The aim of the present study was to prepare and evaluate self-emulsifying drug delivery systems (SEDDS) of gliclazide and glibenclamide. Following conclusions have been drawn from the present study:

1. The analytical and bioanalytical methods developed for the estimation of gliclazide and glibenclamide were found to be sensitive and were successfully applied for the determination of respective drugs. Validation results showed that the methods were accurate, precise, selective and linear over the wide range of concentrations.

2. Based on the solubility data, Palm oil was selected as oil phase, Tween 20 as surfactant, PEG 600 as co-surfactant for formulating SEDDS of gliclazide. For the SEDDS of glibenclamide, Sunflower oil was selected as oil phase, Tween 80 as surfactant, PEG 600 as co-surfactant as these solvents showed higher solubility results.

3. To determine the optimum concentration of oil, surfactant and co-surfactant for the formation of SEDDS, phase diagrams were constructed. For gliclazide, Smix ratio (Surfactant: Cosurfactant) of 4:1 and 3:1 showed the largest nanoemulsification region with infinite dilutions with water. For glibenclamide, Smix ratio of 3:1, 2:1 and 1:1 exhibited the largest nanoemulsification region. In case of both drugs, no significant differences were noticed in the area of nanoemulsion when phase diagrams were constructed in the presence of the respective drugs.

4. SEDDS were formulated successfully with the selected concentrations of oil, surfactant, and cosurfactant for both the drugs. For gliclazide, Formulations Ca1 to Ca4 (Smix ratio 4:1), Cb1 to Cb4 (Smix ratio 3:1) were found to be thermodynamically stable and did not show any signs of phase separation. Formulations Ba1 to Ba6 (Smix ratio 3:1), Bb1 to Bb6 (Smix ratio 2:1), Bc1 (Smix ratio 1:1) were found to be stable during the thermodynamic stability studies and did not show any signs of phase separation during the stress test.

5. Gliclazide SEDDS, Ca1 to Ca4, Cb1 to Cb4 and Glibenclamide SEDDS, Ba1 to Ba5, Bb1 to Bb5 and Bc1 formed clear dispersions and did not show any drug precipitation and thus were considered as stable. All the above SEDDS were found to be isotropic in nature and were robust to dilution in the aqueous media.
6. All the SEDDS on dilution with dilution media of varying pH did not show any drug precipitation or phase separation and the viscosity of the respective systems decreased upon dilution with distilled water.

7. SEDDS of gliclazide with Smix ratio of 4:1 exhibited a lower emulsion droplet size as compared to formulations with Smix ratio of 3:1. Among all the formulations Ca2 showed the minimum emulsion globule size of 133.3 nm with PDI of 0.588 followed by Cb2 with globule size of 159.1 nm with PDI of 0.504.

In case of SEDDS of glibenclamide with Smix ratio of 2:1, the emulsion globule size was found to decrease with the decrease in oil concentration but was higher as compared to Smix ratio of 3:1 with respective oil concentration. Formulation with Smix ratio of 1:1 showed the highest emulsion droplet size. Among all the formulations Ba3 showed the minimum emulsion globule size of 122.9 nm with PDI of 0.549 followed by Bb4 with globule size of 139 nm with PDI of 0.623.

8. In case of gliclazide, both SEDDS (Ca2 and Cb2) showed a very high and immediate drug release as compared to pure gliclazide (8.9±1.1%) and marketed tablet (40.1±1.2%). At the end of 1 h, Ca2 released (98.1±1.2%) and Cb2 (94.2±1.5%) as compared to pure gliclazide (36.7±2.2%) and marketed tablet (82.7±2.3%). Formulation Ca2 showed a higher drug release as compared to Cb2 and also exhibited a smaller emulsion droplet size.

In case of glibenclamide, both the formulations Ba3 and Bb4 showed a very high drug release as compared to pure glibenclamide (12.2±0.67) and marketed tablet (77.2±1.4). Even at the end of 60 min both formulations Ba3 (97.6 ± 1.8) and Bb4 (95.2±2.6) showed a much higher cumulative drug release as compared to pure glibenclamide (31.2±2.2) and marketed tablet (90.3±2.1). Formulation Ba3 showed a higher drug release and smaller emulsion droplet size as compared to Bb4 at every time point upto 60 min.

9. The optimized formulations Ca2 and Ba3 were tested for pharmacokinetic studies in comparison to pure drug and marketed preparations. The optimized formulations showed improved pharmacokinetic activity as compared to pure drug and almost equivalent activity as compared to marketed product.
10. The optimized formulations were found to be stable under accelerated conditions for 6 months with respect to self-emulsification, emulsion droplet size and absence of drug precipitation.

In conclusion, the present study demonstrated successful preparation of self-emulsifying drug delivery systems of gliclazide and glibenclamide.

**Future scope**

- The pilot plant scale up studies are required for the optimized formulation to meet the industrial and regulatory requirements.
- The long term stability studies as per ICH guidelines are required to establish the stability data of these formulations.
- The formulations are to be studied in large number of healthy human subjects to establish the pharmacokinetic profile, safety and efficiency.
- The related technologies can be utilized to other classes of drugs with solubility problem and low and variable bioavailability.
- Extensive research in this SEDDS field is necessary w.r.t. mechanism of drug absorption through SEDDS.