

Oral Bioavailability Enhancement of Glibenclamide by Self-Emulsifying Drug Delivery Systems (SEDDS)

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SUMMARY. The present work was aimed to improve the oral bioavailability of glibenclamide by developing self-emulsifying drug delivery system (SEDDS). Solubility of glibenclamide was determined in oils, surfactant, and cosurfactant. Pseudoternary phase diagrams were constructed to obtain self-nanoemulsifying region. SEDDS were evaluated for thermodynamic stability, droplet size, in vitro dissolution, in vivo pharmacokinetic, and stability studies. Sunflower oil (3.46 ± 0.32 mg/100 mg), Tween 80 (3.75 ± 0.37 mg/100 mg) and PEG 600 (2.98 ± 0.44 mg/100 mg) were selected as oil, surfactant, and cosurfactant, respectively. Surfactant and cosurfactant mix (Smix) of 3:1, 2:1, and 1:1 showed a larger nanoemulsification region and Ba3 (Smix 3:1) showed minimum emulsion globule size of 122.9 nm with PDI of 0.549 and exhibited highest cumulative drug release (97.6 ± 1.8), as compared to pure glibenclamide (31.2 ± 2.2) and marketed tablet (90.3 ± 2.1). Cmax of Ba3 (10.01 ± 2.14 $\mu\text{g/mL}$) was significantly higher than pure drug (7.13 ± 1.16 $\mu\text{g/mL}$) and marketed tablet (9.02 ± 2.23 $\mu\text{g/mL}$) and AUC of Ba3 (140.39 ± 10.14 $\mu\text{g.h/mL}$) was found to be significantly higher than pure glibenclamide (100.12 ± 11.45 $\mu\text{g.h/mL}$), indicating an improvement in the bioavailability of glibenclamide from SEDDS formulation as compared to pure drug.

RESUMEN. El presente trabajo tuvo como objetivo mejorar la biodisponibilidad oral de la glibenclamida mediante el desarrollo del sistema de administración de fármacos autoemulsionantes (SEDDS). La solubilidad de glibenclamida se determinó en aceites, surfactante y cosurfactante. Se construyeron diagramas de fase pseudoternarios para obtener una región auto nanoemulsificante. Los SEDDS se evaluaron para determinar la estabilidad termodinámica, el tamaño de la gota, la disolución in vitro, la farmacocinética in vivo y los estudios de estabilidad. Aceite de girasol (3.46 ± 0.32 mg / 100 mg), Tween 80 (3.75 ± 0.37 mg / 100 mg) y PEG 600 (2.98 ± 0.44 mg / 100 mg) fueron seleccionados como aceite, surfactante y cosurfactante, respectivamente. La mezcla de surfactante y cosurfactante (Smix) de 3:1, 2:1 y 1:1 mostró una región de nanoemulsificación mayor y Ba3 (Smix 3:1) mostró un tamaño de glóbulo de emulsión mínimo de 122.9 nm con un PDI de 0.549 y mostró el fármaco acumulado con más alta liberación (97.6 ± 1.8), en comparación con glibenclamida pura (31.2 ± 2.2) y tabletas comercializadas (90.3 ± 2.1). La C_{máx} de Ba3 (10.01 ± 2.14 $\mu\text{g/mL}$) fue significativamente más alta que el fármaco puro (7.13 ± 1.16 $\mu\text{g/mL}$) y la tableta comercializada (9.02 ± 2.23 $\mu\text{g/mL}$) y el AUC de Ba3 (140.39 ± 10.14 $\mu\text{g.h/mL}$) se encontró que era significativamente mayor que la glibenclamida pura (100.12 ± 11.45 $\mu\text{g.h/mL}$), lo que indica una mejora en la biodisponibilidad de la glibenclamida de la formulación de SEDDS en comparación con el fármaco puro.

KEY WORDS: glibenclamide, nanoemulsion, phase diagram, SEDDS, Smix.

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