Supplementary Material

Tablet preparation

GX, TF, and microcrystalline cellulose were passed through a 40-mesh sieve, thoroughly homogenized with pestle and mortar and granulated with an aqueous solution of tragacanth (5% w/v). The resultant damp mass was passed through a 20-mesh sieve after drying at 40 °C for 3 h and then lubricated with magnesium stearate. Lubricated granules were evaluated through pre-compression parameters to ascertain the flow properties and compressibility of granules (Supplementary Material). Finally, a rotary tablet press fitted with an 11 mm flat surface punch was used to prepare the tablets (300 ± 5 mg). The same procedure was adopted for the preparation of LS tablets. Prepared tablets were then passed through post-compression evaluation such as weight variation, thickness, diameter, hardness, friability and content uniformity (Supplementary Material).

Pre-compression evaluation

Lubricated granules of each formulation were evaluated through different precompression parameters. Angle of repose (θ), bulk density ($D_b$), tapped density ($D_t$), Hausner ratio ($H$) and Carr’s index (C) were calculated to determine the flow properties and compressibility of granules using Equations 1, 2, 3, 4 and 5, respectively. All investigations were carried out thrice and mean values are reported.

$$\tan \theta = \frac{h}{r} \quad (1)$$

$$D_b = \frac{w}{v_b} \quad (2)$$

$$D_t = \frac{w}{v_t} \quad (3)$$
\[ \text{Hausner ratio} (H) = \frac{D_t}{D_b} \]  

(4)

\[ \text{Carr's index} (C) = 100 \times \left(1 - \frac{D_b}{D_t}\right) \]  

(5)

where, in above equations, \( h \) is the height of heap formed, \( r \) is the radius of heap base, \( w \) is weight of granules, \( V_b \) is bulk volume and \( V_t \) is tapped volume.

**Post-compression evaluation**

Various parameters such as weight variation, thickness, diameter, hardness and friability of tablets were evaluated using standard procedures. Tablets (10) of each formulation were randomly chosen and tested for diameter, thickness, and hardness through hardness tester (Pharma Test, PTB 311E, Germany). From each formulation, tablets (20) were randomly taken and weighed on analytical balance (Shimadzu, Japan) for weight variation test. Mean values are calculated and reported. Randomly selected 10 tablets were placed in a friability tester (Pharma Test, PTF 10E, Germany) and rotated for 4 min at 25 rpm. After this, tablets were carefully weighed and friability was then determined as percentage mass loss by Equation 6.

\[ \text{Weight loss} (\%) = \frac{W_i - W_f}{W_i} \times 100 \]  

(6)

where, \( W_i \) and \( W_f \) are the weight of the tablet before and after the friability test, respectively.

**Content uniformity**

Uniform distribution of TF and LS in tablet formulations was analyzed by selecting and crushing 10 tablets of each formulation in pestle and mortar. The resultant powder was
weighed, mixed with methanol in 50 mL flask and filter. The absorbance of TF and LS containing filtrate was noted at 276 and 293 nm, respectively using the UV-1700 PharmSpec spectrophotometer (Shimadzu, Japan). The observed values of absorbance for TF and LS were compared with standard values and the percentage of each drug was then calculated.

Swelling kinetics

The values of normalized ($Q_t$) and equilibrium degree of swellings ($Q_e$) were used to find the second-order swelling kinetics by Equation 7.3,4

$$\frac{t}{Q_t} = \frac{t}{Q_e} + \frac{1}{KQ_e^2}$$

(7)

where $K$ is the second-order rate constant. Swelling of tablets will follow second-order kinetics only if a plot between $t/Q_t$ and $t$ is a straight line with the slope, $t/Q_e$ and intercept, $t/Q_e^2$.

The values of $Q_t$ and $Q_e$ can be calculated using Equation 8 and 9, respectively.

$$Q_t = \frac{W_s - W_i}{W_i} = \frac{W_t}{W_i}$$  \hspace{1cm} (8)

where, $W_i$ is the initial weight of tablet, $W_s$ is the swollen weight of tablet and $W_t$ is the weight of water penetrated in the tablet at time, $t$.

$$Q_e = \frac{W_\infty - W_i}{W_i} = \frac{W_e}{W_i}$$

(9)

where, $W_i$ is the initial weight of tablet at $t = 0$ and $W_\infty$ is the swollen weight of tablet at $t_\infty$. $W_e$ is the weight of water penetrated in the tablet at a time, $t_\infty$.

Drug release kinetics
Zero-order (Eq. 10), first-order (Eq. 11), Higuchi (Eq. 12) and Hixson-Crowell (Eq. 13) models were applied to drug release data for the investigation of drug release kinetics. Among these, the model with the highest value (~1) of coefficient of determination ($R^2$) will be considered the best fit.

$$Q_t = K_0 t$$  \hspace{1cm} (10)

where $K_0$ is the rate constant for zero-order and $Q_t$ is the quantity of released drug from the tablet at time $t$.

$$\log Q = \log Q_0 - \left( \frac{K_1 t}{2.303} \right)$$  \hspace{1cm} (11)

where $K_1$ is the rate constant for first order, $Q_0$ is the quantity of the drug at time $t = 0$ and $Q$ is the amount of drug left in the tablet after time $t$.\(^{5,6}\) (Wagner, 1969; Gibaldi and Feldman, 1967)

$$Q_t = K_H(t)^{1/2}$$  \hspace{1cm} (12)

where $K_H$ is the Higuchi rate constant and $Q_t$ is the quantity of the released drug at time $t$.\(^{7,8}\)

$$Q_0^{1/3} - Q_t^{1/3} = -K_{HC} t$$  \hspace{1cm} (13)

where $K_{HC}$ is the Hixson-Crowell constant, $Q_0$ is quantity of drug in the tablet at $t = 0$, $Q_t$ is the amount of released drug released at time $t$.\(^9\)

**Drug release mechanism**

The drug release from water-swellable polymers is mainly controlled by a diffusion mechanism which can be better explained by power law\(^{10}\) given in Equation 14.
\[ \frac{M_t}{M_\infty} = k_p t^n \]  

(14)

where, \( M_t/M_\infty \) is the fraction of drug released in time \( t \), \( k_p \) is the power-law constant and \( n \) is the diffusion exponent.

The drug release mechanism corresponds to the value of the diffusion coefficient \( (n) \). The drug release from hydrogel follows Fickian diffusion if the value of \( n \) is < 0.45. The mechanism will be non-Fickian diffusion (controlled by both swelling and diffusion) when the value of \( n \) ranges between 0.45 and 0.89. If the value of \( n \) is greater than 0.89, the mechanism is super case-II transport in which the rate of drug release remains constant for longer period of time and shows an exponential increase in drug release at the end due to matrix erosion.\textsuperscript{11,12} (Ritger and Peppas, 1987; Siepmann and Peppas, 2001).

*Swelling kinetics of GXF formulation*

![Swelling kinetics of GXF formulation](image)

**Figure S1.** Second-order swelling kinetics of GXF tablet in buffers of pH 6.8, 7.4 and in deionized water (DW).
Swelling kinetics of GX based TF formulations

Figure S2. Second-order swelling kinetics of GXF and TF formulations (TF1, TF2, TF3) in buffers of pH 1.2 (a), 6.8 (b), 7.4 (c) and deionized water (d).
Swelling kinetics of GX based LS formulations

Figure S3. Second-order swelling kinetics of GXF and LS tablet formulations (LS1, LS2, LS3) in buffers of pH 1.2 (a), 6.8 (b), 7.4 (c) and deionized water (d), respectively.
References


