
| 0          | 98.86±0.68       | 99.85%                      |
| 30         | 98.20±0.99       | 99.74%                      |
| 60         | 98.30±1.50       | 99.51%                      |

DISCUSSION

The calibration curve of GLZ by UV method showed the linearity in absorbance and coefficient of regression found to be 0.9994. The IR studies shows that there is no interaction found between drug and excipients. All the characteristic peaks of GLZ were present in the spectrum of drug (fig. 7) and prepared GLZ nanosponges (fig. 10), indicating compatibility in drug and polymer the spectrum confirmed that there is no significant change in the chemical integrity of the drug [18]. The DSC thermogram pure GLZ shows sharp endothermic peak at 174°C, which is its melting point as it melts with decomposition [19]. Such a sharp endothermic peak indicates that GLZ used was in the pure crystalline state. The thermogram of prepared GLZ nanosponges 1:3 (fig. 14) displayed the nanosponge structure is amorphous as no sharp melting peak is shown.
The percentage yield of different batches was determined by weighing the nanospangles after drying. The percentage yields of different formulations were found to be in the range of 73.8±0.30%–85.6±0.32%. The drug entrapment efficiency found in the range of 62.8±0.22 to 73.1±0.39. The increases concentration of polymer the drug entrapment efficiency also increases. The drug content of different formulation was found to be in range of 77.2±1.07 to 90.6±0.25. The average Particle size was obtained in range of 303±2.36 nm to 680±2.50 nm. The Change in the concentration of polymer results variation in particle size of nanospangles [20]. The average particle size of formulation batch F1 showed minimum particle size i.e. 303±2.36 nm while formulation batch F5 showed maximum particle size i.e. 680±2.50 nm. An increase in the concentration of polymer leads to increase in the particle size of nanospanges. The SEM of the prepared nanospangles revealed a porous nature of GLZ nanospangles (fig. 15). Drug release data for nanospangles. The various release kinetic curves are shown in fig. 3-7. The correlation coefficient equations to find out order of drug release. The various release kinetic model. Hence, it can be concluded that the major mechanism of drug release follows zero-order kinetics [21].

CONCLUSION
Nanosponge is the best novel drug delivery system. For improving the dissolution and bioavailability profile of poorly water-soluble drug. BCS class-2 drug are more suitable drug candidate for formulated into nanospangles. Nanospangles are able to encapsulate variety of various types of drug molecules. Nanospangles prepared by using emulsion solvent diffusion method are simpler and production cost of method is less. Nanospangle prepared by emulsion solvent diffusion method shows good entrapment efficiency ranged between 62.8±0.22 to 73.1±0.39 and optimum drug release is 94.40%. The compatibility of drug and polymer determine by FT-IR, and DSC study. The result of IR and DSC shows drug and polymer are compatible to each other. The nanospangle formulation shows zero order drug release. The outcome of the study concluded that Eudragit S100 are employed as polymer for formulation shows zero order drug release. The outcome of the study concluded that Eudragit S100 are employed as polymer for nanospangelo drug delivery system. World J Pharm Sci 2018;7:575-92.

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