

## FORMULATION AND DEVELOPMENT OF MUCOADHESIVE NASAL DRUG DELIVERY OF ROPINIROL HCL FOR BRAIN TARGETING

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### ABSTRACT

**Objective:** The purpose of this research was to create polymeric nanoparticles of ropinirole HCl for nasal administration utilising the ionic gelation process.

**Methods:** The preparation method was optimized using box-behnken design employing chitosan concentration, guar gum concentration and surfactant concentration as independent variables were as Encapsulation efficiency and mucoadhesion of the formulation were selected as dependent variables. Differential scanning calorimetry and infrared spectroscopy analysis of the drug and polymers revealed that the drug and excipients are physicochemically compatible. Studies on entrapment efficiency, drug content, and *In vitro* release were conducted on the nanoparticles.

**Results:** Each formulation was determined to have a drug content of between 60% and 70% and an entrapment efficiency of between 65% and 84%. *In vitro* drug release tests demonstrated that ropinirole HCl will release between 65 and 81 percent after 5 h.

**Conclusion:** The results showed that the particle size, encapsulation effectiveness, and drug content were all significantly affected by the amounts of chitosan and guar gum.

**Keywords:** Ropinirole HCl, Nanoparticles, Box-behnken, Mucoadhesion, Encapsulation

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### INTRODUCTION

The intranasal route (INDD) has gained prominence in recent decades as a means of administering treatments for the central nervous system (CNS) and related disorders. Evidence suggests that Parkinson's disease is a degenerative movement disorder of neurological system. Dopamine levels drop when cells die off in the midbrain region known as substantia nigra. Alzheimer's disease, Parkinson's disease, brain tumours, migraine, schizophrenia, meningitis, etc., are all disorders of CNS, and despite their enormous frequency and incidence, they remain incurable because medications cannot reach the brain fast enough [1]. Therefore, efficient drug delivery to brain is a necessary initial step in the treatment of such severe illnesses. But, the main problem in doing so is many of drugs do not reach brain from the bloodstream due to the impermeable nature of the Blood-Brain Barrier (BBB). Hence, it is required to developed newer unconventional drug delivery strategies that are mainly influencing the current modes of target site-specific administration in medical practices [2]. One of the most promising and effective methods for improving brain medication delivery is nanotechnology [3]. Improved efficacy [4], decreased toxicity [5], increased patient compliance [6], and prolonged therapeutic effect are only few of the benefits of using a nanoparticle drug delivery system instead of more traditional dosage forms [7].

The formulation scientist has a huge potential to improve the distribution of small-molecule medications and bio-macromolecular pharmaceuticals to brain through nasal route of administration [8]. As a part of novel drug delivery system, brain-targeted drug delivery from nose to brain is possible with the help of a nanocarrier, which can improve drug absorption into the nasal mucosa and offer regulated drug release by boosting mucoadhesion [9]. Therefore, the rationale

behind the current study is to create Ropinirole HCl chitosan nanoparticles for use in brain-specific delivery [10].

### MATERIALS AND METHODS

#### Chemicals and reagents

The drug was purchased from Sigma Aldrich and all chemicals and reagents used in the study were purchased from Merck Laboratories.

#### Pre-formulation studies

Pre-formulation studies are the primary phases in the pharmaceutical development of drug substance into different dosage forms [11].

#### Identification of drug

Melting point analysis and IR spectroscopy analysis were used to positively identify the medication.

#### Physicochemical properties of the drug

The drug ropinirole HCl was studied for Colour, Odour and Appearance.

#### Solubility study

Ropinirole HCl solubility in distilled water is measured using a UV-Visible spectrophotometer (Shimadzu-1800, Japan)  $\lambda_{max}$  249 nm using the Saturation solubility method.

#### Melting point

Ropinirole HCl's melting point was measured using a capillary technique. The melting point was performed by placing little amount of drug sample in capillary tube, sealing off one end, and placing in a melting point device.

### Infrared spectroscopy

Ropinirole HCl was placed in a sample container to acquire an FTIR spectrum. FTIR spectrophotometer was used to capture spectra.

### Drug: excipients compatibility study

FTIR and DSC were used to examine the excipients' compatibility with the medication. It is crucial to study drug-polymer interactions in an experimental setting before formulating a medication. Verifying that the medicine does not react with the polymer and excipient and decrease the product's shelf life is essential.

### FTIR (Fourier transform–infrared spectroscopy) study

FTIR of Ropinirole HCl, Chitosan, Jackfruit mucilage and physical mixtures (1:1ratio) were recorded by using FT-IR spectrophotometer (Shimadzu, I. R Affinity-1) wherein approximately 2-4 mg of given samples were placed in the sample holder. Scanning range was 4,000-400  $\text{cm}^{-1}$  to obtain FT-IR spectrum [12].

### DSC (Differential scanning calorimetry) study

DSC (Mettler Toledo, DSC-1) thermal study was performed on Ropinirole HCl, Chitosan, Jackfruit Mucilage, and their physical combinations. All of the aforementioned samples were crimped and weighed in a DSC aluminium pan (about 4-5 mg). The samples were then heated under nitrogen atmospheres at rate of 100  $^{\circ}\text{C}/\text{min}$  from 300  $^{\circ}\text{C}$  to 3000  $^{\circ}\text{C}$ . Both drug and the drug-excipients mixture had their heat flow rates tested as a function of temperature [13].

### Standard calibration curves of ropinirole HCl

### UV-visible spectroscopy

UV-visible spectrum (UV 1800, Shimadzu) of Ropinirole HCl was obtained by scanning drug solution in pH 6.8 buffer at 400 nm-200 nm; maximum absorbance was observed at 249 nm [14].

### Formulation

This study includes the formulation development of Ropinirole HCl polymeric nanoparticles for Nasal delivery. The major components for the formulation of polymeric Nano particulate system include the drug, polymers and surfactant. After the identification of the drug, various materials were screened as components for the proposed delivery system. These selections were done in the Preliminary batches to decide the proper concentrations of each component to produce small-sized particles with better parameters in the prepared formulation [15].

### Screening of polymer

Formulation of Polymeric nanoparticles by ionic gelation method requires two oppositely charged i.e. polycationic and polyanionic

polymers. For that chitosan a natural polymer is selected due to its polycationic nature, biodegradability and mucoadhesive properties. Also, different anionic charged polymers were screen for further investigations.

### Screening of surfactant

Particle size, polydispersity index (PDI) and zeta potential were measured after nanoparticles were produced with the chosen polymers using various surfactants. Entrapment efficiency was prioritised alongside minimal particle size when choosing the surfactant.

### Formulation of polymeric nanoparticles

The non-ionic surfactant Poloxamer 188 was used in an ionic gelation process to create the chitosan NPs. Chitosan NPs are made by combining cationic chitosan with anionic polymer in two different aqueous phases at room temperature. Overnight, 1.5 mg/ml of chitosan was dissolved in a 1% v/v acetic acid solution with continual stirring. Adjust the pH 5.5 of formed chitosan solution by 0.1N NaOH solution. Add 0.5% Poloxamer 188 to that chitosan solution and allow it to freeze for 15 min to dissolve the surfactant. Ropinirole HCl 50 mg was added into chitosan solution. Spraying 5 ml of JM solution into 50 ml of chitosan solution (1:10) while continuously stirring (800-900 rpm) with a magnetic stirrer for 30 min yielded NPs. After 30 min, a probe sonicator was used to sonicate generated suspension for at least 15 min. Ultra-centrifugation at 15,000 rpm at 10  $^{\circ}\text{C}$  for 45 min removed NPs from the aqueous medium and concentrated them. The pellets were washed with distilled water to ascertain drug concentration and cumulative drug release [16, 17], while the supernatant was used to calculate entrapment efficiency.

### Optimization of formulation using box behnken design

Ropinirole HCl polymeric nanoparticles were created while investigating the combined effect of two-level, three-factor variables using a box Behnken design. In this setup, 15 different permutations were tested, with each of the three components analysed at two different levels. Independent variables included Chitosan concentration and Poloxamer 188 concentration.

Two measures of efficacy were chosen as outcomes for this study: entrapment efficiency (Y1) and mucoadhesion (Y2). These two variables were placed in a box Behnken design with two levels of variation to see how they would affect the desired features of nanoparticle compositions. The influence of three independent factors on the response-dependent variable was investigated using the formulations created by this design of experiment in Design Expert Version 11. Following independent variable were used to formulate nanoparticles as shown in table 1.

**Table 1: Box behnken design parameters and their coded levels**

Independent variable	Level	
	Low	High
Conc of chitosan mg (X1)	1.0	2.0
Conc of surfactant (%) (X2)	0.5	1.5
Dependent variable	Entrapment efficiency(Y1) Mucoadhesion(Y2)	

### Evaluation of nanoparticles formulation

#### Determination of entrapment efficiency

To separate nanoparticles from non-entrapped medication, formulations were centrifuged at 15,000 rpm for 45 min at 10  $^{\circ}\text{C}$  in a Cooling Micro Centrifuge. The free drug concentration in supernatant was measured by UV spectrophotometer at  $\lambda_{\text{max}}$  249 nm. Equation [17] was used to determine the fraction of drugs encapsulated in nanoparticles.

$$\% \text{ EE} = \frac{\text{Total amount of drug added} - \text{Amount of drug in the supernatant}}{\text{Total amount of drug added}} \times 100$$

#### Determination of drug content

In order to create a pellet, nanoparticle compositions were centrifuged at 15,000rpm for 45 min at 10  $^{\circ}\text{C}$ . Resulting pellet was sonicated 15 min while being digested with 0.1 N HCl to produce a transparent liquid. Using a UV spectrophotometer set to a maximum wavelength of 249 nm, the drug concentration was assessed in the nanoparticles by comparing them to a reagent blank consisting of empty nanoparticles that had been manufactured and processed in the same way as the drug-loaded particles. Equation [18, 19] was used to determine the drug's percentage of content.

$$\% \text{ Drug Content} = \frac{\text{Actual drug content}}{\text{Theoretical drug content}} \times 100$$

### In vitro drug release study

Formulations (F1–F15) were tested for drug diffusion *in vitro* utilising dialysis membrane (Mw cut-off 12,000–14,000 Dal). Hi Media, Mumbai, India) that had been rehydrated after an 8-hour soak in phosphate buffer pH 6.8. Franz diffusion cell (20 ml) (Orchid Scientific, India) at 300 rpm, 37±0.5 °C, with membrane attached between donor and receptor compartment. Phosphate buffer, pH 6.6, was injected into the receptor compartment [20].

### Differential scanning calorimetry

DSC was used to examine the temperature reactions of dried nanoparticle compositions. The pellet was weighed out at about 5 mg, and then crimped shut and lid perforated into DSC sample pans. Each sample was examined at temperatures ranging from 30 to 300 °C at a ramp rate of 10 °C/minute [21, 22].

### Stability studies

The optimal nanoparticle formulation F13 underwent a stability analysis in a controlled environment called a stability chamber. Over the course of a three month, we kept the sample at three different temperatures and humidity levels: room temperature, refrigerator temperature, and 37 °C (relative humidity = 75%). After 1, 2 and 3 mo, the entrapment efficiency, mucoadhesion, drug content and visual changes of the optimised batch F13 were assessed [23-29].

## RESULTS AND DISCUSSION

### Pre-formulation studies

**Drug Identification:** Identification of Ropinirole HCl determined by FTIR spectroscopy and Melting Point.

**Description:** Ropinirole HCl complies all physicochemical properties as per British Pharmacopoeia.

### Solubility study

The solubility of ropinirole HCl in distilled water mentioned in table 3.

Table 2: Physicochemical properties of ropinirole HCl

S. No.	Parameter	Standard	Observed	Conclusion
1	Colour	White	White	Complies
2	Odour	Odourless	Odourless	Complies
3	Appearance	Crystalline	Crystalline	Complies

Table 3: Solubility of ropinirole HCl

Solvent	Solubility mg/ml
Distilled water	Standard
	133 mg/ml
	Observed
	140 mg/ml

### Melting point determination

The measured melting point of ropinirole HCl agreed with the reported melting point of ropinirole HCl, falling between 249 and 250 degrees Celsius.

### IR spectrum

A structural peak of ropinirole HCl with corresponds to the functional groups are shown in fig. 1 from this the drug was identified and its interpretation was confirmed.

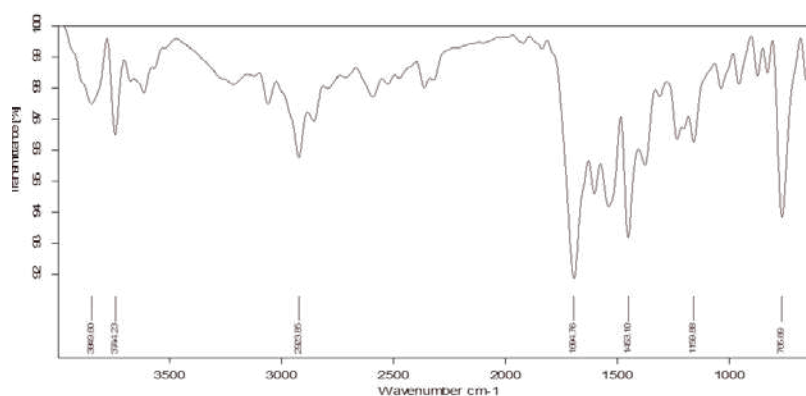


Fig. 1: Peak of ropinirole HCl in IR spectrum

Table 4: FTIR interpretation of ropinirole HCl

Peaks observed (cm <sup>-1</sup> )	Chemical groups interpreted
3744.23	N-H Stretch
1694.76	C=O Stretch
1453.10	C=C Aromatic
1159.88	C-N Stretch

### DSC thermogram

DSC was used to do a thermal investigation of Ropinirole HCl. A Ropinirole HCl sample was placed in an aluminium crucible and heated at a rate of 1000 °C/min from 30 to 3000 °C while thermogram was recorded in a nitrogen environment. In fig. 2 we see the Ropinirole HCl DSC thermogram.

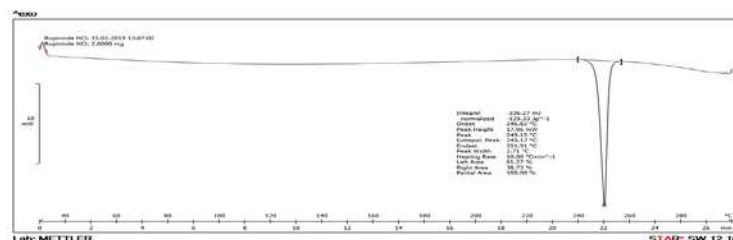


Fig. 2: DSC thermogram of ropinirole HCl

For Ropinirole HCl, the sharp endothermic peak was obtained at ~249.440 °C which is denoting the melting point of pure drug.

#### Standard calibration curve of ropinirol HCL

A standard calibration curve for ropinirole HCl in pH 6.8 buffer at  $\lambda_{max}$  249 nm was plotted, and it was found to be linear between 10 and 60  $\mu\text{g/ml}$ , as expected from Beer's and Lambert's laws. The outcomes are displayed in table 5.

Table 5: Standard calibration curve of ropinirole HCl in phosphate buffer pH 6.8

Concentration ( $\mu\text{g/ml}$ )	Absorbance
5	0.1658
10	0.3308
20	0.7071
30	1.1009
40	1.4460
50	1.8685

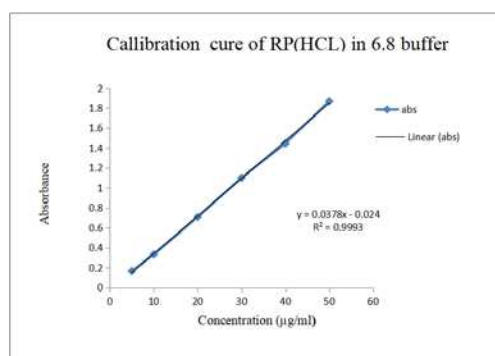


Fig. 3: Standard calibration curve of ropinirole HCl in pH 6.8 buffer

The calibration curve of ropinirole HCl was plotted in phosphate buffer pH 6.8 at 249 nm. The equation obtained was  $y = 0.0378x - 0.024$ . Correlation coefficient ( $R^2$ ) was found to be 0.9993.

#### Formulation development

The Ropinirole HCl-loaded polymeric nanoparticles were formulated containing Chitosan, guar gum and Kolliphor P-188 by ionic gelation method. The selections of the various components were done in the Preliminary batches to decide the proper concentrations of each component to produce small-sized particles with better parameters of the prepared formulation.

Table 6: Prototype formula for the preparation of nanoparticles

S. No.	Ingredient	Quantity
1	Ropinirol HCL	50 mg
2	Chitosan solution	50 ml
3	Guar gum	1 mg/ml

#### Formulation optimization by box behnken design

Entrapment efficiency (Y1) and mucoadhesion (Y2) were chosen as dependent variables, and the concentrations of Chitosan (X1), Guar gum (X2), and Poloxamer P-188 (X3) were chosen as independent factors.

#### Effect of formulation variables on entrapment efficiency

Effects of the independent and dependent variables on the response Y1 (Entrapment efficiency) were examined using an analysis of variance. The contour plots in fig. 4 and 5 were made using the derived regression model to analyse the interactions of the independent factors. Entrapment efficiency of all formulations ranged from  $67.96 \pm 0.03\%$  to  $89.45 \pm 0.39\%$ . Quadratic model was suggested for Entrapment efficiency. The Pred.  $R^2$  of 0.3017 is in reasonable agreement with the Adj.  $R^2$  of 0.7722. Concentration of gum (B) showed a significant effect on the entrapment efficiency. Increase the concentration of chitosan from 1.0-2.0 mg/ml decrease EE but beyond 2.0 mg conc. EE increases. At certain level, an increase in the concentration of Surfactant increases EE but further increase in conc. Of surfactant decrease the Entrapment efficiency.

#### Effect of formulation variables on mucoadhesive force

Effect size and statistical significance of the variables' and interactions' effects on response Y2 (Mucoadhesion) were calculated using analysis of variance. The contour plots in fig. 6 and 7 were made using the derived regression model to analyse the interactions of the independent factors.

Table 7: Formulation batches with their respective composition as per box behnken design

Formulation code	% Entrapment efficiency	% Drug content	Drug release	pH	Mucoadhesive
F1	65.36 $\pm$ 0.030	69.18 $\pm$ 0.01	70.89 $\pm$ 0.01	5	63.89 $\pm$ 0.04
F2	77.98 $\pm$ 0.017	79.43 $\pm$ 0.04	78.15 $\pm$ 0.020	5	66.31 $\pm$ 0.03
F3	76.07 $\pm$ 0.135	76.18 $\pm$ 0.01	71.22 $\pm$ 0.025	5	70.79 $\pm$ 0.08
F4	77.6 $\pm$ 0.050	76.183 $\pm$ 0.01	72.14 $\pm$ 0.01	5	69.2 $\pm$ 0.1
F5	75.18 $\pm$ 0.061	78.25 $\pm$ 0.02	70.75 $\pm$ 0.037	4	69.76 $\pm$ 0.02
F6	75.38 $\pm$ 0.085	80.62 $\pm$ 0.02	65.38 $\pm$ 0.04	4	68.55 $\pm$ 0.03
F7	75.14 $\pm$ 0.015	78.84 $\pm$ 0.04	73.89 $\pm$ 0.03	6	70.23 $\pm$ 0.02
F8	75.92 $\pm$ 0.075	73.81 $\pm$ 0.03	79.21 $\pm$ 0.02	6	69.47 $\pm$ 0.04
F9	73.72 $\pm$ 0.073	79.48 $\pm$ 0.05	73.46 $\pm$ 0.026	4	63.31 $\pm$ 0.02
F10	75.22 $\pm$ 0.050	78.74 $\pm$ 0.04	73.01 $\pm$ 0.005	4	63.89 $\pm$ 0.01
F11	73.25 $\pm$ 0.051	66.54 $\pm$ 0.02	75.19 $\pm$ 0.015	6	58.49 $\pm$ 0.03
F12	75.85 $\pm$ 0.01	70.7 $\pm$ 0.1	94.69 $\pm$ 0.020	6	61.27 $\pm$ 0.02
F13	84.1 $\pm$ 0.060	84.46 $\pm$ 0.03	84.18 $\pm$ 0.015	5	61.9 $\pm$ 0.04
F14	83.1 $\pm$ 0.007	83.46 $\pm$ 0.1	83.12 $\pm$ 0.015	5	60.9 $\pm$ 0.02
F15	83.1 $\pm$ 0.0173	83.46 $\pm$ 0.04	83.2 $\pm$ 0.015	5	60.9 $\pm$ 0.02

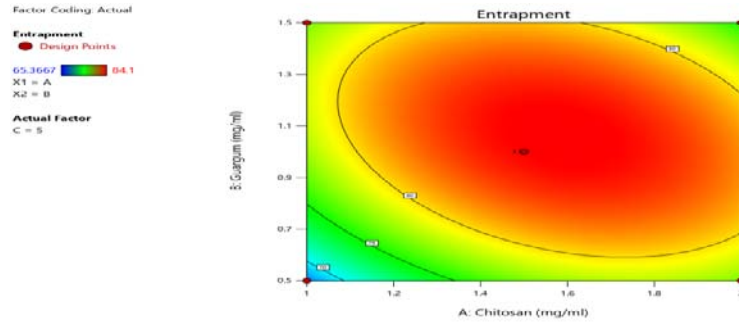
All readings taken in triplicate,  $n = 3 \pm \text{SD}$

From the above graph the Mucoadhesion of all formulations ranged from  $71.96 \pm 0.030\%$  to  $85.45 \pm 0.39\%$ . The Quadratic model was suggested for Mucoadhesion. The Pred.  $R^2$  of 0.3688 is in reasonable agreement with the Adj.  $R^2$  of 0.8895. Concentration of gum (B) showed significant effect on the Mucoadhesion. Increase concentration of chitosan from 1.0-2.0 mg/ml decrease mucoadhesion but beyond 2.0 mg conc. Mucoadhesion increases [24].

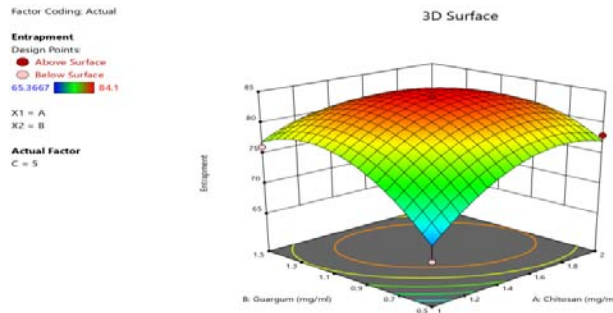
**Evaluation of nanoparticles formulation**

**Determination of entrapment efficiency**

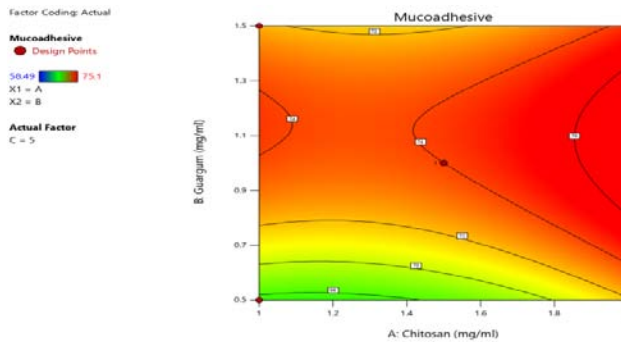
Entrapment efficiency of ropinirole HCl nanoparticles were found to be in the range of  $65.36 \pm 0.03\%$  to  $84.1 \pm 0.39\%$ . It was discovered that chitosan and guar gum concentrations influenced entrapment efficiency. Entrapment efficiency was found to improve with increasing chitosan and gum concentrations. Table 8 displays the findings.



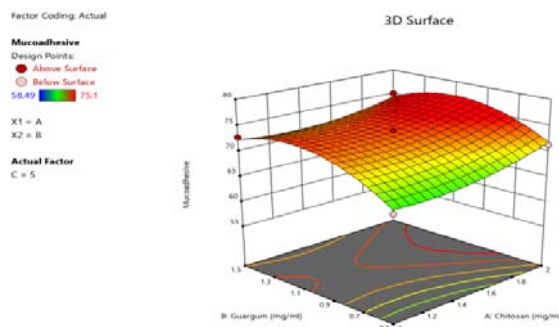
**Fig. 4: Contour surface plot for entrapment efficiency**



**Fig. 5: Three-dimensional surface plot for entrapment efficiency**



**Fig. 6: Contour surface plot for Mucoadhesion**



**Fig. 7: Three dimensional surface plot for entrapment efficiency**

**Table 8: % Entrapment efficiency of ropinirole HCl**

Formulation code	% Entrapment efficiency
F1	65.36±0.030
F2	77.98±0.87
F3	76.07±1.14
F4	77.6±1.03
F5	75.18±0.56
F6	75.38±0.073
F7	75.14±0.039
F8	75.92±0.069
F9	73.72±0.028
F10	75.22±0.39
F11	73.25±0.05
F12	75.85±0.012
<b>F13</b>	<b>84.1±0.051</b>
F14	83.1±0.93
F15	83.1±0.0173

\*All values are expressed in mean±SD (n=3)

It was found that formulations F1, F9 and F11 having minimum concentration of chitosan and gum showed decreased entrapment efficiency. Formulation F13 showed 84.1% maximum entrapment efficiency [25].

#### Drug content

To ensure that each batch of Nano particle dispersion formulation included the same amount of ropinirole HCl, the drug's concentration was measured. You may see the outcomes in table 9.

It was found that, the drug content values of prepared formulation did not show significant difference, suggested that the drug was uniformly dispersed in prepared nanoparticles formulation. The

medication content was shown to rise in tandem with the chitosan concentration. Formulation F13 showed 84.46% maximum drugs content.

**Table 9: % Drug content of ropinirole HCl**

Formulation code	% Drug content
F1	69.18±0.01
F2	79.43±0.04
F3	76.18±0.01
F4	76.183±0.01
F5	78.25±0.02
F6	80.62±0.02
F7	78.84±0.04
F8	73.81±0.03
F9	79.48±0.05
F10	78.74±0.04
F11	66.54±0.02
F12	70.7±0.1
F13	84.46±0.03
F14	83.46±0.1
F15	83.46±0.04

\*All values are expressed in mean±SD (n=3)

#### In vitro drug release study

To learn how mucoadhesive polymers affect the release profile, *in vitro* drug release tests were performed on formulations F1 through F15. Ropinirole HCl was released from nanoparticles in a burst-like fashion initially, followed by a more gradual release. Tables 10 and 11 show the *in vitro* release characteristics of Ropinirole HCl from formulations F1 through F15, respectively [26].

**Table 10: Percent drug release profile of Ropinirole HCl from formulations F1 to F5**

Time	F1	F2	F3	F4	F5
0	0	0	0	0	0
5	10.25±0.020	6.44±0.01	8.19±0.03	1.52±0.02	4.18±0.01
10	18.29±0.03	11.38±0.02	12.98±0.02	7.72±0.03	9.98±0.03
15	32.14±0.02	25.80±0.04	22.54±0.05	11.61±0.01	18.83±0.02
30	43.19±0.04	36.39±0.05	31.18±0.01	22.98±0.06	23.11±0.04
60	61.36±0.06	55.99±0.01	43.87±0.1	35.17±0.02	38.36±0.02
120	74.34±0.02	70.12±0.02	67.72±0.06	48.23±0.1	47.95±0.06
180	83.49±0.03	80.09±0.1	79.43±0.02	68.09±0.02	63.36±0.05
240	94.90±0.04	86.89±0.06	86.54±0.03	79.77±0.02	70.76±0.02
300	70.42±0.03	78.16±0.04	71.25±0.04	73.60±0.02	72.94±0.02

\*All values are expressed in mean±SD (n=3)

**Table 11: Percent drug release profile of ropinirole HCl from formulations F6 to F10**

Time	F6	F7	F8	F9	F10
0	0	0	0	0	0
5	2.055±0.02	10.27±0.1	12.57±0.03	0.540±0.02	11.15±0.04
10	3.58±0.04	18.49±0.02	19.48±0.01	8.187±0.04	18.49±0.01
15	10.31±0.06	20.22±0.04	23.51±0.03	20.67±0.05	19.91±0.02
30	21.18±0.05	30.71±0.05	30.80±0.04	26.16±0.01	25.45±0.03
60	32.73±0.08	39.21±0.02	44.13±0.05	33.08±0.02	31.62±0.03
120	43.33±0.04	46.62±0.1	51.35±0.02	40.10±0.04	41.49±0.02
180	49.61±0.02	51.39±0.03	63.43±0.01	51.12±0.02	43.04±0.04
240	64.55±0.1	64.65±0.03	66.89±0.03	65.11±0.01	50.54±0.01
300	71.61±0.03	74.45±0.04	79.20±0.04	73.99±0.06	73.05±0.01

\*All values are expressed in mean±SD (n=3)

#### Selection of optimized batch

The best formulation (table 13) was obtained by using the software-generated mathematical relationship between factors and variables. Particle size (Y1), zeta potential (Y2), and

entrapment efficiency (Y3) were optimised using a box behnken design. To obtain the optimal formula, the minimum particle size was set between 173.5 nm and 200 nm, the maximum zeta potential was set between 8 mV and 21.5 mV, and the maximum entrapment efficiency was set between 60% and 66.45%.

Formulation F13 was given by software as an optimized formulation with the concentration of Chitosan 1.667 mg, concentration of Muilage 0.5 mg and concentration of Surfactant 0.3%. The software predicted the result of this optimized formulation was minimum particle size 176.73 nm, maximum zeta potential 8.0 mV and highest entrapment efficiency 60.78% [27].

#### Evaluation of optimized batch (F13)

Entrapment efficiency, mucoadhesive and drug release of optimized batch. The observed results of predicted optimized batch for the Entrapment efficiency, Mucoadhesion and drug release were given in table 14 which are significantly close to the predicted value. Stability study results are given in table 15 [28].

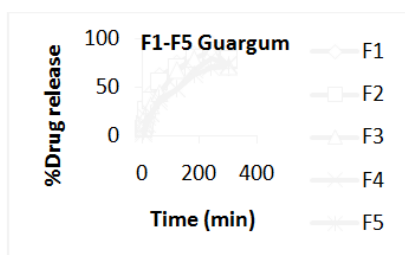


Fig. 8: % Release formulations F1 to F5

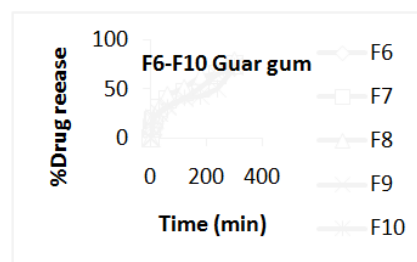


Fig. 9: % Release of drug in formulations F6 to F10

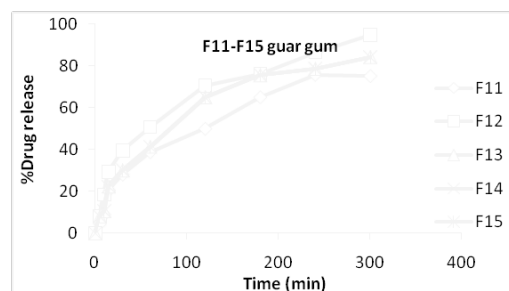


Fig. 10: Percent drug release of formulations F10 to F15

Table 12: Percent drug release profile of ropinirole HCl from formulations F11 to 15

Time	F11	F12	F13	F14	F15
0	0	0	0	0	0
5	4.60±0.02	8.14±0.02	8.06±0.01	8.06±0.06	8.06±0.01
10	9.07±0.03	18.54±0.01	10.64±0.03	10.64±0.02	10.64±0.04
15	20.64±0.1	29.42±0.02	22.41±0.04	22.41±0.01	22.41±0.02
30	28.11±0.05	39.66±0.04	30.10±0.05	30.10±0.03	30.10±0.01
60	38.84±0.02	50.79±0.1	41.35±0.06	41.35±0.04	41.35±0.05
120	50.04±0.08	70.44±0.04	64.91±0.01	64.91±0.01	64.91±0.08
180	65.10±0.03	76.26±0.03	75.42±0.02	75.42±0.02	75.42±0.03
240	75.78±0.02	86.39±0.05	78.44±0.02	78.44±0.08	78.44±0.03
300	75.19±0.02	94.80±0.05	84.11±0.02	84.11±0.02	84.11±0.05

\*All values are expressed in mean±SD (n=3)

Table 13: Formulation of optimized batch

S. No.	Ingredients	Quantity taken
1	Ropinirol HCL	50 mg
2	Chitosan solution	50 ml
3	Guar gum	1 mg/ml

Table 14: Optimized batch (selected)

Formulation code	%Entrapment efficiency	Mucoadhesion	%Drug release
F13	84.1%±0.05	61.90±0.01	84.18%±0.12

\*All values are expressed in mean±SD (n=3)

#### Stability study

The optimized formulation F13 was subjected to the accelerated stability study at 40±2 °C and 75±5% RH for 3 mo as per ICH guidelines. Visual appearance, % drug content, % Entrapment

efficiency and % Mucoadhesive were monitored for 3 mo. The results of the accelerated stability studies revealed no significant change in the parameters. From the data presented in the table 15 shows stable results for 3 mo. Therefore the formulation F13 is considered to be stable [29].

Table 15: Stability for the optimized batch

Formulation code F13	1 Mo	2 Mo	3 Mo
Appearance	No change	No change	No change
% Drug content	84.46±0.03	84.44±0.051	84.38±0.062
%Entrapment efficiency	81.25%±0.032	82.69%±0.011	84.10%±0.025
% Mucoadhesive	61.9±0.04	61.9±0.032	60.9±0.03



**CONCLUSION**

We studied ropinirol HCL as mucoadhesive nasal drug for brain targeting. Ropinirol acts with excipients like chitosan. Ropinirol's physicochemical properties were determined pre-formulation. UV stability was 0.9993 in phosphate buffer at pH 6.8. To construct an efficient Ropinirol HCL mucoadhesive nanoparticle, the box Behnken design assessed entrapment efficiency, drug release, and mucoadhesion force. Entrapment efficiency (F1-F15) and mucoadhesion force (60–70%) ranged from 65.36±0.030 to 83.1±0.0173. Nanoparticles (F1-F15) release 65%–81% of medicines in 5 h. Final formulation: 75.42±0.02 nanoparticle drug release in 5hr. For brain-targeted nasal Ropinirol HCL administration, chitosan and guar gum concentrations dramatically affected particle size, entrapment efficacy, and mucoadhesion.

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**AUTHORS CONTRIBUTIONS**

Conceptualization: GJ, ND, AB; table Work: JL, DK, PS; Supervision: ND, AB, GD; Revisions: HT, ND; Writing and Editing: AS, GD, HT; Proofreading: GJ, DK, PS.

**CONFLICT OF INTERESTS**

The authors declare that there is no conflict of interest

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