CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Available online at: http://www.iajps.com *Research Article*

# APPLICATION OF FREEZE-DRYING TECHNIQUE IN THE DEVELOPMENT AND EVAULATION OF NANOSUSPENSION LOADED ODF OF ANTIPSYCHOTIC DRUG

**Tanushree C*[1], Gowrishankar[2], Chandrakala DC[3]**

[1] Affiliation: Al-Ameen College of Pharmacy, Bangalore-560027, Karnataka

**Article Received:** September 2022 **Accepted:** October 2022 **Published:** November 2022

**Abstract:**

*Lurasidone HCl is antipsychotic drug belonging to BCS class II drug used for the treatment of schizophrenia. It was initially approved by the U.S. Food and Drug Administration (FDA) for the treatment of adults with schizophrenia. Our study was aimed at increasing the solubility of Lurasidone HCl by formulating nanosuspension and then incorporating it into oral dissolving films which were prepared by freeze drying technique to enhance Solubility and stability of film, Bioavailability and patient compliance. Reducing of particle size is achieved by formulating nanosuspension by High Pressure Homogenization Technique in which different stabilizers were screened for stabilizing agent in which Poloxamer 407 were selected based on the particle size and PDI.And the obtained nanosuspension is loaded into the ODF. The polymer is selected by the screening technique based on appearance, film forming, DT, and Folding endurance HPMC E15 is selected as a polymer and glycerine as a plasticizer. Optimization studies were carried out using $3^2$ Central Composite Design. By considering all the evaluation parameters Optimized F7 formulation was the best among all the formulations with the DT 47secs, %Drug content 96.64, and folding endurance of 163.The F7 formulation was evaluated further by carrying out In-vitro dissolution studies and comparison with the In-vitro release profile of film prepared by solvent casting method. The F7 Freeze dried resulted in higher and increased drug release than the heat dried that is 96.11% at the 15th minute for freeze dried film whereas for heat dried 73.78 at $15^{th}$ min. The drug release of the Marketed formulation was found to be 81.18% at the 120th minute.*

***Keywords:*** *Lurasidone HCl, Nanosuspension, ODFs, Freeze dried, solvent casting.*

**Corresponding author:**

**Mrs. Tanushree Chakraborty,**
*Associate Professor*
*Al-Ameen College of Pharmacy*
*Opp Lalbagh Main Gate, Hosur Rd*
*Bangalore -560100*
*Mob-9986897256,E-mail-tanu177@rediffmail.com*

QR code

*Please cite this article in press Tanushree Chakraborty et al,* ***Application Of Freeze-Drying Technique In The Development And Evaulation Of Nanosuspension Loaded Odf Of Antipsychotic Drug.,*** *Indo Am. J. P. Sci, 2022; 09(11).*

## INTRODUCTION:

Schizophrenia is a complex syndrome with a heterogeneous grouping of symptoms. Symptoms of schizophrenia can be divided into 'positive', 'negative' and 'cognitive' categories[1]. For medical treatment of Schizophrenia Atypical (second generation) and typical (first generation) antipsychotic drugs are used. Atypical drugs which have been used for SCZ treatment for ten years are more effective and have fewer side effects than typical drugs. Extrapyramidal side effects and tardive dyskinesia are less common in neurological side effects in atypical medications.[2] Lurasidone is a second-generation antipsychotic agent that initially received regulatory approval for the treatment of adults with schizophrenia in the USA in 2010. Additionally, lurasidone HCl recently received US and Canadian regulatory approval for the treatment of adults with foremost depressive episodes associated with bipolar I disorder (bipolar depression), as either a monotherapy or adjunctive therapy with lithium or valproate[3]. Lurasidone HCl belongs to BCS Class II drugs with poor solubility and high permeability, hence making it an ideal model drug for the envisage research work. Nanotechnology-based techniques have been valuable in combating and improving the solubility profile of poorly soluble drugs. Nanosuspensions have given good results in improving saturation solubility by increasing the surface area of particle size available for dissolution[4]. Screening of stabilizers is done to find the most suitable stabilizer in nanosuspension. Various types of stabilizers are available ionic and non ionic stabilizers .And the formulation of nanosuspension is checked for the effect of process parameters and formulation parameters, based on the Particle size, Polydispersity index and zeta potential a suitable stabilizer is selected. Oral Disintegrating films can further improve the solubility of drugs. Improved stability and bioavailability have been demonstrated for poorly water-soluble drugs. A Oral Disintegrating film that is prepared by using hydrophilic polymers dissolves fast on the tongue.ODF's is prepared by lyophilization process the principle involved in lyophilization is sublimation. Design of Experiment (DoE) is a part of the Quality by Design (QbD) approach which is known as a methodical and scientific style for emerging formulations that include nanosuspensions. The manufacturing processes consider predefined specifications. DoE is a tool for planning formulations to reduce the number of experiments and to observe interactions between formulation variables.[5] A Box-Wilson Central Composite Design, commonly called 'CCD,' contains an surrounded factorial or fractional factorial design with centre points that is amplified with a group of 'star points' that allow assessment of curvature. The central composite design is the furthermost frequently used fractional factorial design used in the response surface model[6]. CCD used to estimate nonlinearity of responses in the given data set and helps to estimate curvature in obtained continuous responses and gives maximum information in a minimum experimental trial, Reduction in the number of trials required to estimate the squared terms in the second-order model and they have been widely used in response to surface modelling and Optimization. Recent technological advancements have diverted many drug companies to explore new prospective in this technology to provides fast, accurate dosing that is expected to increase compliance, particularly among children[7].The formulation of ODF is done by statistical optimization of independent variables influencing the Disintegrating time and % Drug content with central composite design (CCD), a subset of response surface methodology (RSM) in Design-Expert software.The optimized formulation is carried out for invitro dissolution.

## 2.MATERIALS AND METHODS:

### 2.1 Chemicals and Reagents

Lurasidone HCl was a gift sample from Unichem Laboratories Goa.HPMC E15, Glycerine, Potassium dihydrogen orthophosphate, Citric Acid were procured from SD Fine Chemicals Ltd. Ethanol and Methanol from Changshu Hongsheng Fine Chemicals. Poloxamer 407 and SLS from Sigma Life science.

### 2.2 STANDARDIZATION STUDIES

A standardization study of the drug is necessary to confirm identity and purity of the Drug. The drug was screened and tested for the following parameters.

### A) Identification of Drug by FTIR

FTIR spectra of pure drug was determined by using shimadzu FTIR spectrophotometer by KBr pellet method in the wavelength region of 4,000 to 400 cm-1. Drug and KBr were thoroughly mixed in a ratio of 1:100 (1 part of drug sample and 100 parts of KBr). Mixture was subjected to compression in to discs by applying a pressure of five tons for five minutes in a hydraulic press. The pellet was placed in the light path, and the spectrum was obtained by the software.

### B) Determination of λ max Lurasidone HCl by U.V Spectrometric method

The absorption maxima of Lurasidone HCl were determined in methanol using as a solvent. The solution was scanned from 400-200 nm using UV

spectrophotometer (Shimadzu UV-1900 double beam spectrophotometer).

**2.3: FORMULATION STUDIES**

Preparation of Nanosuspension of Lurasidone HCl By High pressure homogenization in which stabilizer is dissolved in distilled water under magnetic stirrer until it dissolves completely. To this stabilizer solvent a drug is added which is previously dissolved in solvent under the magnetic stirrer to become completely wet. To obtain nanosuspension the premixed solution of drug and stabilizer is placed on homogenizer ultraturrax for reducing the particle size at 15000RPM for 15 minutes. Drug to stabilizer ratio were used as 1:1,1:2,1:3.

**2.4: Evaluation of Nanosuspension**

Assessment of Particle Size, Poly Dispersity Index, and Zeta Potential were detected utilizing the dynamic light scattering technique (Nano ZS-90, Malvern Zetasizer. Prior to starting the analysis, the nanosuspension was first diluted with an adequate amount of distilled water with sonication for 1 min. Measurements were performed three times and the mean was calculated.[4]

**2.5: FORMULATION STUDIES OF ODF**

The placebo and Drug loaded Oral dispersible films were prepared by Freeze Drying Technique. To the drug loaded nanosuspension desired quantity of polymer is slowly added under magnetic stirrer for 30mins.Plasticizer is added slowly to the obtained polymeric solution and stirred for 15mins and remaining excipient is added after complete mixing of polymer and plasticizer on magnetic stirrer. The sample is transferred onto the glass cast of 6*3 $cm^2$. The cast were stored in a freezer for 2 h to freeze the sample. The frozen samples were then transferred into the freeze dryer to freeze dry under vacuum suction for 8 h.The obtained oral dispersible films were removed from the Cast and cut the film in 3*3 $cm^2$ and stored in a desiccator for carrying out all the evaluation parameters.

**Table 1: Formulation composition of $3^2$ Central Composite design batches drug loaded film.**

| INGREDIENTS | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Lurasidone(mg) | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 |
| HPMC E-15(mg) | 150 | 175 | 125 | 150 | 125 | 150 | 175 | 125 | 175 |
| Glycerine(ml) | 0.20 | 0.20 | 0.30 | 0.25 | 0.20 | 0.30 | 0.30 | 0.25 | 0.25 |
| Citric Acid(mg) | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Croscarmellose Sodium (mg) | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Purified water(ml) | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Ethanol(ml) | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |

**2.6: PHYSICOCHEMICAL EVALUATION OF ORALLY DISPERSIBLE FILMS**

**1.THICKNESS TEST**

Thickness of a film is determined by using calibrated digital micrometre and then subsequently mean average is calculated. Generally, three readings from all the batches are determined and average is calculated.[5]

**2.FOLDING ENDURANCE**

The method followed to determine endurance value is that the film specimen ($3\times3cm^2$ ) is repeatedly folded at the same place until it breaks or a visible crack is observed. The number of times the film is folded without breaking or without any visible crack is the calculated folding endurance value. This test ensures the tensile strength of the film.[6]

**3.DISINTEGRATION TIME**

Disintegration time indicates the disintegration characteristics and dissolution characteristics of the film. Petri dish method In this method, 2ml of distilled water was placed in a Petri dish and one film was added to the surface of the water and the time required until the oral film was dissolved completely.[7]

**4.WEIGHT VARIATION**

Three films of $3 \times 3$ $cm^2$ size were cut randomly from each film formulation. Films were weighed individually on electronic balance and the mean weight for each batch was calculated.[8]

**5.DRUG CONTENT UNIFORMITY**

The 3×3 cm2 Weight variation piece was first dissolved completely in 10 ml methanol. 1 ml of this solution was diluted to 25 ml using 0.1 N HCl. The drug concentration was determined by measuring the absorbance of the resulting solution at 316 nm against 0.1N HCl as blank using a UV visible spectrophotometer. Mean with SD was recorded.[9]

**6.SURFACE PH**

An electrode pH meter (CONTECH) was employed for this purpose. The pH was measured by bringing the electrode into contact with the surface of the film. The procedure was performed in triplicate samples. Mean with standard deviation was reported.[10]

**7.MOISTURE LOSS %**

Moisture loss % was assessed by recording the initial weight of each OFDF, then putting these films in a desiccator that contained anhydrous calcium carbonate at room temperature for 72 h. After that, OFDFs were taken out from the desiccator and reweighed. This parameter was determined according to the following equation.[11]

Moisture loss % = Initial weight − Final weight /Initial weight × 100

**8.MOISTURE ABSORPTION %**

This parameter was determined by putting pre-weighed films in a desiccator containing potassium chloride saturated solution, to achieve a 80% relative humidity for 24 h, at room temperature. Then, each film was weighed again and the moisture absorption % of each OFDF was assessed using the following equation.[12]

Moisture absorption % = Final weight − Initial weight /Initial weight × 100

**9.*IN VITRO* DISSOLUTION STUDY**

The dissolution medium was composed of 200 mL phosphate buffer with pH of 6.8. Throughout the study, the temperature was adjusted to 37 ± 0.5 ◦C, and the rotation speed was fixed at 50 rpm. Each ODF was put at the bottom of the dissolution apparatus vessel. Then, 1 mL of sample was withdrawn at 2, 4, 6, 8, 10, 12 and 15min time intervals. Then, 1 mL of fresh phosphate buffer was replenished to keep a constant medium volume[47].Finally, Lurasidone HCl concentration was detected spectrophotometrically in each sample at λmax 316 nm. The test was performed three times and the mean % Lurasidone dissolved was estimated.[13]

**10.SCANNING ELECTRONIC MICROSCOPY (SEM)**

Scanning electron microscopy (SEM) is an electron optical imaging technique that provides photographic images and elemental information. SEM is useful for characterizing the morphology and size of microscopic specimens. The sample was placed in an evacuated chamber and scanned in a controlled pattern by an electron beam. Interaction of the electron beam with the specimen produces a variety of physical phenomena that, when detected, are used to form images and provide elemental information about the specimens. Scanning electron microscopy (JSM 840 A) was used to study the surface morphology of the formulation. The samples were analyzed after they were gold sputtered using 25 nm gold film thickness.[14]

**11.COMPARISON OF FREEZE DRIED AND HEAT DRIED FILMS**

The dissolution studies of Freeze dried and Heat dried films is compared. The dissolution medium was composed of 200 mL phosphate buffer with pH of 6.8. Throughout the study, the temperature was adjusted to 37 ± 0.5 ◦C, and the rotation speed was fixed at 50 rpm.

Each ODF was put at the bottom of the dissolution apparatus vessel. Then, 1 mL of sample was withdrawn at 2, 4, 6, 8, 10, 12 and 15min time intervals. Then, 1 mL of fresh phosphate buffer was replenished to keep a constant medium volume. Finally, Lurasidone HCl concentration was detected spectrophotometrically in each sample at λmax 316 nm.

**12. *IN-VITRO* DISSOLUTION OF MARKETED TABLET**

The dissolution medium was composed of 500 mL 0.1N HCl in USP Basket Apparatus. Throughout the study, the temperature was adjusted to 37 ± 0.5 ◦C, and the rotation speed was fixed at 50 rpm. Then, 5 mL of sample was withdrawn at 15, 30, 45, 60, 75, 90 ,105 and 120min time intervals. Then, 5mL of fresh 0.1N HCl was replenished to keep a constant medium volume. Finally, Lurasidone HCl concentration was detected spectrophotometrically in each sample at λmax 316 nm.

## 3. RESULTS AND DISCUSSION:

### 3.1 DRUG POLYMER COMPATIBILITY STUDIES

FTIR spectroscopy was used to determine any drug-excipient in-compatibility. IR spectra were obtained for all the excipients used in the formulation along with the drug to determine their compatibility. IR spectra of all the Drug is shown in Figure no 2. The results obtained from FTIR were checked for the peaks of Lurasidone HCl and it was seen that spectra obtained did not show any considerable change in the peak position of Lurasidone HCl. All the characteristic peaks of Lurasidone HCl were observed in the physical mixture Figure 3. It has been observed that there were no major shifts in the spectral values of the drug, indicating no chemical interaction. Hence, it can be concluded that there is compatibility between the drug and the excipients used and conclude that the drug maintained its identity without undergoing any interaction with the excipients used.

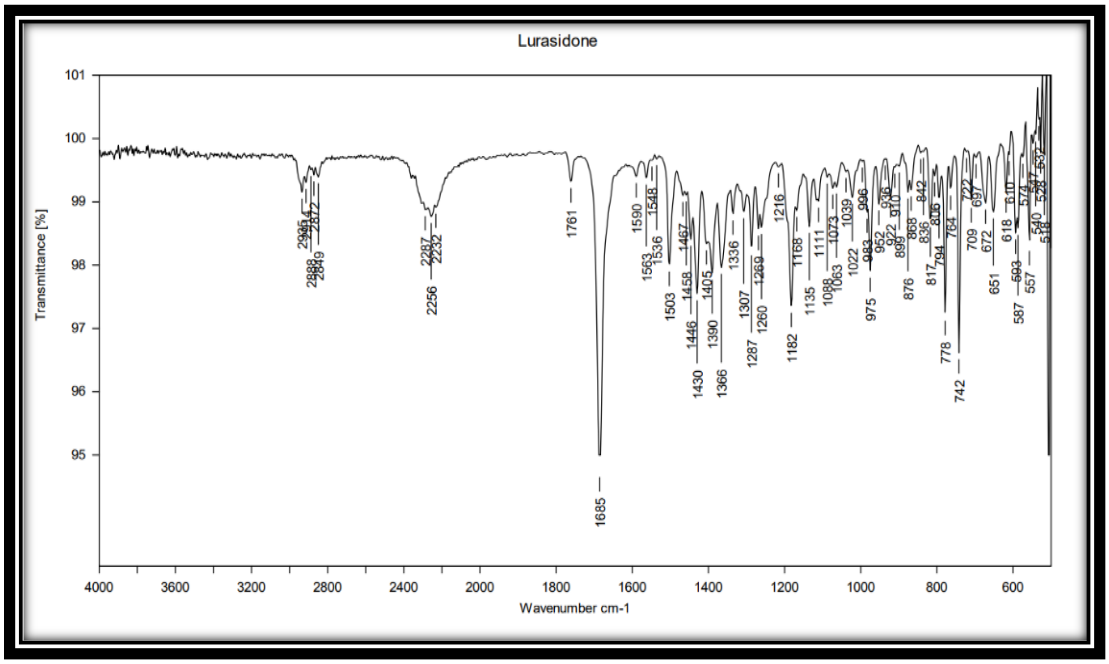


**Figure2: FTIR spectra of pure Lurasidone HCl**

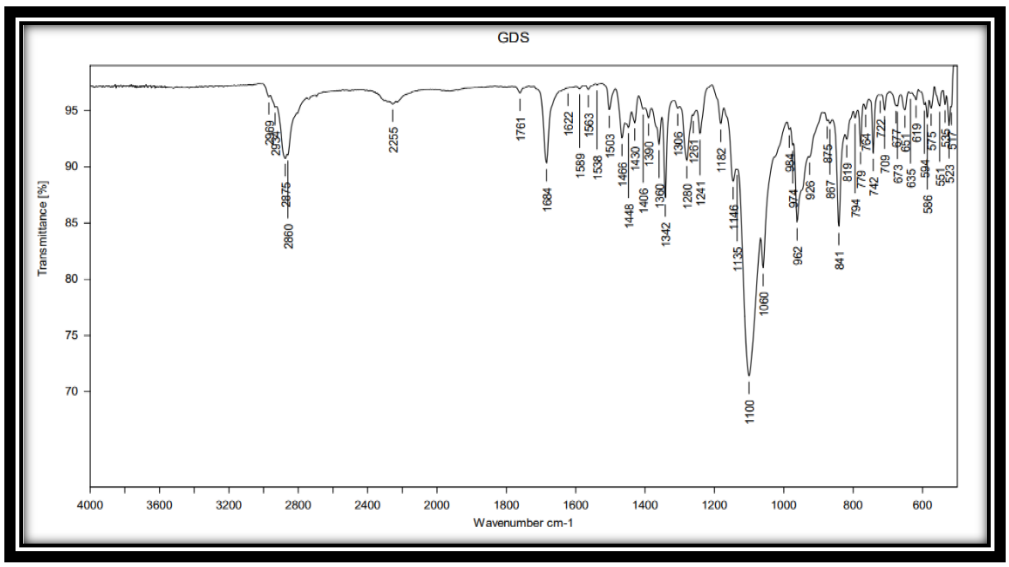


**Figure 3: FTIR spectra of pure drug and PM**

**DETERMINATION OF Λ MAX LURASIDONE HCL BY U.V SPECTROMETRIC METHOD**

Absorption maxima of Lurasidone HCl were determined by preparing a series of concentrated solutions (2-10µg/ml) in Methanol and 0.1 N HCl (10-80ug/ml). Prepared solutions were analyzed spectrophotometrically using (Shimadzu UV-1900 double beamspectrophotometer). Absorption maxima (λ max) of drug in methanol was found to be 316 nm.Figure 4 and table 2.

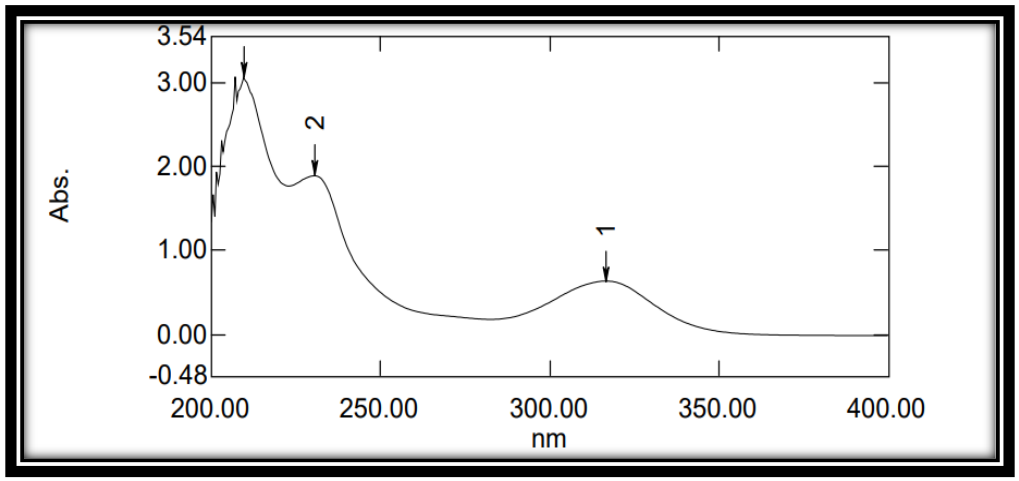


**FIGURE 4: Spectrum of Lurasidone HCl in methanol**

**Table 2: Standard calibration curve data of Lurasidone HCl in Methanol**

| SLNO | CONC µg/ml | ABSORBANCE | | | AVERAGE | SD |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | | |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 2 | 0.08 | 0.07 | 0.08 | 0.076667 | 0.005774 |
| 3 | 4 | 0.138 | 0.137 | 0.136 | 0.137 | 0.001 |
| 4 | 6 | 0.201 | 0.2 | 0.202 | 0.201 | 0.001 |
| 5 | 8 | 0.261 | 0.262 | 0.261 | 0.261333 | 0.000577 |
| 6 | 10 | 0.333 | 0.331 | 0.329 | 0.331 | 0.002 |

### 3.2: EVALUATION OF NANOSUSPENSION

Particle size of the nanosuspension was found to be 100.2nm and PDI of 0.367 in figure 5 and the value of Zeta potential is -37.2 mV figure 6.

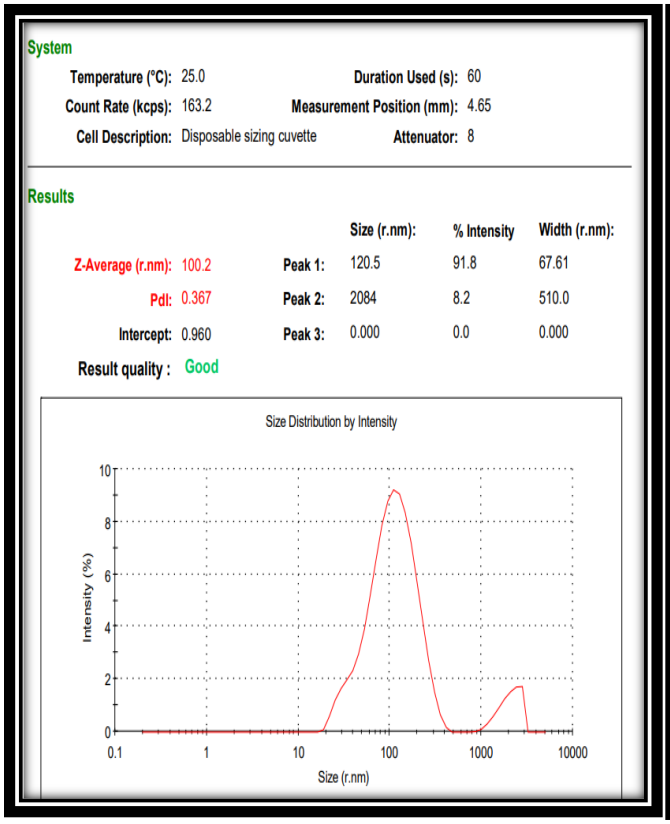


**FIGURE 5:PS AND PDI**

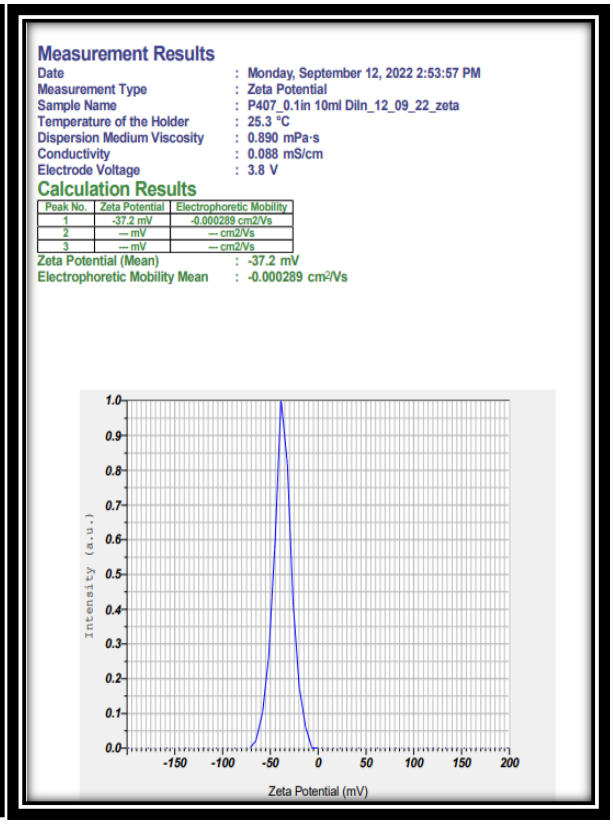


**FIGURE 6: ZETA POTENTIAL**

**3.3: PHYSICOCHEMICAL EVALUATION OF ORALLY DISPERSIBLE FILMS**

The profiles of the optimized films were the appearance of all films were smooth and white. The weight variation of all the optimized film was about 448.6±3.21, 465.3±5.50,540±2.01, 513.4±6.5, 423.3±7.5, 554±9.0, 589.6±9.17, 481±7.93, 518.3±13.01.Folding endurance 145.3±0.09, 157.6±0.06, 116.3±0.06, 154.3±0.06, 109.3±0.03, 151.0±0.04, 167±0.06, 112±0.07, 149.6±0.06 which indicated the film was sufficiently flexible to be processed during cutting and packing and the percentage moisture loss (%)in the optimized film was about 1.25,1.14,0.98,1.17,1.23,0.93,1.59,1.06,1.11. According to Pharmacopeia like USP35, EP8.0, and ChP2015, the disintegration time limit for orally disintegrating tablets was the 60s, however, there is no official guideline available for assaying disintegration time of orally disintegrating films, in our study, the disintegration time of the formulated films was 25.66±0.57 to 44.66±2.51 less than 60 secs. The film had a pH of range 6.22±0.04 to 6.81±0.06 which was within the range of oral cavity pH (6.5-7.5), and the films might not bring about uncomfortable feeling in the oral cavity. The % Drug content of all the optimized formulation is in the range of standard 85-115% according to USP27.Table 3.

From the check point solutions formulation F7 showed a %Drug content of 94.69, folding endurance of 167 with a DT (sec) of 44.6 and %DR of 96.11%. . Graphical presentation of the data helped to find F7 formulation showed highest drug release of 96.11% at 15min which is high compared to all the other formulations and was selected as the ideal formulation for the ODFs. Table 4

**TABLE 3: CHARACTERIZATION OF LURASIDONE HCL FILM**

| FORMULATIONS | THICKNESS Mean±SD | SURFACE pH Mean±SD | DT Mean±SD | FOLDING ENDURANCE Mean±SD |
|---|---|---|---|---|
| F1 | 0.861±0.01 | 6.76±0.09 | 25.66±0.57 | 145.3±0.09 |
| F2 | 0.966±0.01 | 6.57±0.06 | 31.66±1.52 | 157.6±0.06 |
| F3 | 0.832±0.02 | 6.68±0.06 | 40.3±1.52 | 116.3±0.06 |
| F4 | 0.891±0.02 | 6.73±0.06 | 35.6±2.51 | 154.3±0.06 |
| F5 | 0.679±0.04 | 6.67±0.03 | 30.3±1.51 | 109.3±0.03 |
| F6 | 0.806±0.07 | 6.22±0.04 | 41.60±1.51 | 151.0±0.04 |
| F7 | 0.717±0.04 | 6.81±0.06 | 44.66±2.51 | 167±0.06 |
| F8 | 0.653±0.05 | 6.44±0.07 | 33±2.64 | 112±0.07 |
| F9 | 0.683±0.03 | 6.54±0.06 | 36.67±3.21 | 149.6±0.06 |

| FORMULATIONS | Weight Variation Mean±SD | Drug Content% Mean±SD | Moisture Absorption% Mean±SD | Moisture Loss% Mean±SD |
|---|---|---|---|---|
| F1 | 448.6±3.21 | 91.35±1.57 | 4.17 | 1.25 |
| F2 | 465.3±5.50 | 90.98±2.99 | 2.64 | 1.14 |
| F3 | 540±2.01 | 86.92±3.78 | 3.78 | 0.98 |
| F4 | 513.4±6.5 | 89.67±1.32 | 2.05 | 1.17 |
| F5 | 423.3±7.5 | 86.76±2.61 | 3.71 | 1.23 |
| F6 | 554±9.0 | 88.52±1.35 | 4.26 | 0.93 |
| F7 | 589.6±9.17 | 94.69±2.29 | 5.01 | 1.59 |
| F8 | 481±7.93 | 86.01±1.49 | 1.39 | 1.06 |
| F9 | 518.3±13.01 | 92.03±2.48 | 3.64 | 1.11 |

**Table4: In vitro dissolution of F1-F7**

| TIME(min) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| **2** | 29.04 | 32.04 | 31.58 | 27.65 | 32.65 | 28.69 | 37.46 | 35.64 | 36.12 |
| **4** | 39.26 | 41.58 | 43.65 | 38.65 | 46.71 | 36.54 | 45.18 | 48.64 | 47.5 |
| **6** | 52.19 | 49.68 | 49.03 | 40.58 | 49.67 | 41.12 | 51.04 | 54.19 | 57.18 |
| **8** | 60.89 | 61.32 | 58.26 | 55.65 | 59.64 | 56.64 | 61.85 | 66.14 | 63.79 |
| **10** | 82.64 | 78.96 | 77.36 | 69.64 | 61.32 | 72.64 | 86.85 | 82.1 | 83.49 |
| **12** | 88.38 | 84.65 | 80.65 | 79.36 | 72.65 | 84.67 | 90.86 | 83.64 | 88.64 |
| **15** | 90.64 | 88.59 | 85.32 | 83.69 | 81.03 | 89.47 | 96.11 | 87.4 | 90.19 |

**SCANNING ELECTRONIC MICROSCOPY (SEM)**

The SEM micrographs of the films are shown in Figure 7. The freeze-dried film showed more fibrous and porous structure compared to heat fried film. The porosity formed as a result of the release of water molecule from the frozen structure when it was subjected to freeze drying process. sAs a result the drug release of freeze dried film is more when compared to heat dried and the disintegration time is less. It as explained the weaker tensile strength of the freeze dried film.

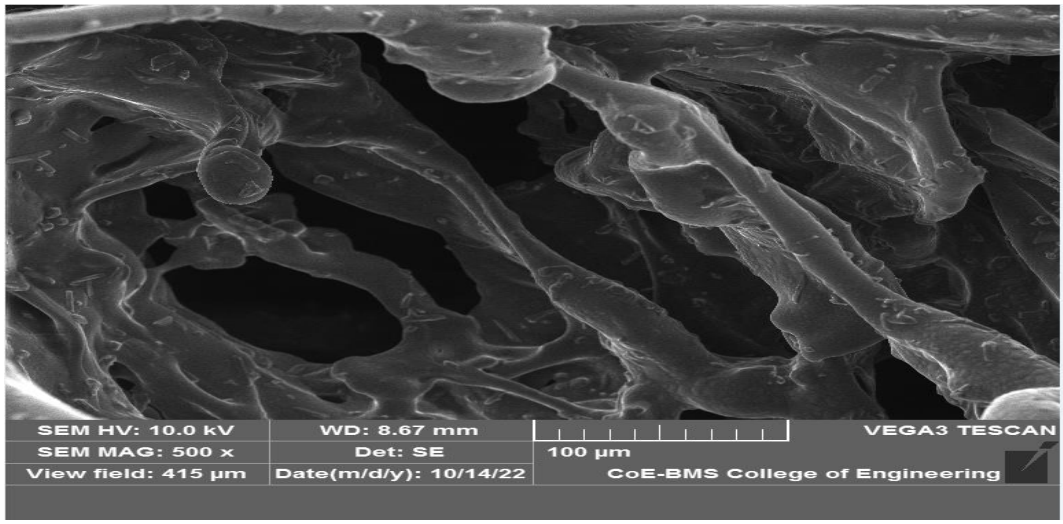


**Figure7: SEM images of optimized film at different magnification**

**COMPARISON OF FREEZE DRIED AND HEAT DRIED FILMS**

The dissolution studies of Freeze dried oral film and Heat dried formulation were carried out(Figure 8), and from the release profile, it was found that the drug release of the oral dispersible film of freeze dried was more. that is 96.11% at the 15th minute when compared with the heat dried the drug release was found to be 73.78% at 15th minute So by considering the above drug release. The F7 shows a better drug release when compared with the heat dried films. Table 6

**Table 6: Dissolution profile of Freeze dried and Heat dried film**

| Time(sec) | Freeze dried Film | Heat dried film |
|---|---|---|
| 2 | 37.46 | 28.14 |
| 4 | 45.18 | 31.04 |
| 6 | 51.04 | 36.18 |
| 8 | 61.85 | 42.97 |
| 10 | 86.85 | 59.64 |
| 12 | 90.86 | 64.78 |
| 15 | 96.11 | 73.78 |

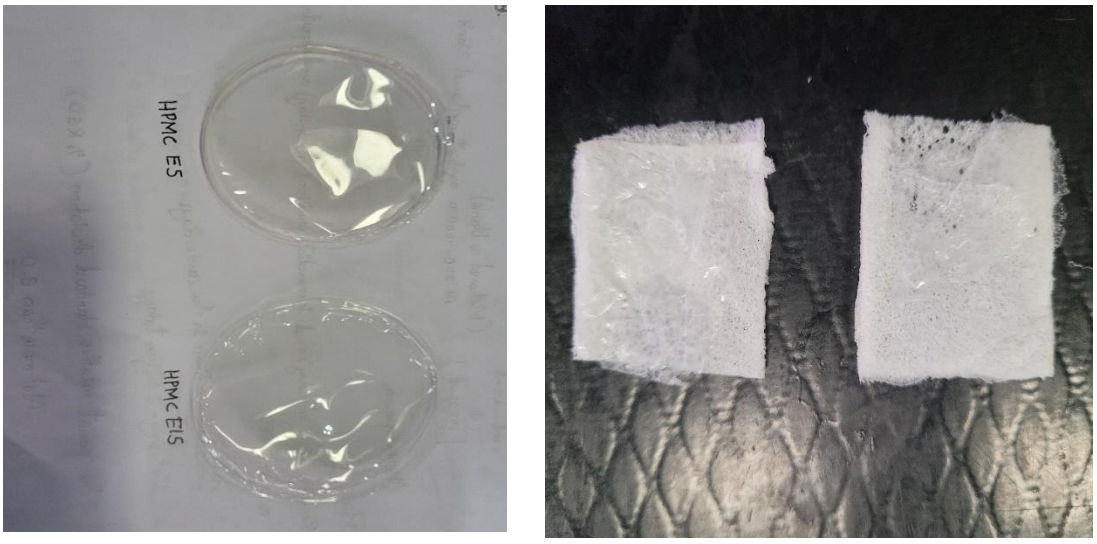


**Figure 8: Pictures of freezed dried and heat dried film**

***IN-VITRO* DISSOLUTION OF MARKETED TABLET**

The dissolution studies of marketed tablet 40mg (Atlura) were carried out, and from the release profile, it was found that the drug release of the tablet was less in terms of %Drug release. The ODF released 96.11% at the 15th minute when compared with the marketed tablet the drug release was found to be 81.18% at 120th minute So by considering the above drug release. The F7 shows a better drug release when compared with the marketed tablet. Table 7

**Table 7: *In-vitro* dissolution of marketed tablet**

| Time (min) | Marketed Tablet %DR |
|---|---|
| 15 | 2.62 |
| 30 | 35.82 |
| 45 | 46.39 |
| 60 | 51.8 |
| 75 | 56.17 |
| 90 | 64.94 |
| 105 | 75.51 |
| 120 | 81.18 |

## 4.CONCLUSION:

This work contributed to the formulation process development of orodispersible films containing poorly soluble API. This innovative dosage form offers many advantages over the conventional dosage forms like tablets, syrups, injections, suppositories etc. The present research work was designed initially to increase the solubility of Lurasidone HCl by preparing Nanosuspension. From the results nanosuspension prepared by high pressure homogenization in the ratio1:1 showed lesser particle size and PDI. Further nanosuspension was loaded into polymer films to obtained oral dispersible films.

The prepared films offered a safe and convenient route for administering the drug without affecting its efficacy. The films were prepared by Freeze drying technique (Lyophilization), and were cut into required size ( $3 * 3 cm^2$ ) Based on the evaluationparameters, the optimized formulation had HPMC E 15 as a polymer, Croscarmellose sodium as a superdisintegrants and Glycerine as a plasticizer. The formulation F7 was found to be the best because it gave disintegration in time 47sec, %Drug content 96.64% and folding endurance of 163. It exhibited good film properties. Based on these parameters F7 was selected for the further studies.

When we compared F7 formulation of freeze dried with the heat dried film formulation the drug release was 96.11% at the 15th minute for freeze dried compared to heat dried film 73.78%.

Therefore, the prepared films proved to be an effective novel drug delivery system. When compared to other conventional dosage forms. films provide a safe effective rote of drug delivery for geriatric and non-cooperative patients. These films offer a new and innovative drug delivery system for treating Schizophrenia and Bipolar disorder.

**5.ACKNOWLEDGEMENT**
Authors are thankful to the Principal, Head of the Department Pharmaceutics, Management of Al Ameen College Of Pharmacy.

**6. CONFLICT OF INTEREST**
We declare that we have no conflict of interest.

**REFERENCES:**

1.Kahn, R. S. & Keefe, R. S. E. Schizophrenia is a cognitive illness: time for a change in focus. JAMA Psychiatry 70, 1107–1112 (2013).
2. A. Dolenc, J. Kristl, S. Baumgartner, O. Planinšek, Advantages of celecoxib nanosuspension formulation and transformation into tablets, Int. J. Pharm. 376 (2009) 204–212
3.Citrome L. Lurasidone in schizophrenia: new information about dosage and place in therapy. Adv Ther 2012; 29: 815-25.
4. Nakarani, M.; Misra, A.K.; Patel, J.K.; Vaghani, S.S. Itraconazole nanosuspension for oral delivery: Formulation, characterization and in vitro comparison with marketed formulation. Daru 2010, 18, 84–90.
5. Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F, Khan A. Orally disintegrating films: A modern expansion in drug delivery system. Saudi pharmaceutical journal. 2016 Sep 1;24(5):537-46.
6. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: A new approach to oral drug delivery system. International journal of pharmaceutical investigation. 2013 Apr;3(2):67.
7.D.R. Choudhary, V.A. Patel, U.K. Chhalotiya, H.V. Patel, A.J. Kundawala, Development and characterization of pharmacokinetic parameters of fast dissolving films containing levocetirizine, Sci. Pharm. 80 (2012) 779–878.
8.A. Dinge, M. Nagarsenker, Formulation and evaluation of fast dissolving films for delivery of triclosan to the oral cavity, AAPS PharmSciTech 9 (2008) 349–356.
9. Soni MM, Patel KR. Formulation and evaluation of fast dissolving films of lurasidone hydrochloride. IntJPharm ResBioSci2016;5:101-23.
10. Senthilkumar K, Vijaya C. Formulation development of mouth dissolving film of etoricoxib for pain management. Advances inP'ceutics; 2015. https://doi.org/10.1155/2015/702963.
11. Satyanarayana, D.A.; Keshavarao, K.P. Fast disintegrating films containing anastrazole as a dosage form for dysphagia patients. Arch. Pharm. Res. 2012, 35, 2171–2182.
12. Shen, C.; Shen, B.; Xu, H.; Bai, J.; Dai, L.; Lv, Q.; Han, J.; Yuan, H. Formulation and optimization of a novel oral fast dissolving film containing drug nanoparticles by Box–Behnken design response surface methodology. Drug Dev. Ind. Pharm. 2014, 40, 649–656.
13.El-Dahmy, R.M.; Elsayed, I.; Elshafeey, A.H.; Abd El Gawad, N.A.; El-Gazayerly, O.N. Optimization of long circulating mixed polymeric micelles containing vinpocetine using simple lattice mixture design, in vitro and in vivo characterization.
14.Mishra R, Amin A. Manufacturing techniques of orally dissolving films. J Pharm Sci 2011;35:70–73