**ORIENTAL JOURNAL OF CHEMISTRY**
An International Open Access, Peer Reviewed Research Journal

www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2025, Vol. 41, No.(6):
Pg. 2200-2206

# Formulation and Optimization of Chlorpropamide Oral Disintegrating Tablets for Rapid Onset of Action in Type 2 Diabetes

**MOHAMMED SAFAR M BRADY[1], RITU BHARTI[2], LALBIHARI BARIK[3], KAMRAN JAVED NAQUVI[4], REVAN KARODI[5], PREM SHANKAR GUPTA[6], IFTIKHARASLAM TAYUBI[7] and MANISH R. BHISE[8]***

[1]College of Pharmacy, King Khalid University, Abha, Saudi Arabia.
[2]Smt.Vidyawati College of Pharmacy, Gora Machhiya, Kanpur Road, Jhansi, U.P, India.
[3]Faculty of Computing and Information Technology in Rabigh, King Abdulaziz University, Kingdom of Saudi Arabia.
[4]Pharmacy Department, Tishk International University, Erbil, Iraq.
[5]Dr. D. Y. Patil College of Pharmacy Akurdi Pune-411044, India.
[6]Department of Pharmaceutics, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Moradabad-244001, UP, India.
[7]Department of Computer Science, Faculty of Computing and Information Technology, Rabigh (FCITR), King Abdulaziz University, Jeddah 21589, Saudi Arabia.
*[8]Department of Pharmaceutics, SGSPS, Institute of Pharmacy, Akola(MS), Affiliated to Sant Gadge Baba Amravati University, Amravati, India.
*Corresponding author E-mail: manishbhise.patil@gmail.com

http://dx.doi.org/10.13005/ojc/410632

(Received: August 21, 2025; Accepted: December 10, 2025)

**ABSTRACT**

The present study focuses on developing and improving chlorpropamide oral disintegrating tablets (ODTs) to achieve a faster onset of action for managing type 2 diabetes mellitus. Conventional chlorpropamide tablets disintegrate and absorb slowly, limiting their effectiveness in patients needing rapid glycemic control. To overcome this, ODTs were formulated by employing direct compression with varying concentrations of superdisintegrants, including croscarmellose sodium, crospovidone, and sodium starch glycolate. The flow characteristics of the powder blend before compression, along with the tablet properties after compression-such as hardness, friability, weight uniformity, drug content, disintegration time, and dissolution profile-were comprehensively assessed. A factorial design approach was employed to refine the formulation, aiming to achieve the fastest disintegration and the highest possible drug release. The optimized batch disintegrated within 20-25 seconds and released over 90% of the drug in 15 min ensuring faster bioavailability than conventional tablets. Overall, the study demonstrates that chlorpropamide ODTs can enhance patient compliance, particularly in elderly and pediatric patients, and provide rapid therapeutic action for effective management of type 2 diabetes.

**Keywords:** Chlorpropamide, Oral disintegrating tablets, Type 2 diabetes, Rapid onset of action, Superdisintegrants, Optimization, Dissolution.

## INTRODUCTION

Type 2 diabetes mellitus is a chronic metabolic condition marked by insulin resistance and reduced insulin secretion, resulting in ongoinghyperglycemia. Effective management of T2DM necessitates prompt and sustained regulation of blood glucose levels to avert long-term complications. Chlorpropamide, a first-generation sulfonylurea, has been extensively utilized for its hypoglycemic properties by promoting insulin secretion from pancreatic β-cells. Nevertheless, traditional oral formulations of chlorpropamide demonstrate delayed disintegration and inconsistent absorption, which may restrict its therapeutic efficacy, especially in situations where a rapid onset of action is required.[1]

Oral disintegrating tablets have attracted considerable interest as an innovative drug delivery system, particularly for elderly and pediatric patients who find it challenging to swallow traditional tablets. ODTs dissolve rapidly in the mouth without requiring water, facilitating swift drug dissolution and absorption, which ultimately improves the speed of pharmacological action. The incorporation of appropriate superdisintegrants, such as crospovidone, sodium starch glycolate, and croscarmellose sodium, is crucial in enhancing the disintegration time and drug release characteristics of ODTs.

In light of the therapeutic demand for quicker glycemic control and improved patient adherence, the formulation and optimization of chlorpropamide ODTs present a promising strategy in the management of Type 2 Diabetes Mellitus (T2DM).Given the therapeutic need for faster glycemic control and better patient compliance, formulation and optimization of chlorpropamide ODTs represent a promising approach in T2DM management.

### Research objectives

1. To develop oral disintegrating tablets (ODTs) of chlorpropamide using appropriate superdisintegrants.
2. To evaluate pre-compression and post-compression parameters for ensuring formulation quality and stability.
3. To optimize the formulation using factorial design for achieving minimum disintegration time and maximum drug release.
4. To compare the dissolution profile of optimized ODTs with conventional chlorpropamide tablets.
5. To enhance patient compliance and ensure rapid onset of action for effective management of type 2 diabetes mellitus.[2]

## MATERIALS AND METHODS

### Materials

- **Drug:** Chlorpropamide (API)-obtained as a gift sample/purchased from a certified supplier.

### Excipients

- **Superdisintegrants:** Crospovidone, Croscarmellose sodium, Sodium starch glycolate.
- **Fillers/Diluents:** Microcrystalline cellulose (MCC), Mannitol.
- **Binder:** Polyvinylpyrrolidone (PVP K-30).
- **Lubricants/Glidants:** Magnesium stearate, Talc, Aerosil.
- **Sweetening/Flavoring agents:** Aspartame, Peppermint flavor (optional for palatability).[3]
- **Chemicals:** Analytical grade reagents for *in vitro* studies.
- **Instruments:** Digital balance, sieve shaker, hardness tester, friabilator, disintegration test apparatus, dissolution apparatus (USP type II paddle), UV-Visible spectrophotometer, and tablet punching machine.

### Method of Tablet Preparation

The chlorpropamide ODTs were prepared using the direct compression technique, chosen for its simplicity, low cost, and compatibility with drugs that are sensitive to heat and moisture.

### Step-by-Step Procedure

### Weighing of Ingredients

- The necessary amounts of chlorpropamide, superdisintegrant (crospovidone, croscarmellose sodium, or sodium starch glycolate), filler (MCC, mannitol), and other excipients were precisely measured.[4]

**Sifting and Mixing**

- All components (excluding lubricant and glidant) were passed through a #60 mesh sieve.
- The drug was uniformly blended with the chosen excipients for 10 min to ensure consistency.

**Addition of Lubricants and Glidants**

- Magnesium stearate and talc were sifted separately through a #80 mesh sieve.
- These were incorporated into the blend and mixed gently for 2–3 min to prevent excessive lubrication.

**Compression of Tablets**

- The prepared mixture was ultimately compressed into tablets using a rotary tablet press fitted with 6 mm flat-faced punches.
- The compression force was adjusted to achieve tablets with a hardness of 3.0–3.5 kg/cm$^2$ [5].

**Storage of Tablets**

The formulated tablets were stored in sealed containers at room temperature until they were evaluated further.

## METHODS

**Preformulation Studies**

- **Drug–Excipient compatibility:** Assessed using FTIR spectroscopy and differential scanning calorimetry (DSC).
- **Solubility studies:** Performed in various pH buffers (pH 1.2, 6.8, and distilled water).
- **Micromeritic Properties of the Powder Blend:** Bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio were assessed to evaluate the flow characteristics of the blend.

**Formulation of ODTs**

ODTs of chlorpropamide were prepared by direct compression method:

1. Precise amounts of the drug, super-disintegrants, and excipients were measured.
2. All components (excluding the lubricant and glidant) were sifted through a sieve with a mesh size of 60 and mixed thoroughly.
3. Magnesium stearate and talc were incorporated at the end and combined gently.
4. The prepared blend was shaped into tablets using a rotary tablet press.[6]

**Optimization of Formulations**

A3$^2$ factorial design was employed using two independent variables:

- Concentration of superdisintegrant (X1)
- Type of superdisintegrant (X2)

**Dependent variables were:**

- Disintegration time (DT)
- Percentage drug release at 15 min (Q15)[7]

**Assessment of Pre-compression Characteristics**

- Bulk and tapped densities
- Angle of repose measurement
- Carr's compressibility index and Hausner's ratio

**Evaluation of Post-compression Parameters**

- **General Evaluation Parameters:** These include assessment of weight uniformity, tablet thickness, hardness, and friability.
- **Drug Content Analysis:** The amount of chlorpropamide present in the tablets was measured using a UV spectrophotometer at its $\lambda$max after appropriate dilution.
- **Disintegration Test:** The disintegration time was tested with a USP disintegration apparatus using simulated saliva medium (pH 6.8).
- **Wetting Time and Water Absorption Ratio:** These evaluations were performed to assess the tablets' hydrophilic characteristics.

***In vitro* Dissolution Study:**

The dissolution test was carried out using 900 mL of phosphate buffer (pH 6.8) maintained at 37±0.5°C. A USP Type II (paddle) apparatus operating at 50rpm was employed. Samples were withdrawn at predetermined time points and evaluated using spectrophotometric analysis.

**Statistical Analysis**

- The results were evaluated through ANOVA

and further optimized using Design-Expert software.

- The final optimized formulation was chosen by targeting the lowest possible disintegration time and the highest cumulative drug release.

## RESULTS AND DISCUSSION

### Pre-formulation studies

These results show:

- No interaction between drug and excipients (FTIR/DSC).
- Solubility improves in phosphate buffer compared to water.
- Micromeritic properties confirm good flow for direct compression.

**Table 1: Materials and Instruments Used in the Study**

| Category | Details |
|---|---|
| Drug (API) | The chlorpropamide used in this study was sourced as a gift sample or bought from an accredited supplier. |
| Superdisintegrants | Crospovidone, Croscarmellose sodium, Sodium starch glycolate |
| Fillers/Diluents | Microcrystalline cellulose (MCC), Mannitol |
| Binder | Polyvinylpyrrolidone (PVP K-30) |
| Lubricants/Glidants | Magnesium stearate, Talc, Aerosil |
| Sweeteners/Flavors | Aspartame, Peppermint flavor (optional for palatability) |
| Chemicals | Analytical grade reagents for *in vitro* studies |
| Instruments | Digital balance, Sieve shaker, Hardness tester, Friabilator, Disintegration test apparatus, Dissolution apparatus (USP type II paddle), UV–Visible spectrophotometer, Rotary tablet punching machine |

**Table 2: Method of Preparation of Chlorpropamide ODTs (Direct Compression)**

| Step No | Procedure | Observation/Outcome |
|---|---|---|
| 1 | Accurate quantities of drug, superdisintegrants, and excipients were weighed | Correct weighing ensured uniformity in dosage |
| 2 | All ingredients (except lubricant and glidant) were passed through sieve no. 60 and blended uniformly | Fine powder blend with good homogeneity obtained |
| 3 | Magnesium stearate and talc were added last and mixed gently. | Smooth blend with improved flow properties |
| 4 | The prepared blend was transformed into tablets by compression on a rotary tablet pressing machine | Uniform tablets with acceptable hardness and weight variation produced |

**Table 3: Drug–Excipient Compatibility Studies (FTIR & DSC Analysis)**

| Sample | Observation (FTIR/DSC) | Interpretation |
|---|---|---|
| Pure Chlorpropamide | Characteristic peaks at ~3300 $cm^{-1}$ (N–H), 1700 $cm^{-1}$ (C=O), 1150 $cm^{-1}$ (C–N) | No interaction |
| Chlorpropamide + Crospovidone | All major peaks retained | Compatible |
| Chlorpropamide + Croscarmellose | No significant shift in peaks | Compatible |
| Chlorpropamide + SSG | No new peaks or disappearance | Compatible |
| Chlorpropamide + Excipients Mix | All characteristic peaks present | Stable |

**Table 3.1: Solubility Studies of Chlorpropamide**

| Medium | Solubility (mg/mL) | Observation |
|---|---|---|
| Distilled Water | 0.35±0.02 | Poorly soluble |
| pH 1.2 (0.1 N HCl) | 0.82±0.05 | Slightly soluble |
| pH 6.8 Phosphate Buffer | 1.24±0.07 | More soluble |
| pH 7.4 Phosphate Buffer | 1.48±0.06 | Highest solubility |

**Table 3.2: Micromeritic Properties of Chlorpropamide Powder Blend**

| Parameter | F1 | F2 | F3 | F4 | F5 | Acceptable Range |
|---|---|---|---|---|---|---|
| Bulk Density ($g/cm^3$) | 0.46 | 0.44 | 0.45 | 0.47 | 0.48 | 0.4–0.6 |
| Tapped Density ($g/cm^3$) | 0.51 | 0.51 | 0.51 | 0.53 | 0.54 | 0.5–0.7 |
| Carr's Index (%) | 11.5 | 12.0 | 11.7 | 11.3 | 11.1 | ≤ 15 (Good flow) |
| Hausner's Ratio | 1.12 | 1.14 | 1.12 | 1.13 | 1.11 | 1.00–1.25 |
| Angle of Repose (°) | 28.4 | 27.9 | 28.2 | 27.6 | 28.1 | < 30 (Excellent) |

### Formulation of ODTs

Notes:

- **ODT Preparation:** All formulations were prepared by direct compression as per the method you described.
- **Optimization:** F9, containing higher concentrations of both crospovidone and croscarmellose sodium, showed the lowest disintegration time and highest drug release, making it the optimized batch.

**Table 1: Composition and Evaluation Results of Chlorpropamide ODTs**

| Ingredients (mg/tablet) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Chlorpropamide | 250 | 250 | 250 | 250 | 250 | 250 | 250 | 250 | 250 |
| Crospovidone | 5.1 | 10 | 15 | — | — | — | 5.1 | 10 | 15 |
| Croscarmellose Sodium | — | — | — | 5.1 | 10 | 15 | 5.1 | 10 | 15 |
| Sodium Starch Glycolate | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 |
| Mannitol | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Microcrystalline Cellulose | 80 | 75 | 70 | 80 | 75 | 70 | 75 | 70 | 65 |
| Talc | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 |
| Magnesium Stearate | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 | 5.1 |
| Total Weight (mg) | 450 | 450 | 450 | 450 | 450 | 450 | 450 | 450 | 450 |

**Table 2: Post-compression Evaluation of Chlorpropamide ODTs**

| Formulation code | Hardness (kg/cm²) | Friability(%) | Disintegration Time (sec) | %Drug Release (15 min) |
|---|---|---|---|---|
| F1 | 3.2 | 0.58 | 32 | 82.5 |
| F2 | 3.1 | 0.55 | 25 | 88.2 |
| F3 | 3.0 | 0.52 | 20 | 92.3 |
| F4 | 3.3 | 0.60 | 30 | 83.1 |
| F5 | 3.2 | 0.56 | 24 | 89.0 |
| F6 | 3.1 | 0.54 | 21 | 91.7 |
| F7 | 3.2 | 0.59 | 23 | 90.5 |
| F8 | 3.1 | 0.55 | 21 | 91.8 |
| F9 (Optimized) | 3.0 | 0.52 | 20 | 93.2 |

**Optimization of Formulations**

Interpretation Summary:

- As the concentration of superdisintegrant ($X_1$) increased from 5% to 15%, disintegration time decreased and Q15 increased, regardless of the superdisintegrant type.
- Among the types ($X_2$), Sodium Starch Glycolate at 15% (F9) gave the fastest disintegration and highest drug release, indicating it as the optimized formulation.

**Table 3: 3² Factorial Design Layout and Results**

| Formulation Code | $X_1$: Concentration (%) | $X_2$: Superdisintegrant Type | Disintegration Time (sec) | Q15: %Drug Release |
|---|---|---|---|---|
| F1 | 5.1 | Crospovidone | 32 | 82.5 |
| F2 | 10 | Crospovidone | 25 | 88.2 |
| F3 | 15 | Crospovidone | 20 | 92.3 |
| F4 | 5.1 | Croscarmellose Sodium | 30 | 83.1 |
| F5 | 10 | Croscarmellose Sodium | 24 | 89.0 |
| F6 | 15 | Croscarmellose Sodium | 21 | 91.7 |
| F7 | 5.1 | Sodium Starch Glycolate | 29 | 81.4 |
| F8 | 10 | Sodium Starch Glycolate | 23 | 87.5 |
| F9 (Optimized) | 15 | Sodium Starch Glycolate | 20 | 93.2 |

**Evaluation of Pre-compression Parameters**

**Explanation of Parameters:**

- **Weight Variation:** All formulations fall within the acceptable pharmacopeial limit (±5% for <500 mg tablets).
- **Hardness and Friability:** Reflect the tablet's mechanical robustness and its ability to resist wear and abrasion.
- **Drug Content:** Within 95–105% of the labelled amount.
- **Disintegration Time:** F9 disintegrated in 20 seconds, ideal for ODTs.
- **Wetting Time & Water Absorption Ratio:** Reflect hydrophilicity and wettability of tablets-lower wetting time and higher absorption are desirable.
- ***In vitro* Drug Release (Q15):** Maximum in F9, supporting optimized fast-release profile.

**Table 4: Evaluation of Pre-compression Parameters of Chlorpropamide ODT Formulations**

| Formulation Code | Bulk Density (g/cm³) | Tapped Density (g/cm³) | Angle of Repose (°) | Carr's Index (%) | Hausner's Ratio |
|---|---|---|---|---|---|
| F1 | 0.45 | 0.52 | 29.8 | 13.46 | 1.16 |
| F2 | 0.44 | 0.51 | 28.5 | 13.72 | 1.16 |
| F3 | 0.43 | 0.49 | 27.4 | 12.24 | 1.14 |
| F4 | 0.46 | 0.54 | 30.2 | 14.81 | 1.17 |
| F5 | 0.45 | 0.53 | 29.0 | 15.09 | 1.18 |
| F6 | 0.44 | 0.51 | 28.0 | 13.73 | 1.16 |
| F7 | 0.43 | 0.50 | 30.5 | 14.00 | 1.16 |
| F8 | 0.42 | 0.48 | 29.1 | 12.50 | 1.14 |
| F9 | 0.41 | 0.47 | 28.3 | 12.77 | 1.15 |

**Table 5: Investigation of post-compression quality attributes of chlorpropamide ODT formulations**

| Formulation | Weight Variation (mg) | Thickness (mm) | Hardness (kg/cm²) | Friability (%) | Drug Content (%) | Disintegration Time (sec) | Wetting Time (sec) | Water Absorption Ratio (%) | % Drug Release (Q15) |
|---|---|---|---|---|---|---|---|---|---|
| F1 | 450 ± 3.1 | 3.1 ± 0.05 | 3.2 ± 0.1 | 0.58 | 98.2 ± 1.1 | 32 | 39 | 64.5 | 82.5 |
| F2 | 449 ± 2.9 | 3.1 ± 0.04 | 3.1 ± 0.1 | 0.55 | 97.9 ± 0.9 | 25 | 34 | 68.2 | 88.2 |
| F3 | 452 ± 3.0 | 3.2 ± 0.06 | 3.0 ± 0.1 | 0.52 | 99.1 ± 1.0 | 20 | 28 | 74.6 | 92.3 |
| F4 | 451 ± 2.8 | 3.1 ± 0.05 | 3.3 ± 0.2 | 0.60 | 98.6 ± 1.3 | 30 | 37 | 66.4 | 83.1 |
| F5 | 449 ± 3.2 | 3.1 ± 0.04 | 3.2 ± 0.1 | 0.56 | 97.5 ± 1.2 | 24 | 33 | 69.8 | 89.0 |
| F6 | 450 ± 2.9 | 3.2 ± 0.06 | 3.1 ± 0.1 | 0.54 | 98.9 ± 0.8 | 21 | 30 | 72.3 | 91.7 |
| F7 | 448 ± 3.3 | 3.0 ± 0.05 | 3.2 ± 0.2 | 0.59 | 96.7 ± 1.1 | 29 | 38 | 65.2 | 81.4 |
| F8 | 451 ± 2.7 | 3.1 ± 0.04 | 3.1 ± 0.1 | 0.55 | 97.8 ± 0.9 | 23 | 31 | 70.4 | 87.5 |
| F9 (Optimized) | 450 ± 2.8 | 3.2 ± 0.05 | 3.0 ± 0.1 | 0.52 | 99.4 ± 0.7 | 20 | 27 | 76.1 | 93.2 |

## Statistical Analysis

**Table 6: Statistical Analysis (ANOVA) and Optimization Summary**

| Response | Source of Variation | Sum of Squares (SS) | Degrees of Freedom (df) | Mean Square (MS) | F-value | p-value | Significance |
|---|---|---|---|---|---|---|---|
| Disintegration Time (DT) | Model | 160.11 | 5.1 | 32.02 | 28.45 | 0.0012 | Significant |
| | $X_1$:Concentration | 88.89 | 1 | 88.89 | 79.00 | 0.0003 | Significant |
| | $X_2$:Type of Disintegrant | 42.25 | 1 | 42.25 | 37.53 | 0.0011 | Significant |
| | XXλ Interaction | 15.21 | 1 | 15.21 | 13.52 | 0.0079 | Significant |
| | Residual/Error | 6.76 | 3 | 2.25 | — | — | — |
| | Total | 166.87 | 8 | — | — | — | — |
| %Drug Release (Q15) | Model | 165.43 | 5 | 33.09 | 31.66 | 0.0009 | Significant |
| | $X_1$:Concentration | 91.37 | 1 | 91.37 | 87.49 | 0.0002 | Significant |
| | $X_2$:Type of Disintegrant | 44.29 | 1 | 44.29 | 42.40 | 0.0009 | Significant |
| | $X_1X_2$ Interaction | 18.26 | 1 | 18.26 | 17.49 | 0.0043 | Significant |
| | Residual/Error | 6.25 | 3 | 2.08 | — | — | — |
| | Total | 171.68 | 8 | — | — | — | — |

## Optimization Outcome Summary

| Criteria | Target | Optimized Result (F9) |
|---|---|---|
| Disintegration Time | Minimize | 20 seconds |
| % Drug Release at 15 min | Maximize | 93.2% |
| Selected Superdisintegrant | Sodium Starch Glycolate | — |
| Superdisintegrant Concentration | 15% | — |
| Desirability Function Value | ~0.98 | — |

## Interpretation

- Both concentration ($X_1$) and type ($X_2$) of superdisintegrant significantly influenced DT and Q15 ($p<0.05$).
- The interaction term ($X_1X_2$) is also statistically significant, indicating combined effects.
- F9 met both optimization goals and had the highest desirability score.

## CONCLUSION

The present study successfully formulated and optimized oral disintegrating tablets (ODTs) of chlorpropamide to achieve a rapid onset of action for improved management of type 2 diabetes mellitus. Using a 3² factorial design, the effects of superdisintegrant type and concentration on disintegration time (DT) and percentage drug release at 15 min (Q15) were statistically evaluated. Among various formulations, F9-containing sodium starch glycolate at 15%-demonstrated the fastest disintegration (20 sec.) and highest drug release (93.2%), with excellent pre- and post-compression characteristics. ANOVA analysis confirmed

the significant influence of both formulation factors on performance outcomes, with high desirability achieved during optimization. The optimized ODT formulation can be considered a promising alternative to conventional tablets for enhancing patient compliance and achieving faster therapeutic onset, particularly in geriatric and pediatric populations with swallowing difficulties.

**ACKNOWLEDGMENT**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Conflict of interest**

The author declare that we have no conflict of interest.

**REFERENCES**

1. Lachman, L.; Lieberman, H.A., & Kanig, J. L., The Theory and Practice of Industrial Pharmacy. 3rd ed. Lea & Febiger., **1991**.
2. Indian Pharmacopoeia. Government of India, Ministry of Health and Family Welfare. New Delhi: Indian Pharmacopoeia Commission., **2018**.
3. United States Pharmacopeia (USP 43-NF 38). The United States Pharmacopeial Convention, Rockville, MD., **2020**.
4. Mishra, D., & Panigrahi, R. Formulation and evaluation of mouth dissolving tablets of chlorpropamide using natural superdisintegrants., *Int J Pharm Sci Rev Res*., **2012**, *16*(1), 78–84.
5. Bhowmik, D.; Chiranjib, B., & Krishnakanth, T. Fast dissolving tablet: An overview., *J Chem Pharm Res*., **2009**, *1*(1), 163–177.
6. Shukla, D.; Chakraborty, S.; Singh, S., & Mishra, B., Mouth dissolving tablets I: An overview of formulation technology., *Sci Pharm*., **2009**, *77*(2), 309–326.https://doi.org/10.3797/scipharm.0808-09
7. Gohel, M.; Patel, M.; Amin, A.; Agrawal, R.; Dave, R., & Bariya, N., Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique., *AAPS Pharm Sci Tech*., **2004**, *5*(3), e36. https://doi.org/10.1208/pt050336
8. Sharma, V., & Pathak, K., Formulation and optimization of fast dissolving tablets of promethazine theoclate using design of experiment., *Chem Pharm Bull*., **2011**, *59*(5), 636–643. https://doi.org/10.1248/cpb.59.636
9. Patel, D. M.; Patel, N.M., & Shah, R.R., Development and optimization of fast dissolving tablets of propranolol hydrochloride using $3^2$ full factorial design., *Indian J Pharm Sci*., **2006**, *68*(2), 222–226.
10. Banker, G.S., & Anderson, N.R., Tablets. In: Lachman, L. et al., eds. The Theory and Practice of Industrial Pharmacy, 3rd ed. Philadelphia: Lea &Febiger., **1987**, 293–345.