where n = number of dissolution points, R_t = percentage of dissolution of the reference product at time t, T_t = percentage of dissolution of the test product at time t.

The similarity factor (f_2) is a logarithmic reciprocal square root transformation of the sum of squared error and calculates the similarity between two dissolution profiles. Similarity factor (f_2) can be expressed as follows:

$$f_2 = 50 \log \left\{ \left[1 + \frac{1}{n} \sum_{t=1}^{n} (R_t - T_t)^2 \right]^{-0.5} 100 \right\}$$

Similarity and dissimilarity factors provide the similarity between two release profiles at selected time points. During comparison, at least 12 units of each product should be compared for at least 3 time points. The standard deviation at each time point for test or reference should not be more than 10%. Dissimilarity value from 0 to 15 and similarity value from 50 to 100 for any two profiles are considered as similar.

6.2. Swelling and erosion characterization for controlled-release dosage form

6.2.1. Swelling characterization

As discussed, drug-release behavior from dosage form is influenced by polymer composition. Solid orals with hydrophilic polymers exhibit swelling phenomena when they come in contact with the dissolution fluid. One of the mechanisms that stand out in most of the release mechanism is "swelling." This swelling phenomenon progressively leads to significant structural changes in the matrix of dosage form. This includes change in porosity and tortuosity of the matrix, which result in change in the diffusion rate of drug release. Swelling index determines the swelling ability of the polymer. Swelling index affects the drug release, retention time and, thus, the overall therapeutic efficacy of the dosage form. Hence, choice of a polymer with proper swelling ability is a prerequisite for the formulation of controlled-release dosage forms. The swelling study involves study of the weight gain by a unit dosage. The swelling study for tablets is performed using USP type 1 (Basket) dissolution apparatus using suitable dissolution medium at 50 rpm at 37 ± 0.5°C. The initial weight of the tablets before the swelling study is noted as W_1. The weight of the tablet after time intervals of 2, 4, 6, 8, and upto 12 h is noted as W_2. The swelling index or percentage of hydration is calculated using the following formula:

$$\text{Swelling index} = \frac{W_2 - W_1}{W_2} \times 100$$

where W_1 is the initial weight of the tablet, W_2 is the weight of the tablet after swelling study [13].

Various studies were conducted to evaluate the influence of the polymer on the tablet's swelling and were correlated with drug release. Recently, Berardi et al. [76] have studied the effect of various coexcipients on swelling and release of drug of various batches of zein tablets. The swelling behavior of zein was compared with that of EC and HPMC. Swelling behavior was determined using an USB microscope connected to a computer that took continuous images of the tablets over a period of 20 h. The overall change in size was extrapolated by image analysis. Drug release was also studied. Zein matrices bursted rapidly and then gradually released the drug. The coexcipients influenced the swelling behavior of zein to a greater extent than EC or HPMC.

Yassin and coworkers conducted swelling study for three excipients, namely HPMC, lactose, and Eudragit RSPO using terahertz-pulsed imaging (TPI) technique. TPI, using the reflection mode, measures 1D swelling of a compact tablet exposed to dissolution media. It can be used as a powerful tool to study diffusion in pharmaceutical compacts [77].

6.2.2. Erosion characterization

The release of drug from a controlled-release tablet involves the formation of a gel layer around the tablet. When a hydrophilic matrix comes into contact with GI fluids, the polymer absorbs water, swells, and forms a gel layer. The polymer swells to its maximum capacity and then erosion takes place. The water-soluble drug release from matrix is because of the mechanism of diffusion, and the poorly soluble drug is dominantly released with the mechanism of tablet erosion. Erosion dictates the release of the insoluble portion of the matrix. For poorly water-soluble drugs, polymeric matrix erosion plays a rate-limiting step for drug release. [78, 79]. Gravimetric method can be used to perform erosion study.

For erosion study, swollen tablets are weighed to determine the extent of water uptake and then dried in a convection oven at 40–60°C for 12 h. Then, the weight of dried tablets is measured. Data are collected at different time intervals. The modified USP paddle apparatus at 100 rpm is utilized, where the agitation was included. This produces a significant difference in erosion when compared with the static condition [80].

$$\%\text{Matrix erosion} = \frac{W_i - W_t}{W_i} \times 100,$$

where W_i is the initial weight of tablet and W_t is the weight of dried matrices at sampling times.

Shameem et al. studied the colonic release of two batches of acetaminophen CR tablets A and B. Tablet A was prepared with 50 mg of EC, and tablet B was