Abstract

Orodispersible drug delivery systems are extensively used to improve bioavailability and patient compliance. Over the past three decades, orodispersible tablets (ODTs) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance, improved solubility and stability profiles.

ODTs are solid dosage forms containing medicinal substances which disintegrate rapidly, usually in a matter of seconds, when placed on the tongue. New ODT technologies address many pharmaceutical and patient needs, ranging from enhanced life-cycle management to convenient dosing for pediatric, geriatric, and psychiatric patients with dysphagia. This has encouraged both academia and industry to generate new orally disintegrating formulations and technological approaches in this field.

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used in the symptomatic treatment of acute and chronic inflammatory diseases and pain. Clinically, nonsteroidal anti-inflammatory drugs (NSAIDs) are the most frequently prescribed preparations. Meloxicam and tenoxicam show high anti-inflammatory and antiarthritic activity.

The aim of this work is to formulate meloxicam and tenoxicam in orodispersible tablets (ODTs) that could enhance the in-vitro dissolution and in-vivo absorption of the drugs. Consequently, the bioavailability of the drugs could be improved.

The work in this thesis is divided into two main parts:

Part I: Formulation and Evaluation of Orodispersible Tablets of Meloxicam.

Chapter 1: Compatibility Study of Meloxicam with Different Excipients.

Chapter 2: Formulation and Evaluation of Meloxicam Orodispersible Tablets.

Chapter 3: Stability Study of Some Selected Meloxicam Orodispersible Tablets.

Part II: Formulation and Evaluation of Orodispersible Tablets of Tenoxicam.

Chapter 1: Compatibility Study of Tenoxicam with Different Excipients.

Chapter 2: Formulation and Evaluation of Tenoxicam Orodispersible Tablets.

Chapter 3: Stability Study of Some Selected Tenoxicam Orodispersible Tablets.

Part I

Formulation and Evaluation of Orodispersible Tablets of Meloxicam

Chapter 1: Compatibility Study of Meloxicam with Different Excipients

The work in this chapter includes:

1. Preparation of meloxicam mixtures with different excipients:

Samples were prepared by mixing of meloxicam and each of the used excipients namely mannitol, Ac-Di-Sol, Explotab, Crospovidone, Starch 1500, magnesium stearate, saccharin sodium, Avicel PH 101, Aerosil 200, camphor, menthol, thymol, PEG 4000, PEG 6000, PVP K25 and PVP K90 in a ratio of (1:1).

Samples were prepared by gentle mixing of drug and excipients in glass morter the accurately weighed 200 mg of each mixture were filled in individual colorless glass vials (2 ml capacity) and tightly sealed. Vials containing meloxicam and excipients alone were also prepared. The prepared samples were stored in oven at 60°C for four weeks. Samples of

the ampoules containing the tested drug-excipient mixtures were removed from the oven daily during the examination period.

2. Evaluation of the prepared meloxicam mixtures with different excipients:

(a) Visual inspection:

The results of visual examination revealed that meloxicam, alone and in mixtures showed no changes in physical appearance when stored at 60°C for four weeks except mixtures of meloxicam with menthol and thymol showed liquefaction after 4 days of storage at 60°C.

(b) Differential Scanning Calorimetry (DSC):

The DSC thermogram of the drug showed one main prominent characteristic endothermic melting peak at 255.81°C. Based on DSC results, all the used additives were found to be compatible with the drug.

(c) Fourier-Transform Infra Red Spectroscopy:

Based on IR results, it could be concluded that, all the excipients under test showed no signs of chemical interaction with the drug.

(d) Thin Layer Chromatography (TLC):

Thin layer chromatographic analysis for plain meloxicam and its physical mixtures with each of aforementioned excipients showed that the color intensity of the developed spots under UV was almost the same and R_f values were nearly equal in all cases indicating that no interaction occurred in these mixtures.

Chapter 2: Formulation and Evaluation of Meloxicam Orodispersible Tablets

The work in this chapter includes:

I) Formulation of meloxicam ODTs: This was carried out by several methods including:

1. Solvent deposition of meloxicam:

In this technique drug was dissolved in a solvent like chloroform to produce a clear solution. The carrier was then dispersed in the solution by stirring, The obtained slurry was stirred by a magnetic stirrer at room temperature till all the solvent evaporates. The resultant mass was then dried, pulverized, and passed through a sieve. Twelve ODT formulae (M1-M12) were prepared by using different carriers. The carriers used were: Crospovidone, Ac-Di-Sol, Explotab and Starch 1500. Each in (1:1, 1:2 and 1:4) w/w drug: carrier ratio. The different blends were prepared and then compressed into tablets (120 mg) containing 7.5 mg of meloxicam using 8 mm punches and die. Mannitol was used as diluent, saccharin sodium (1%) was used as a sweetener and magnesium stearate (0.5%) was used as a lubricant.

2. Preparation of meloxicam ODTs from liquisolid compacts:

Propylene glycol was selected as the liquid vehicle for preparing meloxicam ODTs. Eight liquisolid compacts (M13-M20) were prepared in which drug concentration in liquid medication was (40% w/w), a binary mixture of microcrystalline cellulose–Aerosil 200 (microcrystalline cellulose as the carrier powder and Aerosil 200 as the coating material with a ratio of 20, *R*), different superdisintegrants were tested (each used in two concentrations 5, 10% w/w), 1% saccharin sodium, 0.5% magnesium stearate and mannitol (up to 120 mg) were mixed. The final mixture was compressed into tablets each weighing 120 mg using single punch machine of 8 mm flat punch and die set.

3. Preparation of meloxicam ODTs using sublimation method:

ODTs of meloxicam (M21-M29) were prepared using different subliming agents like camphor, thymol, and menthol. Each was used in three different concentrations (5, 10, 15% w/w). The different blends containing 7.5 mg of meloxicam, saccharin sodium (1%), magnesium stearate (0.5%), subliming agent and mannitol (up to 120 mg) were prepared and then compressed into tablets (120 mg) using 8 mm punches and die. Meloxicam tablets containing the subliming agent were then placed in an oven at 40°C till constant weight was obtained.

4. Preparation of meloxicam ODTs using freeze- drying technique:

Meloxicam ODTs prepared by freeze-drying an aqueous dispersion of meloxicam containing gelatin as a matrix former, mannitol as a sugar alcohol, and glycine as a collapse protectant. In addition, different disintegration accelerators were tested (each in 1% w/v) including PVP K25, PVP K90, PEG 6000, PEG 4000, PEG 400, Tween 80 and Tween 20. Ten formulae (M30-M39) were prepared. Gelatin was used in three different concentrations (0.25%, 0.5% and 1% w/v), while glycine was used at a concentration of 0.886% w/v. Gelatin was first dissolved in distilled water at about 40°C to obtain the required concentration. An accurately weighed amount of meloxicam, mannitol and glycine were mixed then added to the gelatin solution in the predetermined concentration, then dispersed in the prepared aqueous solution using a magnetic stirrer to result in a dose of 7.5 mg meloxicam per 1 ml. One milliliter of the suspension was then poured in each pocket of a PVC blister pack with a diameter of 18 mm and a depth of 5 mm resulting in a dose of 7.5 mg per tablet. The tablet blister packs were then transferred to a freezer at -22°C and kept in the freezer for 24 h. The frozen tablets were placed in a lyophilizer for 24 h. The best of these formulations (based on tablet properties) was taken forward to the next stage which involved the

addition of polymers in order to improve disintegration time and dissolution characteristics. Formula M31containing 0.5% gelatin was elegant tablet and selected for further study.

II) Determination of flowability of the powder formulations:

The flowability of meloxicam and after formulation was determined by measuring angle of repose, Carr's index and Hausner's ratio.

All parameters indicated poor flowability of meloxicam, as the drug has angle of repose equal to 35.5°, Carr's index of 31.11 and Hausner ratio more than 1.25. All the formulae showed angle of repose θ in the range 19.98° to 28.07°, Hausner ratio value close to one and the values of Carr's index for all the formulae were < 21 indicating a good degree of flowability.

III) Evaluation of the prepared meloxicam ODTs:

1. Weight variation test:

All the prepared meloxicam ODTs showed acceptable weight variation range from 118.9 to 122 mg with standard deviation less than 2%.

2. Uniformity of ODTs thickness and diameter:

The values of the tablet diameter were in the range of 0.73 to 1.7 cm while the values of the tablet thickness were in the range of 0.2 to 0.43 cm.

3. Content uniformity:

The mean percentage of meloxicam content in ODTs from all formulae ranged from 95.1 to 102.1% of the initial drug content added. The percentage deviation did not exceed 2% indicating well-mixed products.

4. Friability test:

All tablets formulated with the different excipients showed percentage fines within the permissible limit of 1% except formula M30 prepared by freeze drying method, containing 0.25% gelatin was friable and showed percentage weight loss that exceeded pharmacopoeial limits, (2.6%). Thus this formula was excluded from the study.

5. Hardness:

All meloxicam ODTs showed hardness values ranged from 2.7 – 4.1 kilograms, with standard deviation less than 2%.

6. In-vitro disintegration time:

All the formulations of meloxicam disintegrated in a period less than one minute.

Formula M32 prepared by freeze drying method, containing (1% gelatin) exhibited disintegration time of 110.2 seconds. For this reason this formula was excluded from the study. Formula M31 prepared by freeze drying method, containing (0.5% gelatin) exhibited disintegration time of 67.1 seconds. Thus addition of disintegrant accelerators was done to this formula.

Formula M6 containing Ac-Di-Sol as a carrier in the ratio (1:4) exhibited disintegration time of 5 seconds. Formula M19 prepared by liquisolid method containing (10% Ac-Di-Sol) as the superdisintegrant showed disintegration time of 6 seconds. Formula M23 containing camphor (15% w/w) exhibited disintegration time of 9 seconds. Formula M37 prepared by freeze drying method containing 1% PEG 400 as a disintegration accelerator, exhibited disintegration time of 1 second.

7. In-vitro dissolution testing:

The in vitro dissolution of the formulae was repeated using USP dissolution tester (apparatus II), paddle method. The paddle was rotated at

50 r.p.m in 900 ml of Sorenson's phosphate buffer (pH 6.8) as dissolution medium maintained at 37 ± 0.5°C for 30 minutes.

All formulae showed acceptable dissolution rate, where more than 85% of the labeled dose was dissolved at 30 minutes compared to 77.02% for the market product Mobic® 7.5 tablets.

Formulae M6, M19, M23 and M37 showed the highest dissolution where 99.6, 96.4, 94.3 and 101%, respectively, of the labeled dose was dissolved at 10 minutes.

8. Determination of wetting time and water absorption ratio:

All tablet formulations showed rapid wetting time ranging from 2.5 seconds to 45.8 seconds.

The average water absorption ratios of different prepared ODTs formulations ranged from 17.8 to 600.

9. Moisture uptake:

All tablet formulations showed good stability when exposed to 75% relative humidity and final % increase in weight ranged from 0.5 to 4.9%.

10. Assessment of the taste of the ODTs of the best formulae:

Taste evaluation of the best formulae (M6, M19 and M37) was done. The bitterness scale for M6 ranged from 0 (no bitterness) at 10 seconds and 20 seconds to 0.5 (threshold bitterness) at 60 seconds, while the bitterness scale for formulae (M19 and M37) ranged from 0 (no bitterness) at 10 seconds to 0.5 (threshold bitterness) at 20 seconds to 1 (slight bitterness) at 60 seconds.

10. Kinetic analysis of the dissolution of meloxicam from its ODTs:

The dissolution data were analyzed using linear regression according to zero-order and first-order as well as Higuchi diffusion model. It was revealed that the dissolution of the drug from all the formulations as well as Mobic® 7.5 tablets followed first-order kinetics.

Chapter 3: Stability Study of the Selected Meloxicam Orodispersible Tablets

Based on the findings of in-vitro disintegration and dissolution testing results, the ODTs of formula M6 prepared by solvent deposition on Ac-Di-Sol as a carrier in the ratio of (1:4), formula M19 prepared by liquisolid method containing Ac-Di-Sol in the concentration of (10% w/w) and formula M37 prepared by freeze drying method containing (1% w/v) PEG 400 as a disintegrant accelerator were selected for further stability study as follows:

1. Accelerated stability testing:

The accelerated stability testing was carried out as follow: The ODTs were stored in PVC blisters covered with aluminum foil and stored in thermostatically controlled ovens adjusted at different temperatures, namely, 40°C and 60°C ± 0.5 with relative humidity 75% (maintained using a saturated solution of NaCl for a period of 12 weeks).

The stored ODTs were examined visually for any changes in colour and/or appearance every week. The chemical analysis of the stored meloxicam formulae was carried out for the determination of the amount of drug remained in each formula after 1, 2, 4, 6, 8 and 12 weeks using HPLC stability indicating method.

The mobile phase was a mixture of acetonitrile: water: glacial acetic acid (45:50:5% v/v/v). The mobile phase was delivered into the HPLC apparatus at a flow rate of 1 ml/min, the detection was conducted at 355 nm. Tenoxicam was used as an internal standard.

Visual inspection

None of the stored formulae at different temperatures showed any changes in colour or appearance throughout the storage period.

From the chromatogram of drug, the retention time was 8.3 minutes. The drug showed sharp symmetrical peak with good base line

resolution and minimum tailing. An excellent correlation existed between the peak area ratios and the concentrations (4-20 µg/ml). The plot was highly linear and the correlation coefficient value was 0.9996.

Quantitation:

The percent remaining of meloxicam in the stored formulae at 40°C and 60°C with relative humidity 75% for a period for a period of 12 weeks was calculated and subjected to zero- and first-order; the decomposition of the drug followed first-order kinetics.

The expiration dates were 3.39, 3.1 and 3.6 years for M6, M19 and M37, respectively. The ODTs could be arranged in a descending order according to the chemical stability in the following: M37 > M6 > M19

2. Effect of humidity on meloxicam prepared ODTs:

Aiming to study the effect of storage at high temperatures and humidity on the dissolution of meloxicam from the selected formulae, dissolution testing has been conducted on the samples taken from the stored formulae at 40°C and 75% relative humidity after 4, 8 and 12 weeks as described earlier in chapter 2. It is clear that there is no significant difference in the rate and extent of the drug dissolution.

From the previous results, meloxicam ODT formulae M6, M19 and M37 had mean disintegration time of 5, 6 and 1 minutes, respectively. The percentage meloxicam dissoluted from ODT formulae M6 and M19 within 10 minutes was 99.6% and 96.4, respectively, while for ODT formula M37, the percentage meloxicam dissoluted within 3 minutes was 101%. The predictive shelf life of ODT formulae M6, M19 and M37 was 3.36, 3.1 and 3.67 years, respectively. The applied methods of formulation of meloxicam ODTs could be arranged in a descending order according to the results of in-vitro disintegration, dissolution and chemical stability as follows:

Freeze drying > Solvent deposition > Liquisolid

Part II

Formulation and Evaluation of Orodispersible Tablets of Tenoxicam

Chapter 1: Compatibility Study of Tenoxicam with Different Excipients

In this chapter, compatibility studies were done for tenoxicam with the used excipients. Samples were prepared by mixing of tenoxicam with various excipients namely, mannitol, Ac-Di-Sol, Explotab, Crospovidone, Starch 1500, magnesium stearate, saccharin sodium, Avicel PH 101, Aerosil 200, camphor, menthol, thymol, PEG 4000, PEG 6000, PVP K25 and PVP K90 in a ratio of 1:1. These samples were subjected to visual examination either fresh or after storage for four weeks at 60°C and tested visually for the appearance of any discolouration, caking and/or liquefaction. The samples were subjected to Differential Scanning Calorimetry (DSC), Infrared Spectroscopy (IR) and Thin Layer Chromatography (TLC).

The results of visual inspection revealed that mixtures of tenoxicam with menthol and thymol showed liquefaction after 4 days of storage at 60°C.

Neither the fresh mixtures nor the other stored ones, showed any change in colour or appearance throughout the storage period.

The DSC thermogram of plain tenoxicam showed a characteristic sharp endothermic melting peak at about 216.6°C and one exothermic peak at 218.9°C. Based on DSC results, there was no interaction between the drug and the aforementioned excipients.

IR spectra showed no sign of the chemical interaction between the drug and the tested excipients in the fresh and stored mixtures.

Thin layer chromatography showed that R_f value of the plain drug and its mixtures with the tested excipients was found to be 0.63.

Chapter 2: Formulation and Evaluation of Tenoxicam ODTs

I) Formulation of tenoxicam ODTs: Thirty six formulae were prepared by employing different methods:

1. Preparation of tenoxicam ODTs by solvent deposition method:

ODTs of tenoxicam (T1-T12) were prepared by using different carriers. The carriers used were: Explotab, Ac-Di-Sol, Crospovidone and Starch 1500. Each in (1:1, 1:2 and 1:4) w/w drug: carrier ratio.

2. Preparation of tenoxicam ODTs from liquisolid compacts:

preparation of tenoxicam liquisolid tablets (T13-T20) was done using propylene glycol as a non volatile solvent in a concentration of 40% , Avicel PH 101 as the carrier, Aerosil 200 as the coating material with a ratio of 20, *R*) and different superdisintegrants were tested (each used in two concentrations 5, 10 % w/w).

3. Preparation of tenoxicam ODTs using sublimation method:

ODTs of tenoxicam (T21-T29) were prepared using different subliming agents like camphor, thymol, and menthol. Different concentrations of subliming agent were used (5, 10, 15 % w/w).

4. Preparation of tenoxicam ODTs using freeze- drying technique:

Tenoxicam ODTs prepared by freeze-drying an aqueous dispersion of tenoxicam containing gelatin as a matrix former, mannitol as a sugar alcohol, and glycine as a collapse protectant. In addition, different disintegration accelerators were tested (each in 1% w/v) including PVP K25, PVP K90, PEG 6000, PEG 4000, PEG 400, Tween 80 and Tween 20. Ten formulae (T30-T39) were prepared. Gelatin was used in three different concentrations (0.25%, 0.5% and 1% w/v), while glycine was used at a concentration of 0.886% w/v.

II) Determination of flowability of the powder formulations:

Flowability study of the prepared formulations powder was carried out by determining angle of repose, Carr's index and Hausner's ratio.

For all the formulae, the angle of repose θ was in the range < 30° which indicates good flowability while θ for pure tenoxicam was 35.7° which indicates poor flowability

Concerning Hausner ratio, all the formulae showed acceptable values of Hausner ratio indicating good flowability.

The values of Carr's index for all the formulae were < 21 indicating a good degree of flowability.

III) Evaluation of the prepared tenoxicam ODTs:

1. Weight variation test:

All the prepared tenoxicam ODTs showed acceptable weight variation range from 118.6 to 121.7 mg and from 250.1 to 253.3 mg with standard deviation less than 2%.

2. Uniformity of ODTs thickness and diameter:

The values of the tablet diameter were in the range of 0.73 to 1.64 cm while the values of the tablet thickness were in the range of 0.20 to 0.47 cm.

3. Content Uniformity:

The mean percentage of tenoxicam content in ODTs from all formulae was found to conform to pharmacopoeial limits, (85% - 115%) of the label claim.

4. Friability Test:

Formulae T30 prepared by freeze drying method, containing (0.25%) gelatin was friable and showed percentage weight loss that exceeded pharmacopoeial limits (1.5%). Thus, it was excluded from the study.

Friability testing showed that formulae T31 and T32 prepared by freeze drying method with (0.5% and 1%) gelatin, respectively were non fragile and could be easily handled.

All other prepared tenoxicam ODTs showed percentage fines within acceptable range (less than 1%).

5. Hardness

All tenoxicam ODTs showed hardness values ranged from 2.5-5.2 kilograms, with standard deviation less than 2%.

6. In vitro disintegration time:

All formulae exhibited mean disintegration time less than 1 minute except formulae T3, T6, T9 and T12 had mean disintegration time of 100.4, 120, 76.2 and 180 seconds, respectively.

Formula T32 containing 1% gelatin was very hard and exhibited disintegration time of 143 seconds. It was excluded from the study.

Formula T31 exhibited disintegration time of 84.4 seconds. Thus, addition of disintegration accelerators was done to this formula.

Formulae T5, T19, T23 and T34 exhibited the shortest disintegration times of 9.5, 5.5, 11 and 2 seconds, respectively.

7. In-vitro dissolution testing:

Dissolution of the prepared ODTs was performed using the USP apparatus 2 (paddle method). Studies were carried out at 37 ± 0.5°C in 900 ml of phosphate buffer pH 6.8 for a period of 30 minutes. Rotation speed was 50 r.p.m.

The extent of dissolution of market product Tenoxil® in 30 minutes was 84.9%.

Formulae (T3, T6, T9 and T12), where different superdisintegrants were used in the ratio (1:4) showed lower percentage of drug dissolved.

Formulae T5, T19, T23 and T34 showed the highest dissolution where (92.4, 100.5, 91.3 and 100.8%), respectively, of the labeled dose was dissolved at 10 minutes.

8. Determination of wetting time and water absorption ratio:

All tablet formulations showed rapid wetting time ranging from 2.3 seconds to 114 seconds.

High water absorption ratio of formula T9 may be attributed to the presence of high concentration of the hydrophilic carrier explotab.

9. Moisture uptake:

All tablet formulations showed good stability when exposed to 75% relative humidity and final % increase in weight ranged from 0.9 to 8.9%.

10. Assessment of the taste of the ODTs of the best formulae:

Taste evaluation of the best formulae (T5, T19 and T34) was done. The bitterness scale for T5 ranged from 0 (no bitterness) at 10 seconds to 0.5 (threshold bitterness) at 20 seconds to 1 (slight bitterness) at 60 seconds, for formula T19, the bitteness scale ranged from 0.5 (threshold bitterness) at 10 seconds to 1 (slight bitterness) at 20 seconds to 1.5 (slight to moderate bitterness) at 60 seconds, while the bitterness scale for formula T34 ranged from 0 (no bitterness) at 10 seconds and 20 seconds to 0.5 (threshold bitterness) at 60 seconds

10. Kinetic analysis of the dissolution of meloxicam from its ODTs:

The dissolution of tenoxicam from the different ODTs prepared followed first-order kinetics.

Chapter 3: Stability Study of the Selected Tenoxicam Orodispersible Tablets

Based on the findings of in-vitro disintegration and dissolution testing results, three formulae (T5, T19 and T34) were chosen as the best ones. Formula T5 prepared by solvent deposition on Ac-Di-Sol as a carrier in the ratio of (1:2), formula T19 prepared by liquisolid method containing Ac-Di-Sol as a superdisintegrant in a concentration of (10%

w/w) while formula T34 prepared by freeze drying method containing (1% w/v) PVP K25 as a disintegrant accelerator.

1. Accelerated stability testing:

Accelerated stability studies on tenoxicam ODTs were carried out by storing the tablets in PVC blisters covered with aluminum foil at 40°C and 60°C at 75% relative humidity in ovens for a period of 12 weeks. Samples were withdrawn periodically at 1, 2, 4, 6, 8, and 12 weeks and examined for any physical changes as well as for their drug content using HPLC method.

The mobile phase was a mixture of acetonitrile: water: glacial acetic acid in a ratio of 45: 50: 5, (v/v/v). The mobile phase was delivered into the HPLC apparatus at a flow rate of 1 ml/min, the detection was conducted at 368 nm. Meloxicam was used as an internal standard.

Visual inspection

The formulations showed no significant changes in colour or appearance when stored at elevated temperatures.

A typical chromatogram for tenoxicam in the mobile phase was detected at λ 368 nm. Tenoxicam was well separated and its retention time was 4.6 min. An excellent correlation existed between the peak area ratios and the concentrations (4-20 µg/ml). The plot was highly linear and the correlation coefficient value was 0.9998.

Accuracy and precision

The method was accurate and precise with RSD % value of less than 1%.

The intra-day and inter-day variation

From the ANOVA results there was no significant difference between the results of the intra-day variation and inter-day variation since the p-value was < 0.05.

Quantitation

The percent remaining of tenoxicam for all the stored formulae at 40º and 60ºC for 12 weeks was within the permitted by the USP (90%-110%) up to the end of the storage period.

Kinetic analysis of the stability data revealed that the degradation of tenoxicam from the prepared formulae followed first-order kinetics and the predictive shelf life of formulae T5 , T19 and T34 is 3.67, 3.06 and 3.67 years respectively.

2. Effect of humidity on tenoxicam prepared ODTs:

The dissolution rate of the stored ODTs did not change with increasing temperature and relative humidity.

From the previous results, tenoxicam ODT formulae T5, T19 and T34 had mean disintegration time of 9.5, 5.5 and 2 minutes, respectively. The percentage tenoxicam dissoluted from ODT formula T5 within 30 minutes was 97.5%, while for ODT formulae T19 and T34, the percentage tenoxicam dissoluted within 5 minutes was 100.3% and 100%, respectively. The predictive shelf life of ODT formulae T5, T19 and T34 was 3.04, 3.67 and 3.67 years, respectively. The applied methods of formulation of tenoxicam ODTs could be arranged in a descending order according to the results of in-vitro disintegration, dissolution and chemical stability as follows:

Freeze drying > Liquisolid > Solvent deposition