**INTRODUCTION**

The most preferred route of administration of dosage forms is oral route, due to its potential advantages such as ease of administration, convenient dosing, self-medication, no pain, and patient compliance. Hence, tablets and capsules are the most popular dosage forms [1]. However, the important drawback of these dosage forms is dysphagia [2]. The above-mentioned problem can be solved by developing a fast disintegrating and dissolution rate when compared to the formulations with superdisintegrants alone. The order of superdisintegrants in enhancing the dissolution rate of PLH is crospovidone (CPV) > croscarmellose sodium (CCS) > sodium starch glycolate (SSG). Formulation, EF$_3$ (10% CPV and 1:3; citric acid: NaHCO$_3$ ratio, respectively) had the highest dissolution efficiency at 10 minutes (DE$_{10}$=82.74%); the first order dissolution rate constant (K$_9$=0.141/minutes) with a regression coefficient (r$^2$=0.974) and lesser time for 90% of drug release (t$_{90}$=4 minutes), was considered as the optimal ODT in this study. Formulation EF$_3$ passed the test for stability.

**Conclusion:** Hence, an effective PLH ODT was formulated by the direct compression technique with disintegration by combination of superdisintegrants and effervescent mixture, will fasten the onset of action and enhances the bioavailability of PLH in comparison to its conventional tablets.

**Keywords:** Propranolol HCl, Oral disintegrating tablet, Sodium starch glycolate, Croscarmellose sodium, Crospovidone, Direct compression, In vitro dissolution studies.

**ABSTRACT**

Objective: The current research work is intended to formulate propranolol HCl (PLH) as orally disintegrating tablet (ODT). It is also intending to check the superiority in a combination of superdisintegrants and effervescent mixture than the use of superdisintegrants alone by a direct compression technique. To fasten the onset of action and thereby enhancing the bioavailability of PLH in comparison to its conventional tablets.

Methods: Standard calibration curve of PLH was obtained in pH 6.8 phosphate buffer by spectrophotometric method, drug-excipient compatibility studies were carried by Fourier transform infrared (FT-IR) studies. All the formulations were evaluated for pre and postcompression studies. Accelerated stability studies were carried out up to 6 months for the optimized formulation, EF$_3$.

Results and Discussion: Superdisintegrants used in the study are compatible with PLH. Pre- and post-compression parameters were within the acceptable limits for all formulations. In vitro dissolution kinetic studies indicate the release of PLH from ODT increases as the concentration of superdisintegrants as well as the ratio of citric acid: NaHCO$_3$ of effervescent mixture increases. Formulations with an effervescent mixture are having rapid disintegration and dissolution rate when compared to the formulations with superdisintegrants alone. The order of superdisintegrants in enhancing the dissolution rate of PLH is crospovidone (CPV) > croscarmellose sodium (CCS) > sodium starch glycolate (SSG). Formulation, EF$_3$ (10% CPV and 1:3; citric acid: NaHCO$_3$ ratio, respectively) had the highest dissolution efficiency at 10 minutes (DE$_{10}$=82.74%); the first order dissolution rate constant (K$_9$=0.141/minutes) with a regression coefficient (r$^2$=0.974) and lesser time for 90% of drug release (t$_{90}$=4 minutes), was considered as the optimal ODT in this study. Formulation EF$_3$ passed the test for stability.

Conclusion: Hence, an effective PLH ODT was formulated by the direct compression technique with disintegration by combination of superdisintegrants and effervescent mixture, will fasten the onset of action and enhances the bioavailability of PLH in comparison to its conventional tablets.

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Methods

Standard calibration curve of PLH in pH 6.8 phosphate buffer [9]

Was obtained at the $\lambda_{\text{max}}$ 279 nm using an ultraviolet (UV)-visible spectrophotometer (UV-1700, Shimadzu, Mumbai, India) and represented in (Fig. 1). Which was further used for drug release calculations of in vitro dissolution studies and assay.

Drug-excipient compatibility/Fourier transform infrared (FTIR) studies [10]

FTIR studies were performed on drug and drug: Superdisintegrants (1:1). The samples were appropriately diluted with dried KBr (2 mg sample in 200 mg KBr) and crushed to make pellets under hydraulic pressure of 600 kg and then the resulting pellets were subjected to analysis by an IR spectrophotometer (Shimadzu, FTIR 8700), in the region between 400 and 4000/cm. FTIR spectra of pure PLH and drug: Superdisintegrants (1:1) samples were represented in Fig. 2.

Preparation of PLH ODT [9]

All the formulations were prepared by direct compression method by keeping the amount of PLH constant at 40 mg. The composition of other excipients is varied as mentioned in formulation tables (Tables 1 and 2). In these formulations SSG, CCS and CPV are used as superdisintegrants, mannitol as a directly compressible diluent, aspartame is an artificial sweetener, powder vanilla flavor as flavoring agent, magnesium stearate as a lubricant, talc as glidant, SLS as a surfactant solubility enhancer, citric acid, and NaHCO$_3$ as effervescent mixture. PLH and all the other excipients excluding magnesium stearate and talc were co-sifted through Sieve No. #40 (ASTM), blended uniformly in a poly bag for 10 minutes and lubricated with Sieve No. # 60 (ASTM), passed magnesium stearate and talc and mixed in a poly bag for an additional 2-3 minutes. Tablets were compressed on a tabulating machine (16 station, Cadmach Pharma Machinery Pvt. Ltd., India) fitted with 8 mm standard round punches with an average weight of 200 mg and hardness of 2-3 kg/cm$^2$.

Precompression studies [12]

The directly compressible tablet blends were evaluated for precompression studies.

Angle of repose (θ)

Was determined by funnelling method. The blend was poured through the walls of a funnel, which was fixed at a position such that its lower tip was at a height of exactly 2 cm above hard surface. The blend was
Tapped density (TD)

After the determination of BD, the measuring cylinder was fitted with a TD apparatus. The tapped volume was measured by tapping the powder for 500 times. Later the tapping was done for another 750 times, and the tapped volume was noted (the difference between these two volumes should be <2%). If it is more than 2%, tapping is continued for another 1250 times, and the constant tapped volume was noted. The TD was calculated by the equation.

\[ \text{Tapped density} = \text{weight of powder/tapped volume} \]  

Carr’s index (CI): The percentage of CI is calculated by the equation.

\[ \text{CI} = \left( \frac{\text{tapped density-bulk density}}{\text{tapped density}} \right) \times 100 \]  

Hausner’s ratio (HR): Is a number that correlates to the flowability of powder. It is calculated by the equation.

\[ \text{HR} = \frac{\text{tapped density}}{\text{bulk density}} \]  

Precompression studies of all the formulations were carried out in triplicate; the consolidated results (mean±SD) were tabulated in Table 3.

Postcompression studies

Table weight variation [12]

An electronic balance (Mettler Toledo, 3-MS-S/MS-L, Switzerland) was used to accurately weigh the individual weight of 20 tablets which were randomly selected from each formulation. The (mean±SD) values were calculated.

Friability test [12]

The friability of the 20 tablets from each formulation was tested by a friabilitator (ERWEKA, TAR 120, Germany) at a speed of 25 r pm for
Table 3: Precompression studies of propranolol HCl ODT

| F code | Angle of repose (°) | BD (g/cm³) | TD (g/cm³) | Hausner’s ratio | Carr’s index (%) |
|--------|---------------------|------------|------------|-----------------|------------------|
| DC₁    | 31.08               | 0.528      | 0.692      | 1.31            | 23.69            |
| DC₂    | 30.78               | 0.541      | 0.652      | 1.21            | 17.02            |
| DC₃    | 31.92               | 0.530      | 0.614      | 1.16            | 15.88            |
| DC₄    | 29.53               | 0.538      | 0.639      | 1.18            | 15.30            |
| DC₅    | 29.62               | 0.512      | 0.621      | 1.21            | 15.55            |
| DC₆    | 30.12               | 0.521      | 0.630      | 1.21            | 17.30            |
| DC₇    | 28.17               | 0.543      | 0.640      | 1.17            | 15.15            |
| DC₈    | 29.61               | 0.509      | 0.599      | 1.17            | 15.05            |
| DC₉    | 30.09               | 0.534      | 0.682      | 1.27            | 21.70            |
| EF₁    | 30.68               | 0.540      | 0.633      | 1.17            | 14.69            |
| EF₂    | 29.18               | 0.543      | 0.652      | 1.21            | 16.71            |
| EF₃    | 29.72               | 0.531      | 0.611      | 1.15            | 15.06            |
| EF₄    | 29.32               | 0.572      | 0.670      | 1.17            | 14.62            |
| EF₅    | 27.71               | 0.552      | 0.685      | 1.24            | 19.80            |
| EF₆    | 27.32               | 0.546      | 0.678      | 1.24            | 19.46            |
| EF₇    | 26.45               | 0.543      | 0.689      | 1.26            | 21.11            |
| EF₈    | 29.64               | 0.580      | 0.677      | 1.16            | 14.32            |
| EF₉    | 27.29               | 0.569      | 0.703      | 1.23            | 19.06            |

ODT: Orally disintegrating tablet, BD: Bulk density, TD: Tapped density

4 minutes, the tablets were then de-dusted, reweighed, and percentage weight loss was calculated by the equation,

\[ \% \text{ friability} = \left( \frac{\text{initial weight} - \text{weight after friability}}{\text{initial weight}} \right) \times 100 \]  

\[ \text{Hardness test [12] } \]

To evaluate the diametrical crushing strength, three tablets from each formulation were tested using a hardness tester (Monsanto type hardness tester, MHT-20, Campbell Electronics, India). The mean±SD values were calculated.

\[ \text{Thickness [12] } \]

Of three tablets from each formulation was determined using a vernier caliper (Mitutoyo Corporation, Japan). The mean±SD values were calculated.

\[ \text{In vitro disintegration time and fineness of dispersion [13] } \]

It is specified in the European Pharmacopeia (EP 6.0) that disintegration time determination procedure for ODT is same as that of conventional uncoated tablets and the tablets should be dispersed within <3 minutes. The obtained tablet’s dispersion was passed through a sieve screen with a nominal mesh aperture of 710 mm to confirm the fineness of dispersion. It was carried out in replicates of three tablets from each formulation and mean±SD values were calculated.

\[ \text{Wetting time and water absorption ratio [14] } \]

A piece of tissue paper folded twice was placed in Petri dish having an internal diameter of 5.5 cm, containing 6 mL of water. A tablet was placed on the paper and the time required for complete wetting was measured as wetting time, using a stopwatch. The wetted tablet was then reweighed and water absorption ratio (R) was determined using following equation.

\[ \text{Water absorption ratio (R)=}\left(\frac{W_{w}-W_{j}}{W_{w}}\right)\times 100 \]  

Where, \( W_w \) and \( W_j \) were the weights of the tablet before and after water absorption.

\[ \text{Assay [9] } \]

To evaluate the drug assay, three tablets from each formulation were powdered in motor and pestle. Blend equivalent to 1 mg of PLH was accurately weighed and transferred into a 100 mL volumetric flask. Then, the volume was made up to 100 mL with pH 6.8 phosphate buffer and ultra-sonicated for 2 minutes to extract the PLH from the tablet blend and filtered through 0.45 µm polytetrafluoroethylene (PTFE) filter disc, the filtrate was suitably diluted if necessary and its absorbance was measured by UV-visible spectrophotometer at 279 nm.

Postcompression studies of all the formulations, except friability test were carried out in triplicate (n=3); the consolidated results as (mean±SD) were tabulated in Table 4.

\[ \text{In vitro dissolution studies [9] } \]

Were performed for three tablets form each formulation using the dissolution apparatus (Labindia Disso 2000, Labindia Analytical Instruments Pvt Ltd, India) with USP-II/paddle. Each dissolution flask contains 900 mL of pH 6.8 phosphate buffer; speed of the paddle was maintained at 50 rpm; the temperature was kept stable at 37°C±0.5°C. At required time intervals, 5 mL of dissolution media was withdrawn with a pipette containing 0.45 µ (PTFE) filter disc, suitably diluted if necessary and its absorbance was measured by UV-visible spectrophotometer at 279 nm. Furthermore, 5 mL of fresh pH 6.8 phosphate buffer was replaced to the dissolution flask to keep the volume of dissolution medium constant. The dissolution profiles were represented graphically in Fig. 3.

\[ \text{In vitro dissolution kinetics [15] } \]

The in vitro drug release data were fitted into kinetic models to plot dissolution profiles (cum% drug dissolved versus time) and first order plots (log% drug undissolved versus time) as per the following equations.

\[ \text{Zero order: } Q_{t} = Q_{0} + K_{t} t \]  

\[ \text{First order: } \log Q_{t} = \log Q_{0} - K_{t} t/2.303 \]  

Where, \( Q_{0} \) is the amount of the drug dissolved in time t, \( Q_{t} \) is the initial amount of drug in the solution; \( K_{0} \) and \( K_{t} \) refers to the rate constants of zero and first order, respectively.

\[ \text{In vitro dissolution kinetic parameters } \]

Dissolution efficiency at 10 minutes (DE₁₀), at 12 minutes (DE₁₂), at 14 minutes (DE₁₄), and time for 90% drug release (t₀.₉₀) were calculated from dissolution profiles. Equations for calculating \( \text{DE}_{10} \) and \( \text{DE}_{12} \) were used in the following equations.

\[ \text{DE}_{10} = \frac{1}{2} (C_{i} + C_{j})(t_{2} - t_{1}) \]  

\[ \text{DE}_{12} = \frac{1}{2} (C_{i} + C_{j})(t_{3} - t_{2}) \]  

\[ \text{t}_{12} = \text{t}_{0.90} \]  

Where, Cᵢ and Cⱼ were the absorbance readings for the tablet sample at the beginning of dissolution and a reference point, respectively.
Table 4: Postcompression studies of propranolol HCl ODT

| F code | Weight variation (kg/cm²) | Thickness (mm) | Friability* (%) | Wetting time (seconds) | In vitro DT (seconds) | Water absorption ratio (%) | Assay (%) |
|--------|--------------------------|----------------|-----------------|------------------------|-----------------------|---------------------------|-----------|
| DC     | 0.202±2.97               | 2.8±0.24       | 3.5±0.24        | 0.74                   | 50.00±0.01            | 98.02±0.30                | 6.21±0.61 | 94.24±0.97 |
| DC     | 0.205±0.97               | 2.9±0.16       | 3.5±0.48        | 0.66                   | 44.6±1.21             | 90.12±1.53                | 9.41±0.02 | 95.68±0.48 |
| DC     | 0.202±0.99               | 2.7±0.24       | 3.5±0.48        | 0.49                   | 42.6±1.77             | 89.16±0.90                | 1.30±0.53 | 95.47±0.12 |
| DC     | 0.204±1.47               | 2.9±0.12       | 3.4±0.97        | 0.49                   | 58.6±1.11             | 117.2±1.33                | 6.53±1.12 | 94.24±0.44 |
| DC     | 0.201±0.99               | 2.8±0.12       | 3.5±0.24        | 0.49                   | 54.6±2.21             | 115.2±2.08                | 8.11±1.55 | 94.56±0.16 |
| DC     | 0.207±0.48               | 2.9±0.16       | 3.5±0.97        | 0.66                   | 54.25±1.10            | 102.3±0.88                | 11.66±0.77 | 96.47±0.48 |
| DC     | 0.202±1.98               | 2.9±0.16       | 3.4±0.79        | 0.80                   | 59.6±1.12             | 122.2±2.5                | 3.41±0.01 | 95.29±0.12 |
| DC     | 0.204±2.45               | 2.7±0.24       | 3.5±0.48        | 0.82                   | 56.33±0.87            | 117.2±1.15                | 4.86±0.99 | 95.29±0.44 |
| DC     | 0.203±1.47               | 2.8±0.24       | 3.5±0.48        | 0.40                   | 56.12±2.21            | 113.0±2.10                | 5.87±1.44 | 94.66±0.12 |
| EF     | 0.206±1.60               | 2.6±0.16       | 3.5±0.48        | 0.25                   | 16.6±1.12             | 26.3±0.44                 | 2.33±0.42 | 94.40±0.44 |
| EF     | 0.202±1.68               | 2.7±0.24       | 3.5±0.24        | 0.49                   | 13.33±0.88            | 22.0±1.33                 | 2.73±0.71 | 97.3±0.12  |
| EF     | 0.203±0.97               | 2.7±0.24       | 3.5±0.48        | 0.41                   | 11.0±0.12             | 13.6±1.11                 | 2.59±0.12 | 96.57±0.48 |
| EF     | 0.206±0.58               | 2.7±0.24       | 3.5±0.79        | 0.41                   | 16.0±0.66             | 29.6±0.88                 | 9.36±1.02 | 95.69±0.11 |
| EF     | 0.209±1.25               | 2.8±0.24       | 3.5±0.48        | 0.33                   | 19.0±0.66             | 28.2±0.66                 | 21.3±2.45 | 95.21±0.12 |
| EF     | 0.202±1.13               | 2.9±0.16       | 3.4±0.48        | 0.33                   | 20.32±0.88            | 27.0±1.33                 | 22.5±2.93 | 96.02±0.12 |
| EF     | 0.204±0.78               | 2.6±0.16       | 3.5±0.97        | 0.49                   | 24.3±1.11             | 37.0±1.33                 | 18.45±1.34 | 98.72±0.16 |
| EF     | 0.207±0.79               | 2.7±0.24       | 3.5±0.79        | 0.49                   | 23.0±0.66             | 35.6±0.44                 | 20.7±2.25 | 94.88±0.66 |
| EF     | 0.204±0.58               | 2.8±0.24       | 3.5±0.79        | 0.66                   | 26.3±0.44             | 34.6±1.78                 | 2.14±1.13 | 97.57±0.66 |

*Except friability test all other were performed as n=3 and the values are given as mean±SD. ODT: Orally disintegrating tablet

RESULTS AND DISCUSSION

Standard calibration curve of PLH in pH 6.8 phosphate buffer
Based on the measurement of absorbance at 279 nm in pH 6.8 phosphate buffer in the concentration range of 10-50 µg/ml, a straight line with an equation: y=0.0193x+0.0151 and a regression coefficient (r²) of 0.99983 was obtained (Fig. 1).

Drug-excipient compatibility/FTIR studies
The FTIR spectrum of PLH showed a characteristic secondary amine –NH stretch at 3280/cm, a C-H stretch at 2964/cm, an arylC¼C stretch at 1579/cm, an aryl O–CH symmetric stretch at 1240/cm, an aryl O–CH asymmetric stretch at 1030/cm, and a peak at 798/cm due to alpha-substituted naphthalene. Comparison of FTIR spectra of pure drug with the drug: Superdisintegrant (1:1 ratio) samples indicate the chemical stability of drug in the 6 month-accelerated stability sample of formulation EF, was compared with the drug alone by FTIR studies (Shimadzu, FTIR 8700), recorded in the region of 400-4000/cm, by KBr pellet method. The consolidated results of postcompression studies on accelerated stability samples of formulation EF, except friability test were carried out in triplicate and the results as mean±SD were tabulated in Table 6. FTIR spectra of pure PLH and 6 month-accelerated stability sample of formulation EF, were represented in Fig. 4. In vitro dissolution profiles of accelerated stability samples of formulation EF, were represented graphically in Fig. 5.
absence of chemical interaction between PLH and superdisintegrants used in the study (Fig. 2).

**Precompression studies**

Of the directly compressible blends of all formulations, reveals that the angle of repose was found between 26° 45' and 31° 92'; BD between 0.59 and 0.580 g/cm³; TD between 0.611 and 0.703 g/cm³; HR between 1.15 and 1.31, and CI between 15.05% and 23.69%. The micromeritic studies indicate better flow and compression characteristics of all the formulations. In these formulations sugar based excipient (Mannitol) is used as diluent, which impart good flow and compressibility to the directly compressible blends. It also exhibits the high aqueous solubility and sweetness, and hence, impart taste masking property and a pleasing mouth feel[18] (Table 3).

**Postcompression studies**

Of all the formulations, reveals that the weight variation of tablets was found to be 0.201-0.208%. The average thickness of tablets was found to be 3.4-3.5 mm. The average hardness of the tablets was 2.6-2.9 Kg/cm², indicating satisfactory mechanical strength. The % weight loss in the friability test ranges from 0.25% to 0.82%, which was N-methyltryptamine 1% as per official requirement of Indian Pharmacopoeia indicating a good mechanical strength of tablets. Assay of all the prepared batches is within 94.24-98.72% of the labeled content, indicating content uniformity of all the formulation. The wetting time of all the formulations was obtained in the range of 11.00-59.66 seconds. As the concentration of superdisintegrant increases, there is a significant decrease in the wetting time and in vitro disintegration time. Wetting is related to the inner structure of the tablets, hydrophilicity of the components and swelling mechanism of superdisintegrant. The water absorption ratio was related to the hydrophilicity of the matrix. This phenomenon was similar even with the combination of superdisintegrants with effervescent mixture in different ratios (1:1; 1:2, and 1:3). The order of superdisintegrant’s efficiency is CPV>CCS>SSG. The formulation EF₃ (with 10% of CPV+1:3 ratio of citric acid: NaHCO₃ respectively) which shows minutes wetting time of 1.100 seconds; minutes in vitro disintegration time of 1.366 seconds and max water absorption ratio of 25.39% is an optimized formulation (Table 4). Decrease in the wetting and disintegration times were clearly observed in formulations with a combination of superdisintegrants and effervescent mixture than the formulations with superdisintegrants alone. This is due to the synergistic effect of a combination of two approaches, namely superdisintegrants addition with effervesence approach. The evolved CO₂ gas accelerated the breakdown of the tablets [19].

**In vitro dissolution studies**

Dissolution profiles are represented graphically in Figs. 1 and 2 indicate that the release rate increases with an increase in concentration of superdisintegrant. Based on the values of Kₑ, the order of superdisintegrants in enhancing the dissolution rate of PLH in its ODT is (CPV>CCS>SSG). Formulations with a combination of superdisintegrants and effervescent mixture are having rapid disintegration and dissolution rate when compared to the formulations with superdisintegrants alone. A combination of two approaches, namely superdisintegrant addition with effervesence approach resulted in an increase in the drug dissolution rate, could be due to the synergistic effect of superdisintegrant and CO₂ produced due to the wetting of the tablets. The evolved gas accelerated the breakdown of the tablets as indicated by their lesser disintegration times [19]. Dissolution rate also enhances with an increase in citric acid: NaHCO₃ ratio of effervescent mixture (1:1<1:2<1:3) as it requires three molecules of sodium bicarbonate to neutralize one molecule of citric acid. Hence, the desired ratio of citric acid: NaHCO₃=1:3.44 by weight [20]. Formulation EF₃ (with 10% CPV AND 1:3, citric acid: NaHCO₃ ratio, 2.6-2.9 Kg/cm² wetting time of 11.00 seconds; 1.366 minutes in vitro disintegration time and 25.39% max water absorption ratio is an optimized formulation (Table 3).

**Table 5: In vitro dissolution kinetics of propranolol HCl ODT**

| F code | tₑ (minutes) | Dₑ (%) | First order dissolution rate constant; Kₑ (minutes⁻¹) | First order regression coefficient (r²) |
|--------|--------------|--------|-----------------------------------------------------|--------------------------------------|
| DC₁    | 18           | 46.35  | 0.110                                               | 0.667                                |
| DC₂    | 16           | 50.40  | 0.113                                               | 0.652                                |
| DC₃    | 14           | 53.44  | 0.118                                               | 0.653                                |
| DC₄    | >24          | 30.82  | 0.123                                               | 0.788                                |
| DC₅    | 24           | 38.92  | 0.133                                               | 0.809                                |
| DC₆    | 24           | 41.72  | 0.140                                               | 0.802                                |
| DC₇    | >24          | 29.97  | 0.127                                               | 0.908                                |
| DC₈    | >24          | 31.47  | 0.131                                               | 0.915                                |
| DC₉    | >24          | 34.64  | 0.149                                               | 0.927                                |
| EF₁    | 6            | 80.00  | 0.129                                               | 0.973                                |
| EF₂    | 6            | 81.84  | 0.136                                               | 0.979                                |
| EF₃    | 4            | 82.74  | 0.141                                               | 0.974                                |
| EF₄    | 8            | 75.39  | 0.074                                               | 0.993                                |
| EF₅    | 8            | 76.32  | 0.086                                               | 0.969                                |
| EF₆    | 6            | 77.86  | 0.094                                               | 0.966                                |
| EF₇    | 14           | 68.83  | 0.064                                               | 0.935                                |
| EF₈    | 14           | 69.89  | 0.068                                               | 0.982                                |
| EF₉    | 10           | 71.92  | 0.080                                               | 0.993                                |

ODT: Orally disintegrating tablet

**Table 6: Postcompression studies on accelerated stability samples of formulation EF₃**

| Parameter                  | Initial | 45°C/75% RH 1 month | 45°C/75% RH 2 month | 45°C/75% RH 3 month | 45°C/75% RH 6 month |
|----------------------------|---------|---------------------|---------------------|---------------------|---------------------|
| Weight variation (%)       | 0.206±0.97 | 0.223±0.21          | 0.241±0.32          | 0.244±0.14          | 0.252±0.52          |
| Hardness (kg/cm³)          | 2.7±0.24 | 2.6±0.12            | 2.6±0.35            | 2.5±0.12            | 2.5±0.33            |
| Thickness (mm)             | 3.5±0.48 | 3.5±0.32            | 3.5±0.11            | 3.5±0.54            | 3.5±0.43            |
| Friability (%w/w)          | 0.41     | 0.43                | 0.51                | 0.53                | 0.50                |
| Dissolution (seconds)      | 11.00±1.12 | 11.35±0.12          | 12.35±0.34          | 12.5±0.38           | 12.55±0.42          |
| Wetting time (seconds)     | 13.66±1.11 | 14.12±0.13          | 14.76±0.32          | 14.23±0.45          | 14.52±0.21          |
| Water absorption ratio (%) | 25.39±5.15 | 25.78±0.15          | 26.23±0.22          | 27.35±0.42          | 27.11±0.35          |
| Assay (%)                  | 96.57±0.48 | 96.52±0.12          | 96.40±0.44          | 95.29±0.44          | 94.66±0.12          |

*Except friability test all other were performed as n=3 and the values are given as mean±SD. RH: Relative humidity.
respectively) released 90% of drug within lesser time of 4 minutes than others, was considered as the optimal ODT (Fig. 3).

**In vitro dissolution kinetics**
Formulation EF$_3$ had the highest DE$_{10}$ (82.74%); $K_1$ (0.141/minutes) with $r^2$ (0.974) and the lowest $t_{90}$ (4 minutes). Hence, it is the optimal ODT (Table 5).

**Accelerated stability studies**
As there were no significant differences in postcompression and in vitro dissolution profiles of initial and accelerated stability samples up to 6 months, formulation EF$_3$ passes the test for stability. FTIR spectrum of pure PLH is having primary amide group and two secondary amino groups. Two N-H stretching bands resulting from symmetrical and asymmetrical stretching in 3400-3520/cm correspond to primary amide group [18]. An FTIR spectrum of 6 month-accelerated stability sample of optimized formulation (EF$_3$) shows the same functional groups at the corresponding frequencies as that of pure drug. This, indicates no significant chemical interaction and change in functional groups of PLH occurred during the accelerated stability study of optimized formulation, EF$_3$ (Table 6, Figs. 4 and 5).

**CONCLUSION**
In the view of above findings, there is drug-excipient compatibility between PLH and superdisintegrants used in the study. All the formulations passed the pre- and post-compression parameters. The release rate of PLH from ODT increases as the concentration of superdisintegrants as well as the ratio of citric acid: NaHCO$_3$ of effervescent mixture increases. Formulations with an effervescent mixture are having rapid disintegration and dissolution rate when compared to the formulations with superdisintegrants alone. The order of superdisintegrants in enhancing the dissolution rate of PLH is CPV>CCS>SSG. Formulation EF$_3$ (with 10% CPV and 1:3, citric acid: NaHCO$_3$ ratio respectively) had the highest DE$_{10}$ (82.74%); $K_1$ (0.141/minutes) with $r^2$ (0.974) and the lowest $t_{90}$ (4 minutes), was considered as the optimal ODT. An accelerated stability study on EF$_3$ in the final pack up to 6 months indicates it passed the test for stability. Therefore, an effective PLH ODT was formulated by the direct compression technique with disintegration attained by a combination of superdisintegrants and effervescent mixture. This PLH ODT will better manage the hypertension, by fastening the onset of action and enhancing the bioavailability of PLH in comparison to its conventional tablets.

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