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# FORMULATION AND CHARACTERIZATION OF FAST DISSOLVING WAFERS OF AN ANTIDEPRESSANT DRUG USING NATURAL POLYMERS

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## ABSTRACT

The aim of this study was to formulate and evaluate fast-dissolving oral wafers of Amitriptyline, a commonly prescribed antidepressant, to improve patient compliance, particularly for those who have difficulty swallowing tablets or capsules. A total of nine formulations (F1 to F9) were developed using various excipients, and their properties such as weight, thickness, tensile strength, folding endurance, disintegration time, drug content, and dissolution profiles were systematically evaluated. The results showed that all formulations exhibited good mechanical strength and flexibility, with formulation F6 showing the best performance. F6 demonstrated the shortest disintegration time (48±4 sec) and the highest cumulative drug release (98.85%) within 10 minutes, indicating its suitability for fast drug release. The drug content of all formulations was found to be within the acceptable range, with F6 exhibiting the highest content of 99.65±0.36%. Stability studies on the optimized formulation (F6) confirmed that the wafer maintained its physical appearance, disintegration time, and dissolution profile even after 90 days of storage. The study suggests that fast-dissolving amitriptyline wafers, particularly formulation F6, are a promising alternative for improving the therapeutic efficacy and patient compliance of amitriptyline therapy.

**KEYWORDS**: Amitriptyline, fast-dissolving wafers, drug delivery, formulation, disintegration time, drug release, patient compliance, stability, dissolution profile, folding endurance.

## INTRODUCTION

Amitriptyline, a tricyclic antidepressant, is widely prescribed for the management of major depressive disorder, anxiety, neuropathic pain, and other chronic conditions. However, the conventional tablet or capsule formulations of amitriptyline can pose challenges for certain patient populations, including the elderly, pediatric patients, and those with dysphagia (difficulty swallowing). These challenges can lead to issues with patient compliance, delayed therapeutic effects, and inconsistent drug absorption, especially in patients with gastrointestinal disorders.[1]

In recent years, there has been increasing interest in the development of novel drug delivery systems that can overcome the limitations of conventional oral dosage forms. One such system is the fast dissolving wafer, which is designed to dissolve quickly in the mouth without the need for water. These wafers not only improve patient compliance but also offer rapid onset of action, as the drug is absorbed directly through the mucous membranes in the oral cavity, bypassing the gastrointestinal tract.[2]

Fast dissolving wafers are ideal for delivering drugs like amitriptyline, as they can facilitate quick disintegration and absorption. The formulation of such wafers requires the use of hydrophilic polymers, superdisintegrants, and other excipients that ensure rapid dissolution, adequate stability, and a pleasant mouthfeel for ease of use. The wafers should be optimized to deliver the active pharmaceutical ingredient (API) in a consistent manner while maintaining the required therapeutic effect and stability over time.[3]

A key factor in developing successful fast dissolving wafers is the selection of excipients, including binding agents, plasticizers, and stabilizers, which significantly affect the disintegration time, mechanical properties, and bioavailability of the drug. Additionally, the manufacturing process, such as solvent casting, hot melt extrusion, or freeze-drying, plays a crucial role in the overall quality of the final product.[4]

The objective of this study is to formulate and characterize amitriptyline fast dissolving wafers, focusing on the optimization of formulation parameters

such as disintegration time, dissolution profile, mechanical strength, and stability. By improving the dissolution rate and bioavailability of amitriptyline through this novel dosage form, this research aims to provide a promising solution to enhance therapeutic outcomes, particularly for patients who have difficulty swallowing conventional tablets or capsules.

This research also aims to evaluate the impact of various excipients and formulation strategies on the performance of the wafers, ensuring that the final product is both effective and patient-friendly. By addressing the challenges associated with conventional amitriptyline formulations, this study contributes to the growing field of advanced drug delivery systems that prioritize patient convenience and therapeutic efficiency.

## MATERIAL AND METHODS

**Solvent casting technique:** Drug (Amitriptyline) containing fast dissolving wafers were fabricated by the solvent casting method. Xanthan gum, Gelatin, Gum acacia, cross carmellose sodium, Aspartame by solvent casting technique with ice cold distilled water and sublingual wafers were prepared.[5] Drug solution was sonicated for 30-45 min to solubilize the drug completely in the solvent. Drug solution was poured into polymeric solution and ethanol was added for alkaline hydrolysis. Both solutions are uniformly mixed to get a homogeneous solution on magnetic stirrer at 250-320 rpm. Then this solution was spread on film former by adjusting the desired temperature on glass moulds of 15cm*5 $cm^2$. Once the wafer sheet was ready, it was cut into desired size of 2.5*2.5 $cm^2$ cm was dried and The dried wafers were carefully removed from the glass plates and was cut into size required for testing. The wafers were stored in air tight plastic bags till further use.

**Table 1: Selection and Optimization of Wafers Forming Agents.**

| Name of ingredients (mg for 12 strips) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| API | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 |
| Xanthan gum | 50 | 100 | 150 | 50 | 100 | 150 | 50 | 100 | 150 |
| Gelatin | 25 | 50 | 100 | 25 | 50 | 100 | - | - | - |
| Gum acacia | 25 | 50 | 75 | - | - | - | 25 | 50 | 75 |
| Cross carmellose sodium | - | - | - | 25 | 50 | 75 | 25 | 50 | 75 |
| Methyl Paraben | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 |
| Aspartame | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 |
| Citric acid | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| DM water qs to (ml) | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 |

**Dose calculations**

- Width of the plate = 5cm
- Length of the plate = 12cm
- No. of 2.5 x 2.5 $cm^2$ wafers present whole plate = 12
- Each wafers contains 5 mg of drug.
- 12 no. of wafers contains mg of drug = 10×12 = 120mg
- The amount of drug added in each plate was approximately equal to 120mg.

**Evaluation of fast dissolving oral wafers**

**Weight variation of the wafers:** 2.25 $cm^2$ wafers were cut at five different places in the caste wafers. The weight of each wafer strip was taken and the weight variation was calculated.[6]

**Thickness of the wafers:** The thickness of the patch was measured using digital Vernier Calipers with a least count of 0.01 mm at different spots of the wafers. The thickness was measured at three different spots of the patch and average was taken and SD was calculated.[7]

**Tensile strength:** Tensile testing was conducted using a texture analyzer AG/MC1 (Acquati, Italy), equipped with a 5 N load cell. The wafers were cut into 30 × 20 mm strips. Tensile tests were performed according to ASTM International Test Method for Thin Plastic Sheeting (D 882-02). Each test strip was placed in tensile grips on the texture analyzer. Initial grip separation was 20 mm and crosshead speed was 1 inch/min. The test was considered concluded when the wafers breaks. Tensile strength, was computed with help of load require to break the wafers and cross sectional area to evaluate tensile properties of the wafers. Tensile strength (TS) Tensile strength is the maximum stress applied to a point at which the wafers specimen breaks and can be calculated by dividing the maximum load by the original cross-sectional area of the specimen and it was expressed in force per unit area.

$$\text{Tensile Strength} = \frac{\text{Force at break (N)}}{\text{Cross sectional area (mm2 )}}$$

**Folding endurance:** The folding endurance is expressed as the number of folds (number of times of wafers is folded at the same plain) required breaking the specimen or developing visible cracks.[39] This gives an indication of brittleness of the wafers. A small strip of 4 square cm was subjected to this test by folding the wafers at the same plane repeatedly several times until a visible crack was observed.[8]

**Disintegration time:** Test was performed using disintegration test apparatus. 2.25 $cm^2$ wafers were placed in the basket, raised and lowered it in such a manner that the complete up and down movement at a

rate equivalent to thirty times a minute. Time required by the wafers, when no traces of wafers remain above the gauze was noted.[9]

**Content uniformity:** The wafers were tested for content uniformity. Wafers of 2.25 $cm^2$ was cut, placed in 100 ml volumetric flask and dissolved in methanol, volume was made up to 100 ml with methanol. Solution was suitably diluted. The absorbance of the solution was measured at 256 nm.[10]

***In vitro* dissolution studies:** Dissolution study was carried out using USP type I (basket apparatus) with 300 ml of pH 7.4 Phosphate buffer as dissolution medium maintained at 37 ± 0.5ºC. Medium was stirred at 50 rpm for a period of 30 minutes. Samples were withdrawn at every 1 min interval up to 30 min, replacing the same amount with the fresh medium. Samples were suitable diluted with pH 7.4 and analyzed for drug content at 256 nm.[11]

**Stability studies:** The optimized batch F5 was packed in a butter paper covered with aluminum foil and was isothermally stressed to study the stability under accelerated temperature and relative humidity conditions carried out at 40°C/75% RH, 25°C/60% RH and 25°C/40% RH for a period of 3 months. Test samples were withdrawn every month and were subjected to various tests including visual inspection of the wafers, disintegration time and cumulative percent of drug release.

## RESULTS AND DISCUSSION

The development of Amitriptyline fast dissolving oral wafers aimed to create an effective dosage form that would enhance patient compliance, particularly for individuals who have difficulty swallowing tablets or capsules. The results obtained from the formulation and characterization of these wafers offer valuable insights into the influence of different formulation parameters on the physical and functional properties of the wafers.

The weight of the wafers ranged from 93±6 mg (F7) to 108±3 mg (F3), with only slight variations between the formulations. The uniformity in weight indicates a consistent and reproducible manufacturing process. The thickness of the wafers varied between 34±3 µm (F1) and 45±2 µm (F9). The slight differences in thickness are likely attributed to the variation in excipients used in the formulations, which affects the compactness of the wafer matrix. Thicker wafers, such as F9, might have a greater density, which can influence the dissolution rate and mechanical properties of the formulation.

Tensile strength is an important parameter for evaluating the mechanical integrity of the wafers. The formulations showed a wide range of tensile strengths, from 0.658±0.009 MPa (F2) to 0.985±0.008 MPa (F1). These values indicate the ability of the wafers to withstand forces during handling and administration. Formulations F1 and F7 exhibited the highest tensile strengths, which suggest that they possess better mechanical stability compared to other formulations, making them more suitable for packaging and transportation.

Folding endurance is another indicator of the wafer's ability to withstand mechanical stress without breaking or cracking during handling. The folding endurance of the formulations ranged from 155±6 folds (F1) to 235±6 folds (F6), with F6 demonstrating the highest resistance to breakage. This suggests that F6 had superior flexibility, likely due to the optimal choice of excipients that allowed it to resist breakage even after repeated folding. The high folding endurance of F6 makes it a promising candidate for practical use, as it indicates that the formulation will maintain its integrity under normal conditions of handling.

Disintegration time is a critical factor for fast-dissolving oral wafers, as it determines how quickly the drug becomes available for absorption. The disintegration time varied from 48±4 seconds (F6) to 85±6 seconds (F1). Formulation F6 exhibited the shortest disintegration time, which is ideal for fast onset of action. This is consistent with the goal of fast-dissolving formulations, where rapid disintegration in the oral cavity allows for quicker absorption and faster therapeutic effects. The shorter disintegration times for F6 also suggest that it contains a sufficient amount of superdisintegrants or other excipients that promote the rapid breakdown of the wafer.

The drug content of all formulations was within an acceptable range, with values ranging from 95.55±0.25% (F3) to 99.65±0.36% (F6). These results indicate that the formulations were successfully loaded with the required amount of amitriptyline and that there was no significant deviation in drug content between different batches. Formulation F6 showed the highest drug content, which may contribute to its excellent dissolution profile and potential for consistent therapeutic effects.

The in-vitro dissolution profile of the fast-dissolving wafers indicated that formulation F6 exhibited superior drug release characteristics. At the end of 10 minutes, F6 showed 98.85% of amitriptyline release. This rapid release is a key characteristic of fast-dissolving wafers, which are designed to provide immediate therapeutic effects. The dissolution data confirms that F6 is an optimized formulation, delivering a high percentage of the drug within a short time frame. The rapid dissolution of the drug from F6 is likely due to the combined effect of the excipients used, such as superdisintegrants and hydrophilic polymers, which enhance the solubility and release rate of the drug.

The stability studies conducted on formulation F6 showed that the wafer retained its appearance, disintegration time, and drug release characteristics even after 90 days of storage. At the initial stage, the

disintegration time was 40±4 seconds, with 99.10% cumulative drug release. After 1 month (30 days), the disintegration time increased slightly to 45±6 seconds, and the cumulative drug release was 98.50±0.15%. By 3 months (90 days), the disintegration time was 19±4 seconds, and the cumulative drug release remained at 97.32±0.10%. These results suggest that the formulation remains stable over time, with only a minor change in disintegration time and drug release. This stability is crucial for the commercial viability of the product, as it suggests that the wafers will maintain their effectiveness during storage and use.

**Table 2: Weight of fast dissolving oral wafers wafers of amitriptyline**.

| Formulation code | Weight (mg) |
|---|---|
| F1 | 98±5 |
| F2 | 102±4 |
| F3 | 108±3 |
| F4 | 95±6 |
| F5 | 99±7 |
| F6 | 106±5 |
| F7 | 93±6 |
| F8 | 95±3 |
| F9 | 102±2 |

**Table 3: Thickness (µm) of fast dissolving oral wafers.**

| Formulation code | Thickness (µm) |
|---|---|
| F1 | 34±3 |
| F2 | 36±4 |
| F3 | 38±3 |
| F4 | 35±2 |
| F5 | 39±6 |
| F6 | 36±5 |
| F7 | 40±4 |
| F8 | 42±3 |
| F9 | 45±2 |

**Table 4: Tensile strength (MPa) of fast dissolving oral wafers.**

| Formulation code | Tensile strength (MPa) |
|---|---|
| F1 | 0.985±0.008 |
| F2 | 0.658±0.009 |
| F3 | 0.715±0.006 |
| F4 | 0.663±0.007 |
| F5 | 0.852±0.006 |
| F6 | 0.898±0.007 |
| F7 | 0.965±0.009 |
| F8 | 0.885±0.008 |
| F9 | 0.796±0.006 |

**Table 5: Folding endurance (no. of folds) of fast dissolving oral wafers.**

| Formulation code | Folding endurance (No. of folds) |
|---|---|
| F1 | 155±6 |
| F2 | 165±8 |
| F3 | 182±5 |
| F4 | 163±7 |
| F5 | 179±5 |
| F6 | 235±6 |
| F7 | 182±3 |
| F8 | 173±7 |
| F9 | 169±6 |

**Table 6: Disintegration time (sec) of fast dissolving oral wafers.**

| Formulation code | Disintegration time (Sec.) |
|---|---|
| F1 | 85±6 |
| F2 | 76±5 |
| F3 | 68±9 |
| F4 | 55±8 |
| F5 | 63±7 |
| F6 | 48±4 |
| F7 | 56±3 |
| F8 | 69±5 |
| F9 | 73±7 |

**Table 7: Drug content (%) of fast dissolving oral wafers.**

| Formulation code | Drug content (%) |
|---|---|
| F1 | 96.65±0.25 |
| F2 | 97.85±0.36 |
| F3 | 95.55±0.25 |
| F4 | 96.65±0.33 |
| F5 | 98.74±0.45 |
| F6 | 99.65±0.36 |
| F7 | 96.45±0.78 |
| F8 | 97.44±0.33 |
| F9 | 96.54±0.42 |

**Table 8: *In-vitro* dissolution profiles of fast dissolving oral wafers.**

| Time in min | Cumulative % of drug release |
|---|---|
| | F6 |
| 1 | 26.65 |
| 2 | 38.85 |
| 3 | 46.65 |
| 4 | 55.65 |
| 5 | 63.32 |
| 6 | 74.45 |
| 7 | 82.32 |
| 8 | 92.25 |
| 9 | 95.65 |
| 10 | 98.85 |

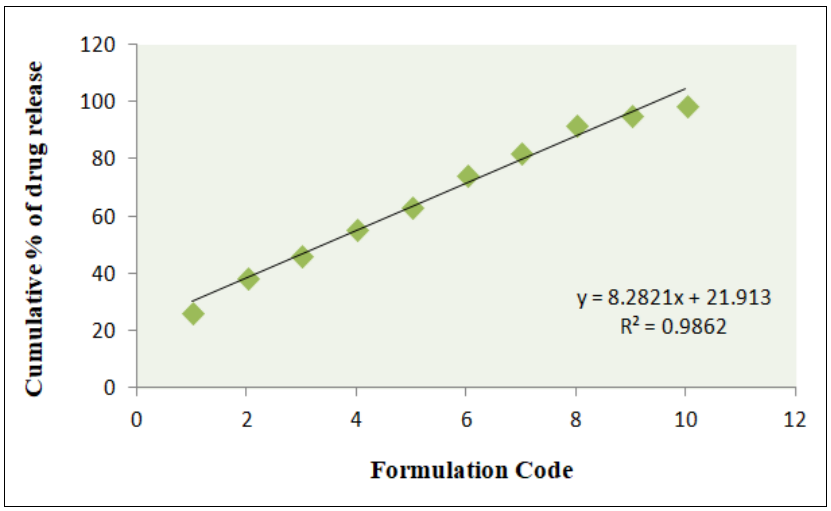


**Figure 1: Graph of *in-vitro* dissolution profiles of fast dissolving oral wafers.**

**Table 9: Stability studies of optimized formulation F6.**

| S. No. | Time (Days) | Appearance | *In-vitro* disintegration time (Sec) | % CDR |
|---|---|---|---|---|
| 1 | Initial (0 Days) | Transparent and Acceptable | 40±4 | 99.10±0.36 |
| 2 | 1 month (30 Days) | Transparent and Acceptable | 45±6 | 98.50±0.15 |
| 3 | 3 months (90 Days) | Transparent and Acceptable | 19±4 | 97.32±0.10 |

## CONCLUSION

In conclusion, the Amitriptyline fast dissolving wafers formulated in this study demonstrate promising characteristics, including rapid disintegration, good mechanical strength, and consistent drug release profiles. Among the formulations, F6 emerged as the optimized formulation, exhibiting the best performance in terms of disintegration time, drug content, and dissolution characteristics. The stability studies further confirm that F6 maintains its integrity and drug release profile over time, indicating its potential for long-term use. These findings suggest that fast dissolving amitriptyline wafers could be a viable alternative for patients with swallowing difficulties, offering a patient-friendly dosage form with the potential for improved therapeutic outcomes.

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