Mass transfer and modeling release of Olanzapine from Glycerol monooleate

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ABSTRACT SUMMARY
The aim of this study was to prepare the water-insoluble olanzapine using glycerol monooleate (GMO) and plasticizer such as PEG to investigate the swelling properties of matrix and to evaluate effect of percentage of Olanzapine and weight ratio of PEG/GMO, water/GMO on percentage of swelling also to calculate the diffusion coefficient of gel prepared. This study was performed to give the applicability of the lumped model to describe the release mechanism of drug.

INTRODUCTION
Drug delivery developed due to the various type of mass transport process such as drug diffusion, drug dissolution and swelling of polymer, osmotic effect, erosion of polymer and other phenomena. If process happened in a sequence stages and one of the steps is slower than all the other, therefore the slowest one is the release rate-limiting step. (1)

When a glassy or dry polymer contacts with water or any other medium, the solvent penetrates into the free spaces on the surface and solvent has entered into the matrix with special velocity, simultaneously and cause to enchantment radius of polymer molecules. This phenomenon is seen macroscopically and called “swelling of the matrix”. Thickness of swollen matrix increases with time and time derived for the increase in radius is a characteristic of system.

EXPERIMENTAL METHODS
Plain matrices: The molten GMO and PEG and Olanzapine mixed by vortex then pH of solutions were measured (pH of all the samples indicated below 4). Water added to prepared solution and mixed by vortex for 10 min.

Swelling studies: Swelling studies were performed by equilibrium weight gain method. The studies were carried out using USP 24 Type II dissolution test apparatus (Electrolab, TDT-06P, and India). The water uptake obtained from the following equation:

\[ \text{Swelling} = 100 \frac{W_t - W_0}{W_0} \]  
Eq.1

Where \( W_0 \) is initial weight of the gel and \( W_t \) is final weight of gel at time \( t \).

Diffusion coefficient of drug in GMO matrices
To evaluate the diffusion coefficient, we used approximate solution. The approximate solution of this equation as follows:

\[ \frac{M_t}{M_{\infty}} = (1 + \alpha)(1 - x) \]
\[ \alpha = \frac{A}{\pi R^2 K_p} \]  
Eq.2

Where \( x \) can be calculated from:

\[ \frac{D t}{a^2} = \frac{3}{40} \alpha^3 \left[ \frac{1}{x} - 1 \right]^3 + \frac{3(\alpha + 5)}{160} \alpha^2 \left[ \frac{1}{x} - 1 \right]^2 + \frac{3 \alpha^2(5 - 3 \alpha)}{80} \left[ \frac{1}{x} - 1 - \ln \left( \frac{1}{x} \right) \right] \]  
Eq.3

At the first \( x \) was calculated from ratio of \( \frac{M_t}{M_{\infty}} \) at different time and then right – hand side of equation 3 was plotted versus time. Slope of this line is \( \frac{D}{a^2} \) from which \( D \) can be obtained.

Mathematical modeling: Mathematical models of drug delivery systems can be employed to provide information about diffusion processes and drug release (2-3).

Lumped model: If we assumed the resistance of drug release at the interface of particle and medium, internal resistance is neglected. According to this assumption, a logarithmic equation (Eq.2) was used to describe the release of drug.

\[ C - C_{eq} / C_0 - C_{eq} = \exp(-kt) \]  
Eq.4

Where \( C \) is concentration of drug in medium at time \( t \) and \( C_0 \) is initially concentration, \( C_{eq} \) is equilibrium concentration of drug, \( k \) is constant equation.

RESULTS AND DISCUSSION
Swelling studies: Effect of amount of drug on water uptake is shown in Figure 1. It was shown that the water uptake decreased with increasing the percentage of loading. Addition of PEG 300 had also caused significant effect on water uptake (see Figure 2). Water uptake increased with enhance in amount of PEG 300 which could explain that incorporation of hydrophilic material transformed the cubic phase into lamellar phase and lamellar formation did not resist water uptake.

Whereas when water/GMO increased, amount of k decreased because cubic phase formed and mechanism of drug penetration controlled by degree of swelling.

CONCLUSION
In this paper we investigated the effect of percentage of Olanzapine and weight ratio of PEG/GMO, water/GMO on percentage of swelling. Release of Olanzapine from gel inserts was mainly occurred with swelling and diffusion controlled mechanism together. We used the lumped model to describe the mechanism of drug release.

REFERENCES