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Formulation and Evaluation of Nano Suspension Based Oro Disoersible Film of Aripiprazole

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Abstract:
The present study was aimed to enhance the solubility and dissolution of BCS class 4 drug aripiprazole, by nano formulation approach. Acid-base neutralization method had been used to produced nanosuspension. The nanosuspensions remained stable without any aggregations with particle size 209.6nm and PDI 0.247. Zeta potential was found to be 3.5mV. Drug content, Entrapment and solubility of nanosuspension formulations were determined. *In vitro* drug release of the selected formulation has shown a drug release of 95.63% by the end of 1 hr, whereas plain drug suspension has shown only 12.3% release. XRD and DSC studies revealed that the solid form of aripiprazole altered from the crystalline state to the amorphous state after incorporation into nanosuspensions. Hence, from the results, it can be concluded that Aripiprazole, when formulated by acid-base neutralization method as a nanosuspension, leads to enhanced solubility, dissolution, and stability.
Objective: The aim of this study is to prepare fast-dissolving oral films containing Aripiprazole. However, the candidate's poor solubility is a major concern in achieving the required bioavailability from the films. Thus, this approach is designed to address solubility issues via solid acid-base neutralization, method and prepare the oral films containing the nanosuspensions of the drug.
Method: The nanosuspensions prepared using an acid phase (Conc HCL) and a basic phase (NAOH) with adding of poloxamer 407. Various molar concentrations of acidic phase and basic phase were studied using acid-base neutralization method. The nanosuspension ratios which exhibited maximum solubility dissolution rate , drug content and drug release was further incorporated into oral film. The film consisted of hydroxypropyl methylcellulose (HPMC) as a film-forming polymer , tween-80 (a plasticizer), poloxamer, citric acid (a saliva stimulant), and saccharin as sweetener. Various physical parameters, drug content, solubility, disintegration time in vitro release profiles, and other factors were evaluated for the oral films.

Keywords: Aripiprazole, HPMC, nanosuspensions, oral dispersible films, increased solubility, dissolution, bioavailability.

1.INTRODUCTION

Schizophrenia and other psychotic disorders are categorized under the spectrum of primary psychotic disorders in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Individuals with psychosis experience various neuropsychiatric symptoms, such as hallucinations,

delusions, thought disorders, unusual motor behaviors, negative symptoms, cognitive impairments, and emotional disturbances. The longstanding theory that schizophrenia is linked to elevated levels of the neurotransmitter dopamine in the brain stems mainly from observations that dopamine agonists can induce or exacerbate psychotic symptoms.(1)

Antipsychotic drugs are the best choice for treating above mentioned psychiatric disorders.

Blocking dopamine D2 receptors is considered a crucial, and possibly even sufficient, neuropharmacological action for the effectiveness of most antipsychotic drugs, particularly in treating symptoms like hallucinations, delusions, and schizophrenia. By inhibiting these receptors, antipsychotic medications help to reduce the overactivity of dopamine, which is believed to play a significant role in the manifestation of psychotic symptoms.

However, clinical studies reveal a significant issue with patient noncompliance regarding these medications. Many patients do not adhere to their prescribed treatment regimens for various reasons, including side effects, lack of insight into their condition, or the complexity of their medication schedules. This noncompliance has severe consequences. Patients who do not consistently take their medications are at a higher risk of being rehospitalized, requiring emergency room visits, and experiencing homelessness. Additionally, their symptoms often worsen without continuous treatment, leading to a decline in their overall mental health and quality of life. Effective management of schizophrenia and other psychotic disorders, therefore, not only involves prescribing the correct medication but also ensuring that patients adhere to their treatment plans through supportive measures and interventions.(2)

Nanosuspensions are water-based suspensions that contain drug substances with particle sizes in the submicron range, along with stabilizers to maintain their stability. These stabilizers include excipients that help in the nanogrinding process of the drug particles, prevent the particles from growing into larger crystals or clumping together during storage, and maintain the suspension's pH. Additionally, preservatives and other components might be included for further processing, such as converting the suspension into a solid form, or for patient administration, such as adding sweeteners and colorants.(3)

Bioavailability refers to the extent and rate at which an active substance is absorbed from a pharmaceutical form and becomes available at the site of action.(4) From a pharmacokinetic perspective, bioavailability data for a specific formulation estimate the relative fraction of the orally administered dose that enters the systemic circulation compared to a solution, suspension, or intravenous dosage form. These studies also provide valuable pharmacokinetic information related to distribution, elimination, nutrient effects on drug absorption, dose proportionality, and the linearity of pharmacokinetics for active and inactive components. Additionally, bioavailability data can indirectly reveal the drug's physicochemical properties before entering the systemic circulation, such as solubility or permeability and the impact of pre-systemic enzymes or transporters.

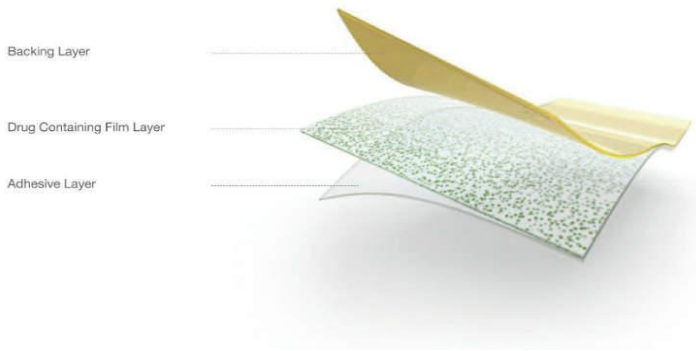
Depending on a drug's physicochemical properties, either solubility or the permeation rate across the intestinal epithelium may limit the drug's entry into systemic circulation. For drugs in BCS classes II and IV, solubility is the rate-limiting factor, leading to low oral bioavailability. Consequently, only a small amount of the drug reaches the systemic circulation, necessitating frequent dosing and potentially increasing dose-dependent systemic side effects. This challenge has spurred the development of advanced, efficient, and novel techniques to administer poorly soluble compounds at safe and effective therapeutic levels.(5)

Oral administration is considered the most convenient route for drug delivery due to lower production costs, suitability for self-medication, higher patient safety, and better compliance. However, an orally

administered drug must meet specific criteria: sufficient solubility in gastrointestinal (GI) fluids, stability against acidic and enzymatic degradation in the GI tract, and the ability to permeate the intestinal barrier to reach the systemic circulation in adequate amounts. Developing suitable oral formulations for poorly water-soluble drugs is a major challenge for formulation scientists, as the first step in oral absorption is the dissolution of the drug in GI lumen contents. Poor aqueous solubility is a significant hurdle for oral drug delivery. To address this, various physical and chemical approaches (e.g., reducing particle size, modifying crystal habits, creating polymorphs and pseudo-polymorphs, forming inclusion complexes with cyclodextrins, using micro emulsifying systems, amorphous solid dispersions, soluble prodrugs, and salt formation) are employed to overcome solubility and bioavailability issues.(6)

Oral films are very thin strips designed for placement on the patient's tongue or any oral mucosal tissue. When exposed to saliva, the film rapidly hydrates and adheres to the application site. It then quickly disintegrates and dissolves, releasing the medication for oromucosal absorption. With modifications in the formula, these films can also maintain their quick-dissolving properties to allow for gastrointestinal absorption when swallowed. Oral films promote patient compliance due to their appealing form and ease of administration. They are particularly useful for bedridden and non-cooperative patients, as they are easily administered and difficult to spit out. Thus, oral films are a suitable alternative for patients with swallowing difficulties and offer a more convenient dosage form compared to conventional oral dosage forms.(7)

Fast dissolving oral film formulations include key components such as water-soluble polymers, plasticizers, active pharmaceutical ingredients, sweetening agents, saliva-stimulating agents, flavoring agents, coloring agents, stabilizing and thickening agents, permeation enhancers, and super disintegrants. These ingredients combine to form a convenient and effective medication delivery system.



A typical oral film

Aripiprazole is an antipsychotic medication that is used to treat the symptoms of schizophrenia It is also used together with other medications to treat major depressive disorders in adults. It belongs to biopharmaceutics classification system (BCS) class II, has a poor water solubility. Aripiprazole reaches peak plasma concentration within 4 hours of administration, and steady state occurs within 10-12 days of dosing. Oral bioavailability is 95%, and can be administered with or without food.(9)

Being a class II BCS drug, the drug solubility is a major concern. Therefore, a suitable technique is required to improve the solubility, thus dose and dose related side effects can be minimized.

Solid dispersions have attracted considerable interest as an efficient means of improving the dissolution rate and hence bioavailability of a range of hydrophobic drugs. Solid dispersions of poorly water-soluble

drugs with water-soluble carriers reduce the incidence of these problems and enhanced dissolution. A solid dispersion is one of the most promising approaches for solubility enhancement.(9)

Advantages of Orally Fast Dissolving Films(10)

1. Can be administered without water, anytime and anywhere.
2. Provide rapid disintegration and dissolution in the oral cavity due to a larger surface area.
3. Flexible and portable, making them easy to transport, handle, and store.
4. Suitable for geriatric and pediatric patients, as well as those with swallowing difficulties, mental illness, developmental disabilities, uncooperative behavior, reduced liquid intake, or nausea.
5. Beneficial for conditions requiring ultra-rapid onset of action, such as motion sickness, acute pain, sudden allergic attacks, or coughing.
6. Offer long-term stability since the drug remains in solid form until consumed, combining the stability of solid dosage forms with the bioavailability of liquid dosage forms.
7. Ensure precise dosing with each strip, compared to liquid formulations.

Disadvantages of oral dissolving films:

1. **Dose Limitations**: High doses are difficult to incorporate into ODFs, usually needing to stay below 40 mg per 4 cm^2.
2. **Bitter Medications**: Not suitable for bitter-tasting medications due to the challenge of effective taste masking.
3. **Dose Homogeneity**: Achieving uniform drug distribution within the film is technically complex.
4. **Special Packaging**: Requires specialized packaging to maintain stability and protect from moisture.
5. **Irritation**: Drugs that irritate the oral mucosa are unsuitable for administration via ODFs

Method of preparation of nano suspension

Acid Base Neutralization method

Basic phase (NaOH)+ Drug +Acidic phase (HCL)+polaxomer

Neutralised nanoparticles

When creating neutralized nanoparticles, the process begins by preparing a basic phase using sodium hydroxide (NaOH) and polaxomer. This mixture is combined with an acidic phase containing hydrochloric acid (HCl) and drug. The interaction between the basic and acidic phases leads to the neutralization of the nanoparticles. Stir the mixture continuously for one hour at 600-800 rpm. This mixture is then homogenized for 15 minutes for further particle size reduction. The final solution is poured into a petri dish and kept at room temperature which forms powder after evaporation. The resulting formulation yields neutralized nanoparticles that may have improved stability and bioavailability, making them suitable for preparing an oral film.(11)

Evaluation of drug induced nano particles:

4.5.1 Clarity

The clarity of the nanosuspension was assessed simply by observing its visual appearance.

Fourier transform (FTIR)

Attenuated total reflectance-fourier transform infrared spectrum (ATR-FTIR) was used to identify if any

interaction exists between the drug and the carrier used. Samples were analysed in an IR spectrophotometer (Alpha-II (Bruker) in a region between 4000-400cm^{-1} .

pH Measurement of Prepared Nanosuspensions

The pH levels of the nanosuspensions from all selected formulations were measured using a digital pH meter from Digisun Electronics System, Hyderabad. The pH meter's glass electrode was directly immersed in the samples at room temperature, and the measurements were conducted three times for accuracy.(12)(13)(14)

Solubility Study of Nanosuspension

The solubility characteristics of aripiprazole nanosuspension were analyzed using a paddle method in a dissolution system (LABINDIA DS 8000). This was carried out in different media such as hydrochloric acid at pH 1.2, phosphate buffer at pH 6.8, and. The study was performed at a stirring speed of 50 rpm and a temperature of 37±0.5°C. Excess aripiprazole nanosuspension was added to each medium, and samples were taken at intervals, ultracentrifuged at 5000 rpm for 30 minutes, and then analyzed using a UV spectrophotometer at a wavelength of 287 nm. This was repeated until constant solubility readings were obtained. For comparison, the solubility of pure aripiprazole was also measured under the same conditions in all the media.

Drug content determination

Nanosuspension particles were taken (20mg,30mg and 60mg for subsequent 1:1, 1:2, and 1:3 ratios) was weighted into a 10ml of volumetric flask using distilled water and 6.8 pH buffer. The samples were subjected to mechanical stirring for 24hrs. After 24 hours, the sample was filtered. The filtrate volume of 1 ml was initially diluted to 10 ml in a volumetric flask and subsequently diluted again with 1 ml to reach a final volume of 10 ml in another volumetric flask using methanol. The solution was measured for the concentration of drug using Shimadzu UV spectrometer at the observed) max.

Particle Size Distribution and Polydispersity Index (PDI)

The particle size was analyzed using Photon Correlation Spectroscopy (PCS) with a Horiba Nanoparticle Analyzer (Nanopartica SZ-100). This method provided the mean particle diameter, also known as the z-average, along with the Polydispersity Index (PDI) and zeta potential, all measured at a temperature of 25°C.

4.5.6 Determination of Zeta Potential

The zeta potential, which indicates the surface charge properties and contributes to the long-term physical stability of the nanosuspension, was measured using a HORIBA SCIENTIFIC SZ-100 Zeta Sizer. Samples of the selected formulations were placed in an electrophoretic cell and measured three times at 25±1°C, with the average value reported. To achieve electrostatic stability, a zeta potential of at least ±30 mV is required, while a combination of electrostatic and steric stabilization requires at least ±20 mV. When an electric field is applied, particle movement within the measurement volume causes fluctuations in light intensity, which are processed by the digital signal processor and computer to produce a frequency spectrum. This spectrum is then used to calculate the electrophoretic mobility and, consequently, the zeta potential.

Differential Scanning Calorimetry (DSC) Analysis

The Differential Scanning Calorimetry (DSC) analysis of the pure drug (aripiprazole) and nanosuspension was conducted using a DSC 1 calorimeter from Mettler Toledo, Switzerland. The analysis was carried out under a nitrogen atmosphere with a flow rate of 20 ml/min. Approximately 3 mg of each sample was

accurately weighed and placed into aluminum pans, which were then sealed with a cover that had a small pinhole. The heating process was performed at a scan rate of 10°C per minute over a temperature range from 25°C to 250°C. An empty pan was used as a reference.

The fundamental principle of DSC is that when a sample undergoes a physical change, such as a phase transition, it requires more or less heat to maintain the same temperature as the reference pan. Whether more or less heat is needed depends on whether the process is endothermic (absorbing heat) or exothermic (releasing heat). In endothermic processes, the sample requires more heat to reach the same temperature, while in exothermic processes, it requires less. By measuring the difference in heat flow between the sample and the reference, the DSC can quantify the amount of heat absorbed or released during these transitions.

Powder X-Ray Diffraction (XRD) Analysis

The crystalline structure of the pure drug (aripiprazole) and aripiprazole nanosuspension was examined using a Powder X-Ray Diffractometer (XRD-6000, Shimadzu-Japan). The freeze-dried samples were scanned over a 2θ range of 3° to 45° using a continuous scan mode. The analysis was conducted at an operating voltage of 40 kV and a current of 30 mA. The scan was performed with a step size of 0.050° (2θ) and each step was held for 60 seconds to ensure accurate data collection.

Stability studies

Short term stability studies were carried out at 40℃ ± 2℃/75% ± 5% RH for 4 weeks to determine physical and chemical stability.

In Vitro Dissolution Studies

The in vitro release of aripiprazole from the nanosuspension, pure drug, each containing an equivalent of 5 mg of the drug, was evaluated using a Type II apparatus (paddle type). The test was conducted in 900 ml of pH 6.8 buffer, with the medium stirred at a speed of 25 rpm and maintained at a temperature of 37°C. The aripiprazole nanosuspension, pure drug, were added to the dissolution vessel, and the test was run continuously.

At specific time intervals 1-hour period, 1 ml samples were withdrawn from the dissolution medium and immediately replaced with 1 ml of fresh buffer to maintain consistent conditions. The collected samples were diluted appropriately with Ph 6.8 buffer, and their was measured using a UV spectrophotometer at a wavelength of 287 nm to determine the amount of drug released over time.

Preparation of Aripiprazole oral films.

Selected aripiprazole nanosuspension (1 molar) oral dispersible films (ODFs) were prepared using the solvent casting method. First, specific amounts of HPMC 15cp (300mg) , Tween 80 (0.9ml), citric acid 75mg were carefully measured and added to mixture of ethanol 12ml and water 3ml .This mixture was stirred for 45 minutes at 300rpm using a magnetic stirrer. The resulting mixture was then evenly spread onto a petri dish and dried at room temperature. Once dried, the films were carefully removed with a sharp blade, cut into appropriate sizes to contain 5 mg of aripiprazole, and then stored and evaluated.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
HPMC	300mg	450mg	375mg	450mg	300mg	375mg	375mg	300mg	450mg
Tween 80	0.9ml	1.05ml	1.05ml	0.9ml	0.75ml	0.9ml	0.75ml	1.05ml	0.75ml
Citric acid (in mg)	75	75	75	75	75	75	75	75	75
saccharin (mg)	75	75	75	75	75	75	75	75	75
methanol	12ml	12ml	12ml	12ml	12ml	12ml	12ml	12ml	12ml

water	3ml	3ml	3ml	3ml	3ml	3ml	3ml	3ml	3ml

Formulations F1-F9

Evaluation of Aripiprazole oral dissolving films

Drug content

Three film samples, each with an area of 6.2 cm² and containing 5 mg of Aripiprazole, were cut from different locations on the films. These samples were then dissolved in methanol to extract the drug. The extracted solutions were diluted with a pH 6.8 buffer and analyzed for drug content using a UV spectrophotometer (UV-1900i by Shimadzu, Tokyo) at the wavelength of maximum absorbance. A blank solution was prepared from a film without the drug for comparison. The experiment was conducted three times to ensure the accuracy and reliability of the results.

Film Thickness:

The thickness of the films was determined using a screw gauge, and the average thickness was calculated. Measurements were taken at five different spots across the film to ensure consistency. The percentage reduction in thickness from the wet to dry state was calculated using the quotient of the wet-to-dry film thickness.

Folding Endurance:

To evaluate folding endurance, films from each formulation were randomly selected and tested under bright light. The films were repeatedly folded at the same spot until any cracks or visible fissures appeared. This test measured the number of folds the films could withstand before breaking. Each test was conducted three times to ensure the accuracy and consistency of the results.

Disintegration time

The disintegration time of the oral films, each with an area of 3.14 cm², was evaluated by placing them in a 2 ml solution of phosphate buffer with a pH of 6.8. The films took 90 seconds to fully disintegrate.

In Vitro Dissolution Study:

4.9.5.1 Drug Release in 900 ml PBS:

The in vitro dissolution study was performed using a USP Type II dissolution apparatus. The dissolution medium consisted of 900 ml of phosphate buffer (pH 6.8) . The study was conducted at a temperature range of 37-40.5°C with the apparatus set to a rotational speed of 50 RPM. Oral dissolving patches (ODPs) from the desired formulation were placed in the apparatus, and samples were taken at specific time intervals—2,5,10, 20, 30, and 60, minutes. After each sampling, the volume was replenished with an equal amount of blank solution. The samples were then filtered, and the drug concentration was measured at the wavelength of maximum absorbance (λmax). A comparative analysis was also conducted against the pure drug and the selected formulation.

Fourier Transform Infrared Spectroscopy (FTIR):

Attenuated Total Reflectance-Fourier Transform Infrared Spectroscopy (ATR-FTIR) was used to detect any potential interactions between the drug and the carrier used in the formulation. The samples were analyzed using an IR spectrophotometer (Alpha-II by Bruker) within a wavelength range of 4000-400 cm^{-1}.

4.9.7 Moisture Uptake Studies:

The films were weighed and then placed in a desiccator containing a 1% aluminum chloride solution, where they were exposed to moisture for 24 hours. After this period, the films were re-weighed, and the

percentage of moisture content was calculated based on the weight difference.

4.9.8 Stability Studies:

Stability studies for the film formulations were conducted at two different storage conditions: 40°C ± 2°C with 75 ± 5% relative humidity (RH), and room temperature (25°C ± 2°C) with 65 ± 5% RH. These conditions were maintained for one month. At the end of the month, the drug content and physical properties of the films were assessed for both storage conditions.

Results

Melting point

Melting point of Aripiprazole was found to be 140^0c and it's meeting the standards as specified in official limits i.e., 140-143^0C.

Table 10 Melting point studies

Trails	Observed values
Trail 1	140^0C
Trail 2	139^oC
Trail 3	142^0C
Average 140^0C	

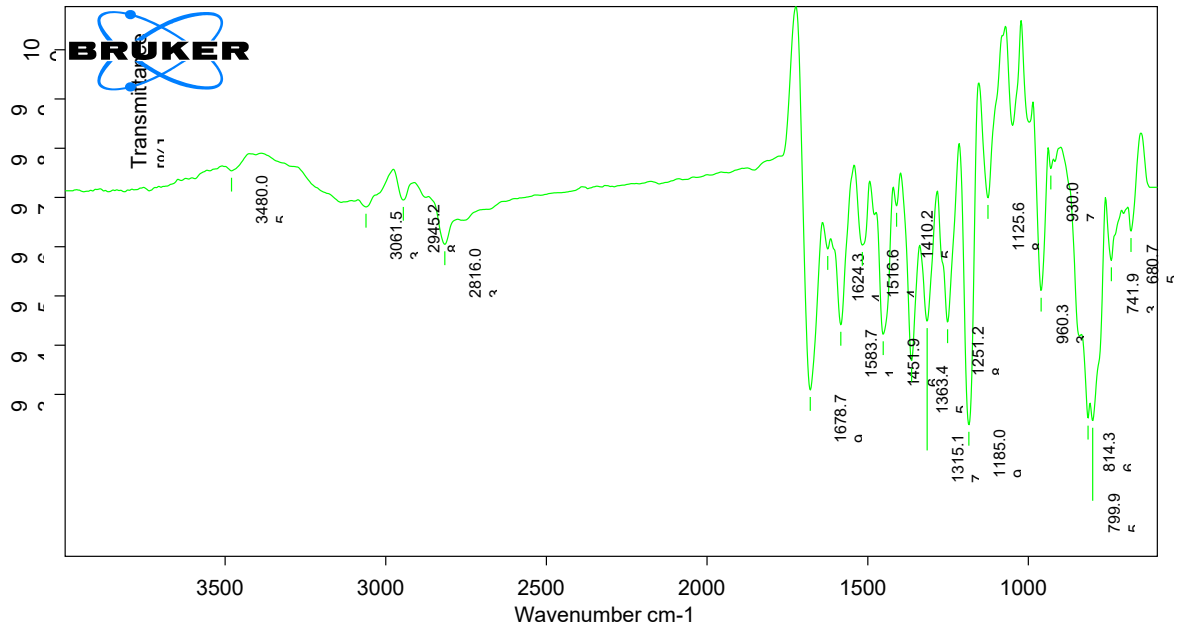
Initial solubility of drug aripiprazole

- aripiprazole is soluble in Methanol, Ethanol
- Practically insoluble in waterS

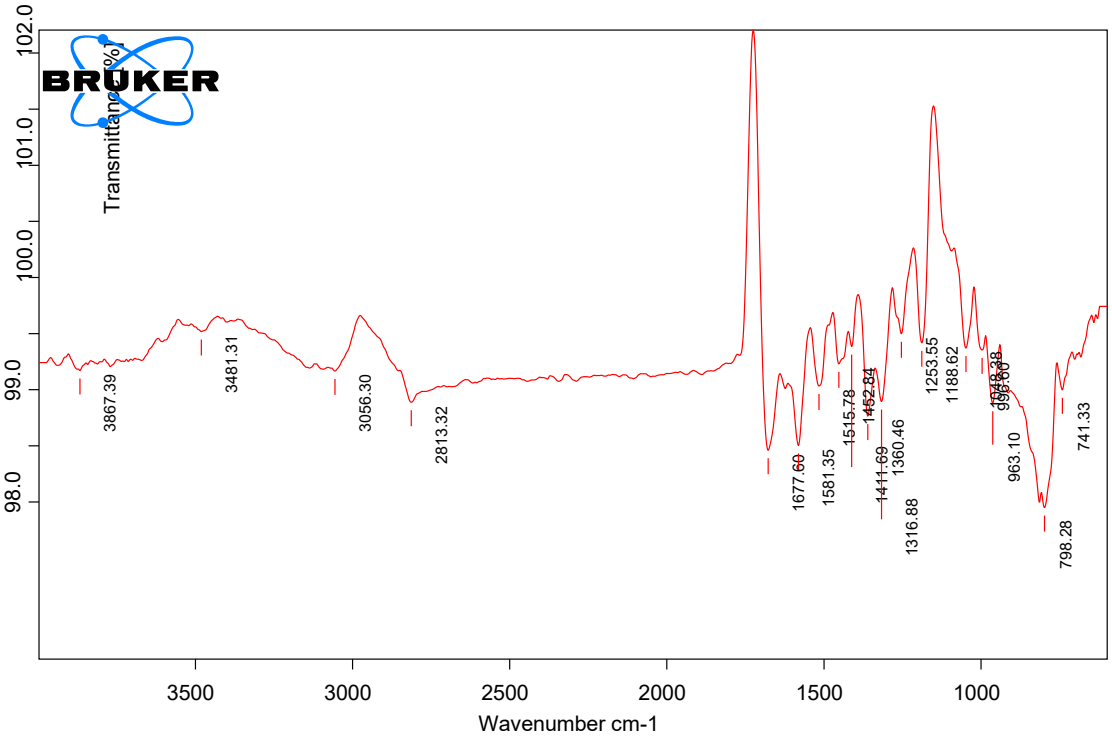
Drug content

Pure drug	**48%**
Nanoparticle	**89%**

FTIR – COMPATIBILITY STUDIES



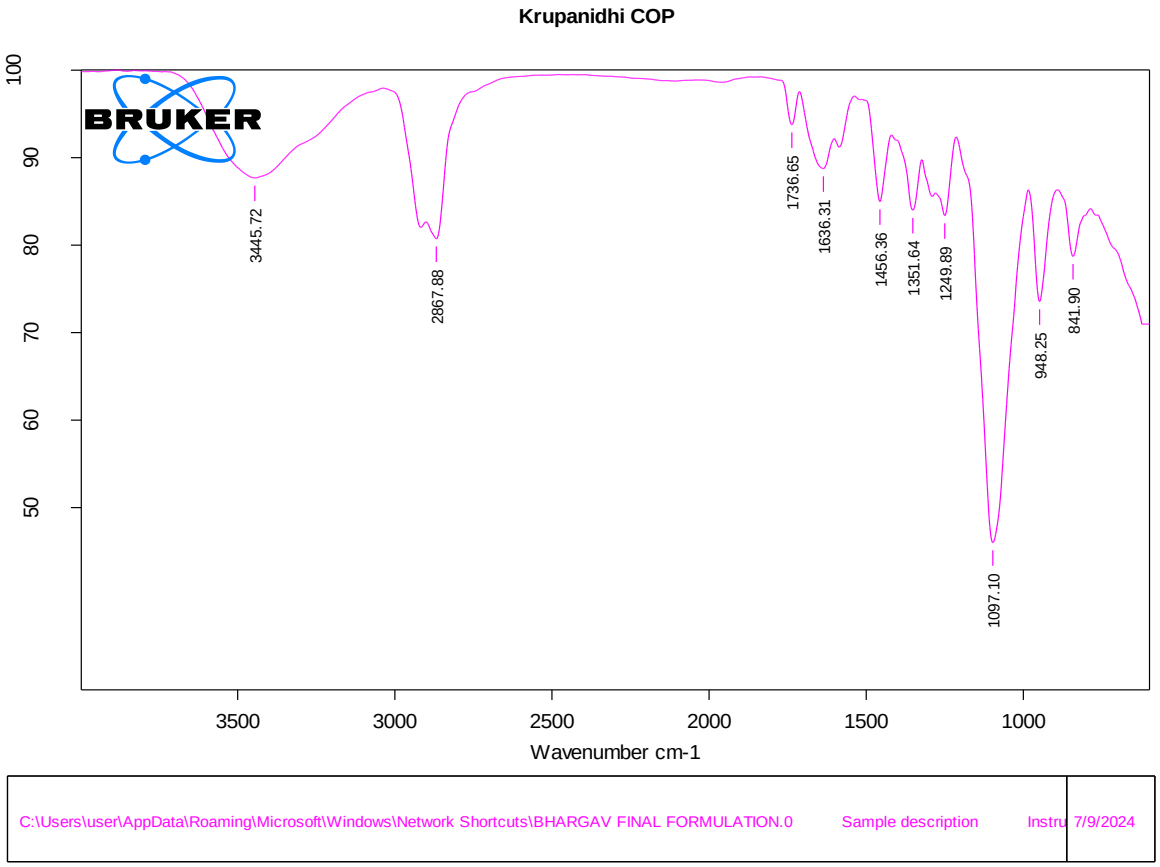
PURE DRUG



Pure drug + polymer

ALL EXCIPIENTS

Final formulation



Particle size
Nanosuspension
Drug
Zeta potential

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HORIBA Scientific

HORIBA SZ-100 for Windows [Z Type] Ver2.00

SZ-100

Measurement Results

Date	:	Wednesday, May 08, 2024 3:25:43 AM
Measurement Type	:	Particle Size
Sample Name	:	1M suspension_06_05_24_size
Scattering Angle	:	90
Temperature of the Holder	:	25.2 °C
Dispersion Medium Viscosity	:	0.891 mPa·s
Transmission Intensity before Meas.	:	26470
Distribution Form	:	Standard
Distribution Form(Dispersity)	:	Polydisperse
Representation of Result	:	Scattering Light Intensity
Count Rate	:	2240 kCPS

Calculation Results

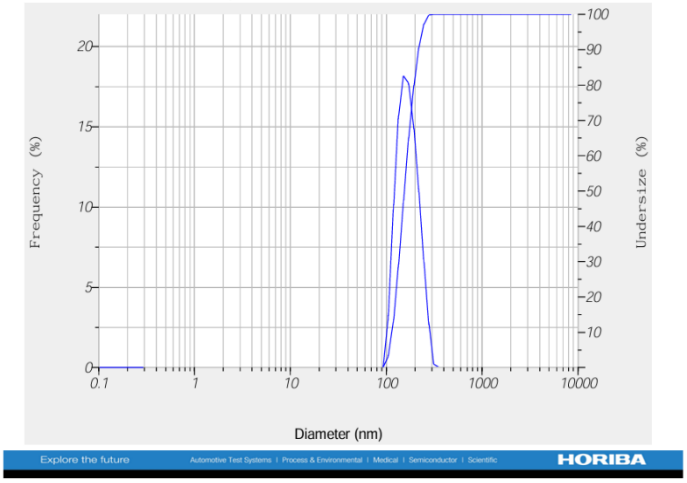
Peak No.	S.P.Area Ratio	Mean	S. D.	Mode
1	1.00	190.9 nm	51.3 nm	162.6 nm
2	---	--- nm	--- nm	--- nm
3	---	--- nm	--- nm	--- nm
Total	1.00	190.9 nm	51.3 nm	162.6 nm

Cumulant Operations

Z-Average	:	209.6 nm
PI	:	0.247

Molecular Weight Measurement

Molecular Weight	:	---
Parameters for Molecular Weight Calculation	:	---



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HORIBA SZ-100 for Windows [Z Type] Ver2.00

SZ-100

Measurement Results

Date	:	Wednesday, May 08, 2024 3:17:19 AM
Measurement Type	:	Particle Size
Sample Name	:	1M Powder_06_05_24_size
Scattering Angle	:	90
Temperature of the Holder	:	25.3 °C
Dispersion Medium Viscosity	:	0.889 mPa·s
Transmission Intensity before Meas.	:	26144
Distribution Form	:	Standard
Distribution Form(Dispersity)	:	Polydisperse
Representation of Result	:	Scattering Light Intensity
Count Rate	:	2088 kCPS

Calculation Results

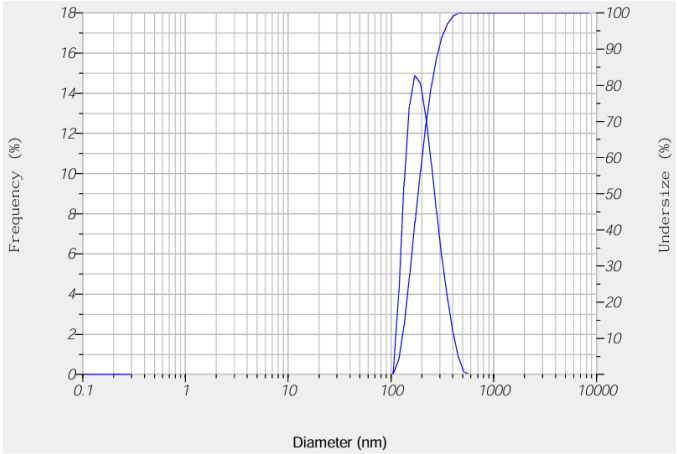
Peak No.	S.P.Area Ratio	Mean	S. D.	Mode
1	1.00	199.2 nm	66.1 nm	161.9 nm
2	---	--- nm	--- nm	--- nm
3	---	--- nm	--- nm	--- nm
Total	1.00	199.2 nm	66.1 nm	161.9 nm

Cumulant Operations

Z-Average	:	207.6 nm
PI	:	0.372

Molecular Weight Measurement

Molecular Weight	:	---
Parameters for Molecular Weight Calculation	:	---



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HORIBA Scientific

HORIBA SZ-100 for Windows [Z Type] Ver2.00

SZ-100

Measurement Results

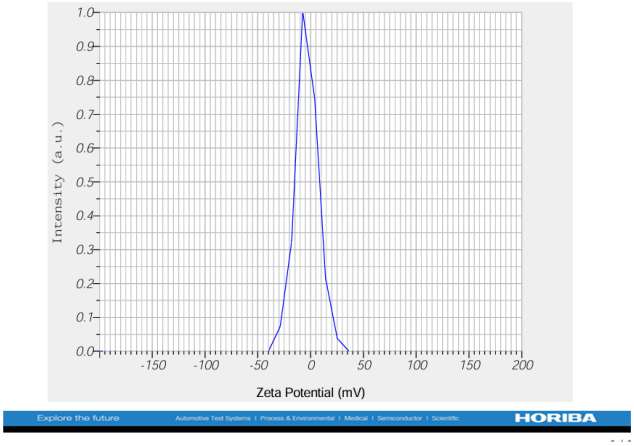
Measurement Results

Date	:	Wednesday, May 08, 2024 3:38:27 AM
Measurement Type	:	Zeta Potential
Sample Name	:	1M suspension_06_05_24_zeta
Temperature of the Holder	:	25.2 °C
Dispersion Medium Viscosity	:	0.892 mPa·s
Conductivity	:	5.046 mS/cm
Electrode Voltage	:	2.3 V

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-3.5 mV	-0.000027 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean)	:	-3.5 mV
Electrophoretic Mobility Mean	:	-0.000027 cm²/Vs



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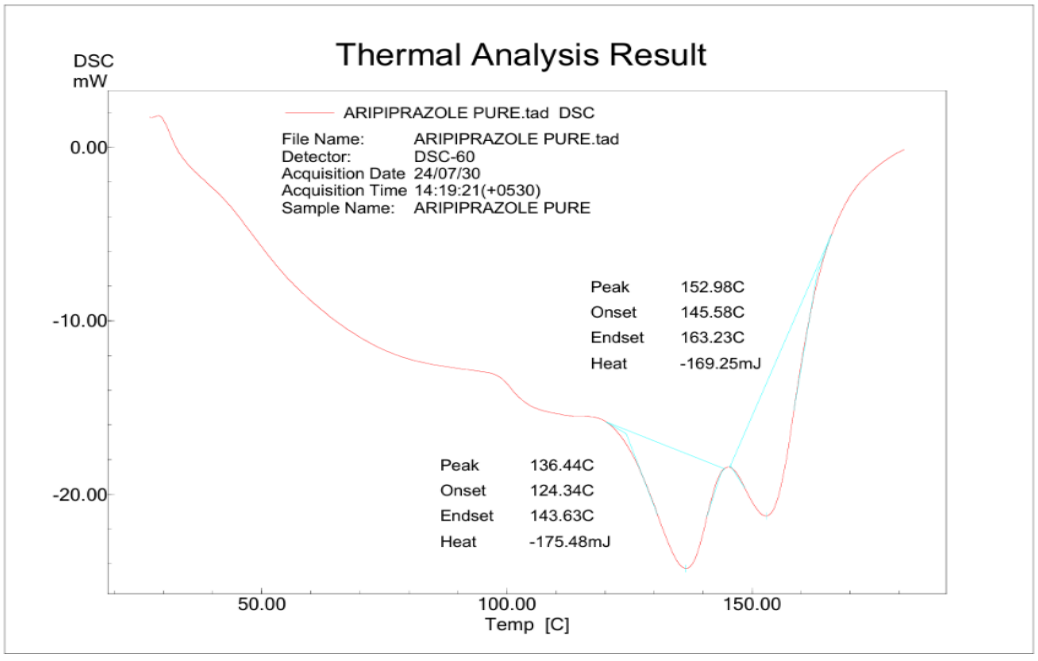
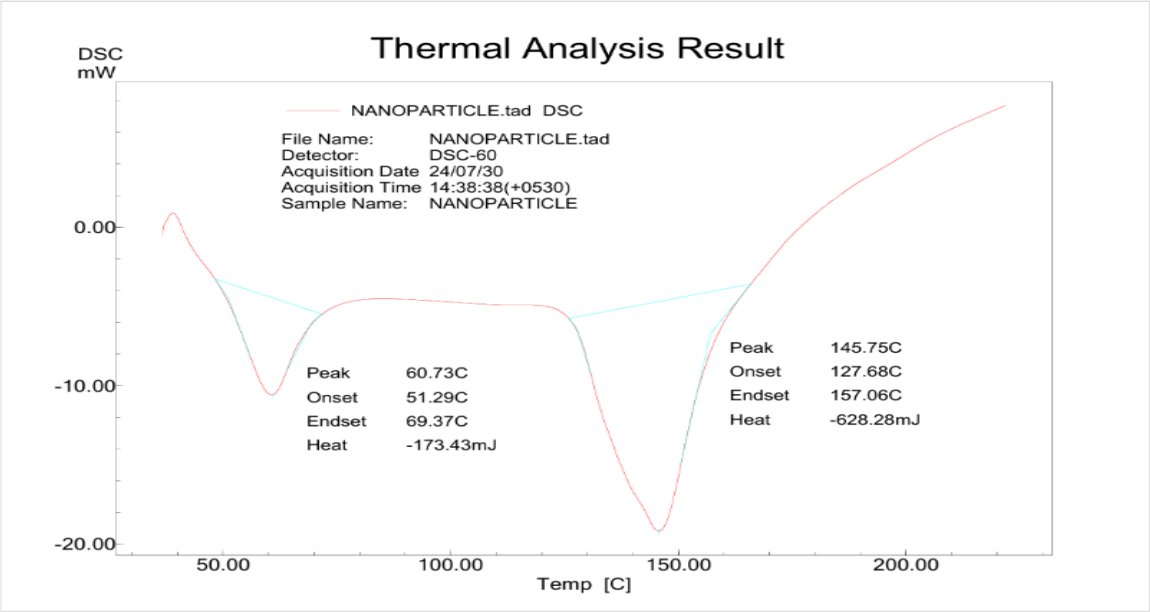
DSC analysis

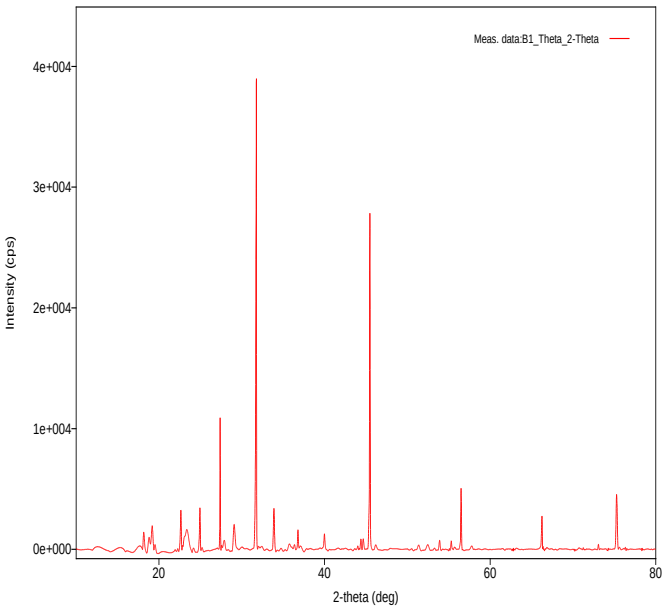
PURE DRUG - ARIPIPRAZOLE

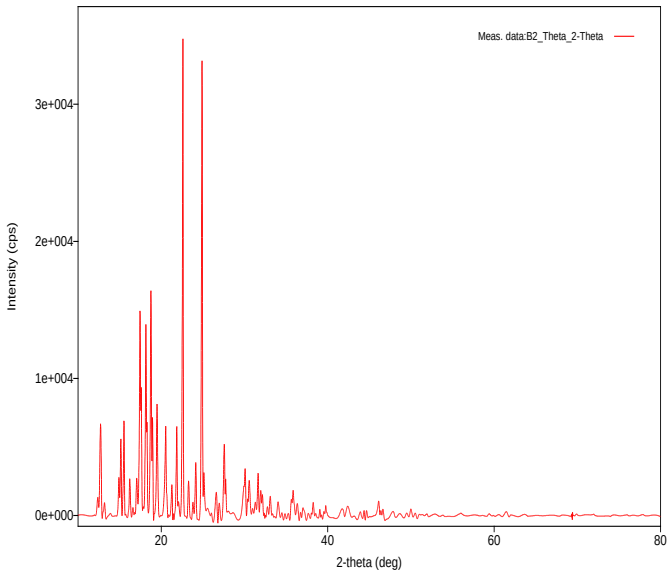




DSC – Nanoparticle

Powder X Ray Diffraction





formulations	absorbance	DC-%
f1	0.382	96.36±0.29
f2	0.371	94.63±0.15
f3	0.353	89.17±0.29
f4	0.387	98±0.17
f5	0.369	93.6±0.13
f6	0.363	92.1±0.12

f7	0.383	97.1±0.24
f8	0.377	94.01±0.25
f9	0.353	89.07±0.45

Drug content

***In vitro* drug release profile**

Dissolution rate of oral films , nano suspension and pure drug in pH 6.8 buffer

S. NO	Time(min)	CDR (%)		
		Pure drug	Oral films	Nano suspension
1	2	0	53.865±0.240	39.11±0.29
2	5	0	80.85±0.129	75.19±0.26
3	10	0.720	98.81±0.088	98.61±0.31
4	20	1.740	36.02±0.438	49.70±0.15
5	30	1.860	22.62±0.322	35.10±0.29
6	1 hour	2.560	22.74±0.149	22.65±0.28

Parameters evaluated for 1:1 molar nano suspension oral films

Sl. NO.	Evaluation of oral films	Results
1	Folding endurance	>200 (150 folds)
2	Drug content (%)	96.9 ± 0.17
3	Moisture content (%)	0.13 ± 0.010
4	Moisture uptake	0.15 ±0.011
5	Thickness	2.27 ± 0.15

Stability studies data

Parameters	40^0C at 5%RH		25^0C at 5%RH	
	0 days	30 days	0 days	30 days
Physical evaluation	Clear and transparent	Clear and slightly opaque	Clear and transparent film	Clear and slightly opaque film
Drug content (%)	94.9	93.7	94.9	94.8

CONCLUSION

Addressing the challenge of water-insoluble pharmaceuticals, which often suffer from low solubility and bioavailability, nanosuspensions present a novel and practical solution. However, the aggregation of nanoparticles within these suspensions can pose significant issues, potentially compromising their

effectiveness. To mitigate this problem, Oral Fast Dissolving Films (OFDFs) have emerged as an innovative approach to stabilize and optimize nanosuspensions**.**

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