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FORMULATION AND EVALUATION OF CONTROLLED RELEASE MICROSPHERE

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ABSTRACT
Aim: The aim of present study was formulation and evaluation of Perospirone loaded controlled released microspheres by solvent evaporation technique. Method: Gellon gum is biocompatible polymer used as a retardant material. Drug loading, polymer type and solvent type, such process conditions were investigated. The formulated microspheres were characterized for their particle size, drug release, drug loading. The in vitro studies were carried out. The prepared microspheres were free flowing, white in color, free flowing with spherical shape. Entrapment efficiency of microspheres was found in the range between 34.5 to 53%. The formulation F2 had highest cumulative drug release of 98.26% as compared to other formulation. Conclusion: The study concluded that, the prepared microspheres formulation of gellan gum is better for the formulation of controlled release microspheres of Perospirone.

KEYWORDS: Pulsatile drug delivery, Perospirone, Antipsychotic, Solvent evaporation technique.

INTRODUCTION
Microspheres are small circular particles, with a diameter of 10µm to 1000µm. The Microsphere plays an important role in improving the availability of generic drugs and minimizing side effects. The main advantage of using microspheres as a drug delivery system is the controlled release of drug content. Microencapsulation used to delay drug withdrawal in dosage forms and reduce side effects, increase the patient's compliance.[1,2] In this method, the aqueous insoluble core (drug) is coated with a non-aqueous coating (polymer) by the process of emulsion solvent diffusion evaporation to stabilize the drug delivery system.[2] Microspheres can be made in a variety of ways including an emulsification process with single or double solvent evaporation system spray-drying process or phase separation process. Microspheres can be formed by dissolving staring material in specific solvents and then dispersing them into another immiscible solution. Over time the complete evaporation of the final solution will produce a fine powder called water-soluble microspheres. There are two types of microspheres,[2,3]

• Microcapsules
• Micrometrics

MATERIALS AND METHODS
MATERIALS: Perospirone was purchased from Fusion lab Mumbai, Gellon gum was purshed from LOBA chem. Ltd., Mumbai, Dichloromethane was purchased from LOBA chem. Mumbai. All other reagents used in the study were of analytical grade and were used as received.

METHOD OF PREPARATION[13]
This is the method widely used in the microencapsulation process. Polymer's calculated quantity was dissolved in Dichloromethane (10 ml) to form a homogenous solution. Afterword drug's calculated quantity was mixed with polymer solution and mixed thoroughly. The resulting mixture was then added in a thin stream of 300ml of aqueous solution containing 0.4% PVA solution while stirring at 500 rpm to emulsify the added dispersion in fine droplets. The solvent Dichloromethane was then removed by evaporation during continuous stirring at room temperature for 3 hours to produce spherical microspheres. During 3 hours of stirring period, Dichloromethane was completely removed by evaporation. Dichloromethane was used as polymer solvent, aqueous solution as a microencapsulating vehicle. The microspheres were collected by vacuum filtration and washed repeatedly and dried to get free flowing microspheres the composition of microsphere is given in the table (1).

RESULTS AND DISCUSSION

1. Preformulation studies

1. Physicochemical properties of drug

Drug name	Organoleptic property	Observed Melting Point	Solubility
Perospirone	White color	95°C - 96°C	Soluble in water, sparingly soluble in methanol

2. Determination of λmax of Perospirone in distilled water

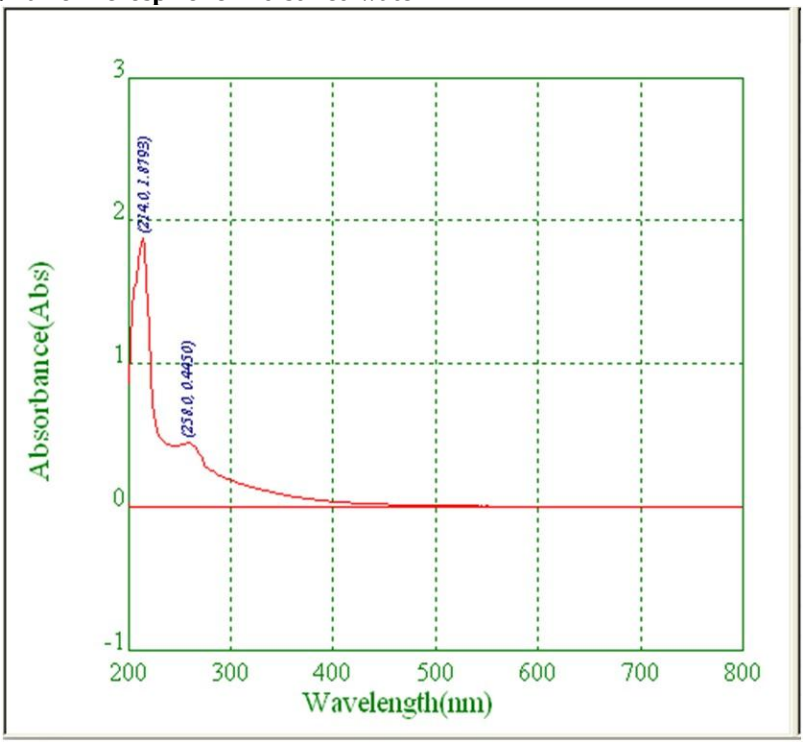

Figure 1: UV Spectra of Perospirone in distilled water.

Absorption maximum was found to be at 219 nm. Hence, it was selected as λmax for further studies.

1.1. Determination of λmax of Perospirone in phosphate buffer pH 6.6.

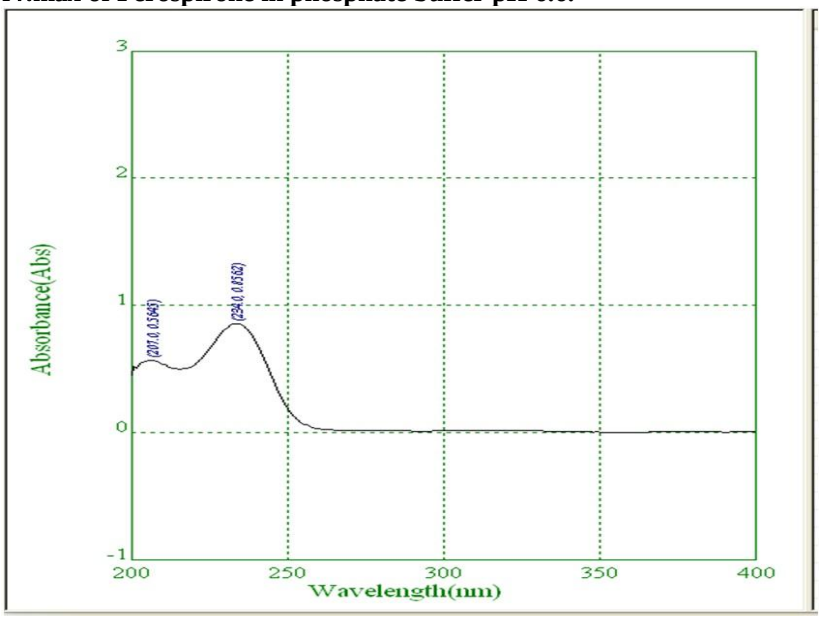

Figure 2: UV Spectra of Perospirone in phosphate buffer pH 6.6.

Absorption maximum was found to be at 241 nm. Hence, it was selected as λmax for further studies.

1.2 Calibration curve of Perospirone in distilled water

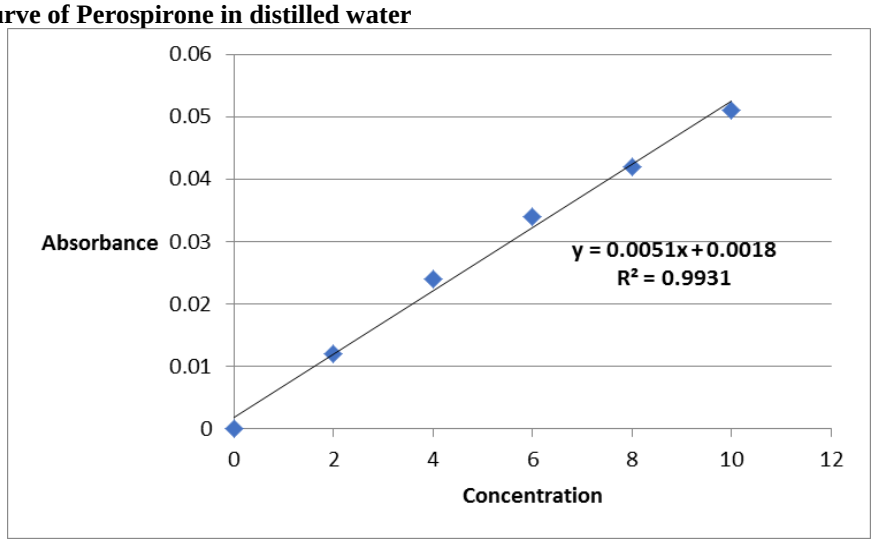

Figure 3: Calibration curve of Perospirone in distilled water.

1.3 Calibration curve of perospirone in phosphate buffer pH 6.6

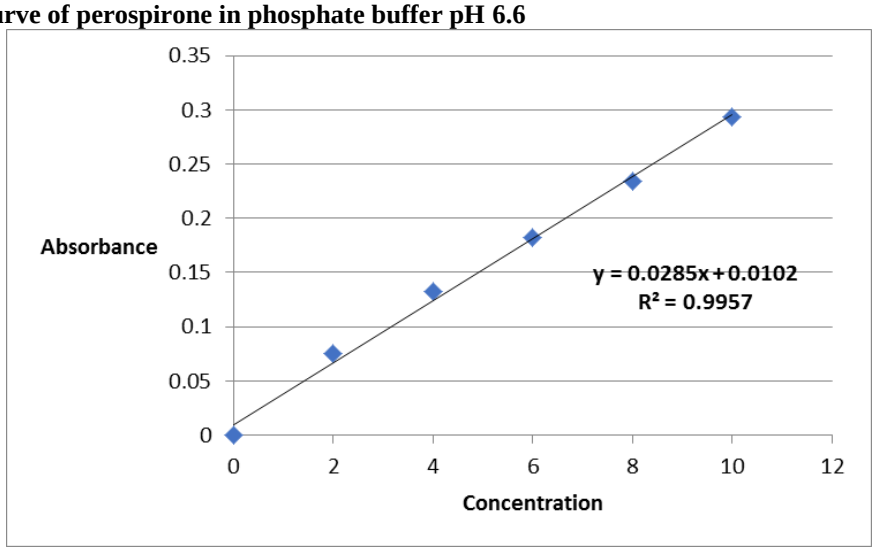

Figure 4: Calibration curve of perospirone in pH 6.6.

2. Drug and polymer interaction study

2.1. Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectrum of pure drug, polymer and physical mixtures were shown in Figure 7.5 -7.6.

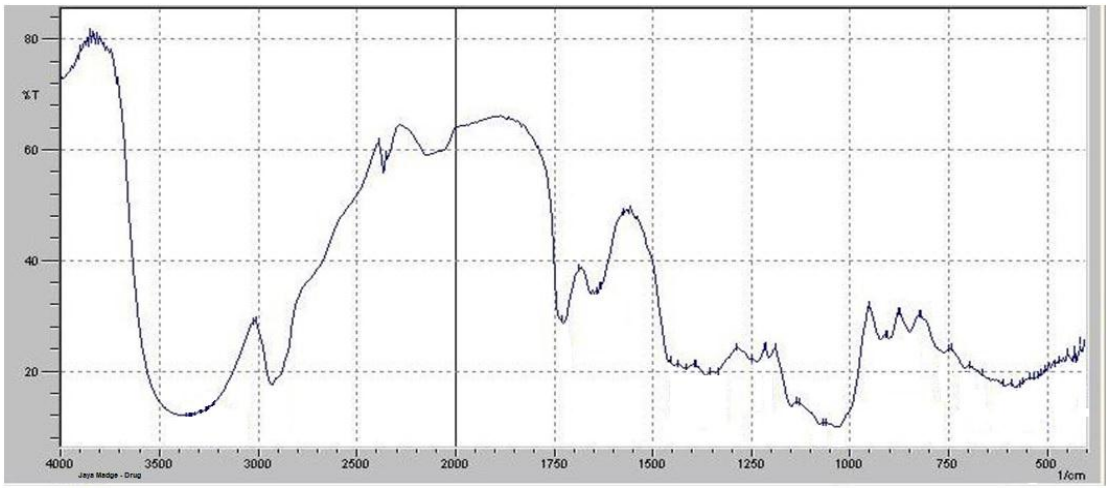

Figure 5: FTIR spectra of Perospirone.

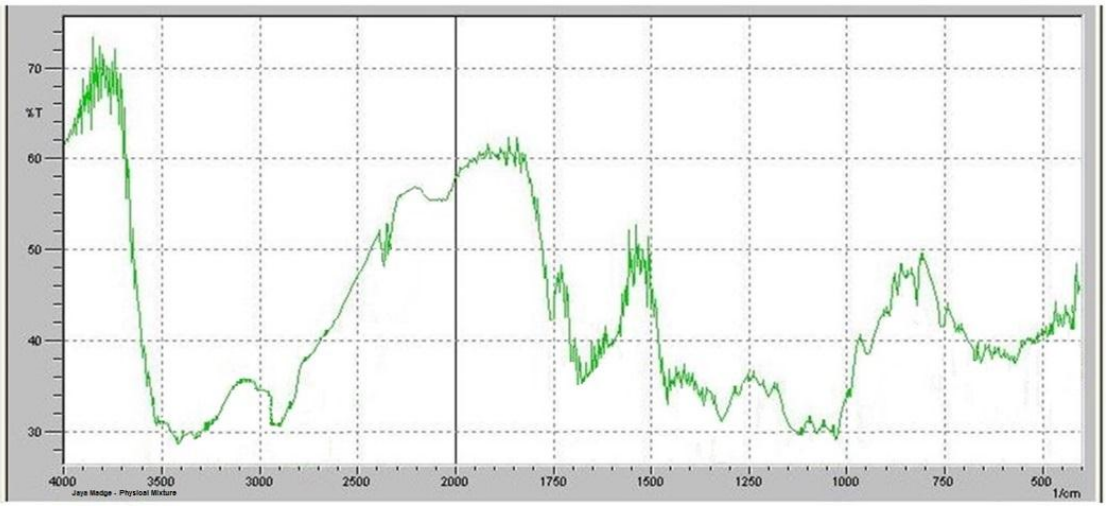

Figure 6: FTIR spectra of Perospirone + Gellan Gum.

The possible interaction between the drug and polymer was studied by FTIR spectroscopy. There was no considerable change in the positions of characteristic absorption bands and bonds of various functional groups present in the drug. This observation clearly suggests that the perospirone shows no prominent change in its characteristics even in its physical mixture. The results of FTIR spectra indicated the interaction between drug and polymer. It showed that perospirone was compatible with gellan gum.

3. Differential Scanning Calorimetry (DSC)

The thermal analysis of drug was studied using differential scanning calorimetry (DSC) shown in Figure 7.7-7.8. Perospirone have shown melting sharp endotherm at 89.66°C whereas, thermogram of physical mixture shows respective endothermic peak at 64.95°C for gellan gum.

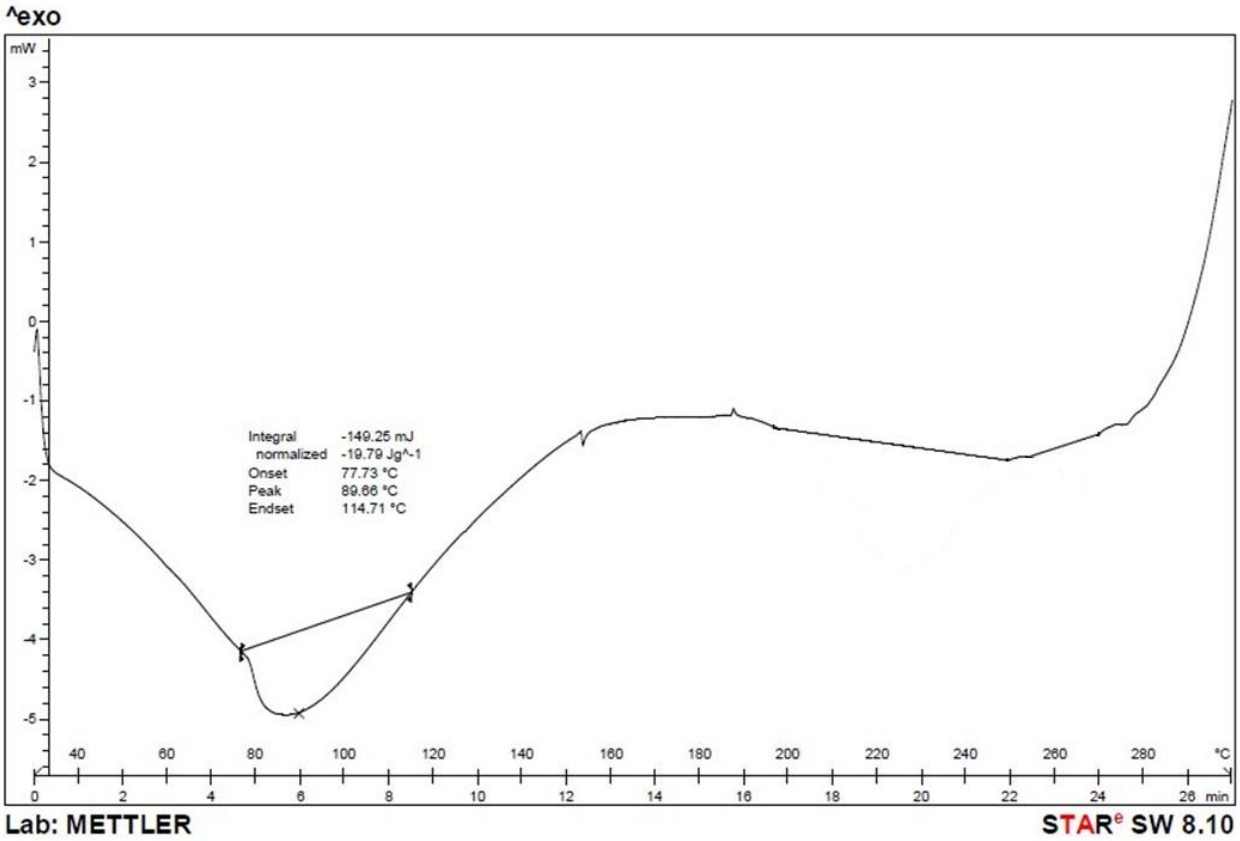

Figure 7: DSC of Perospirone.

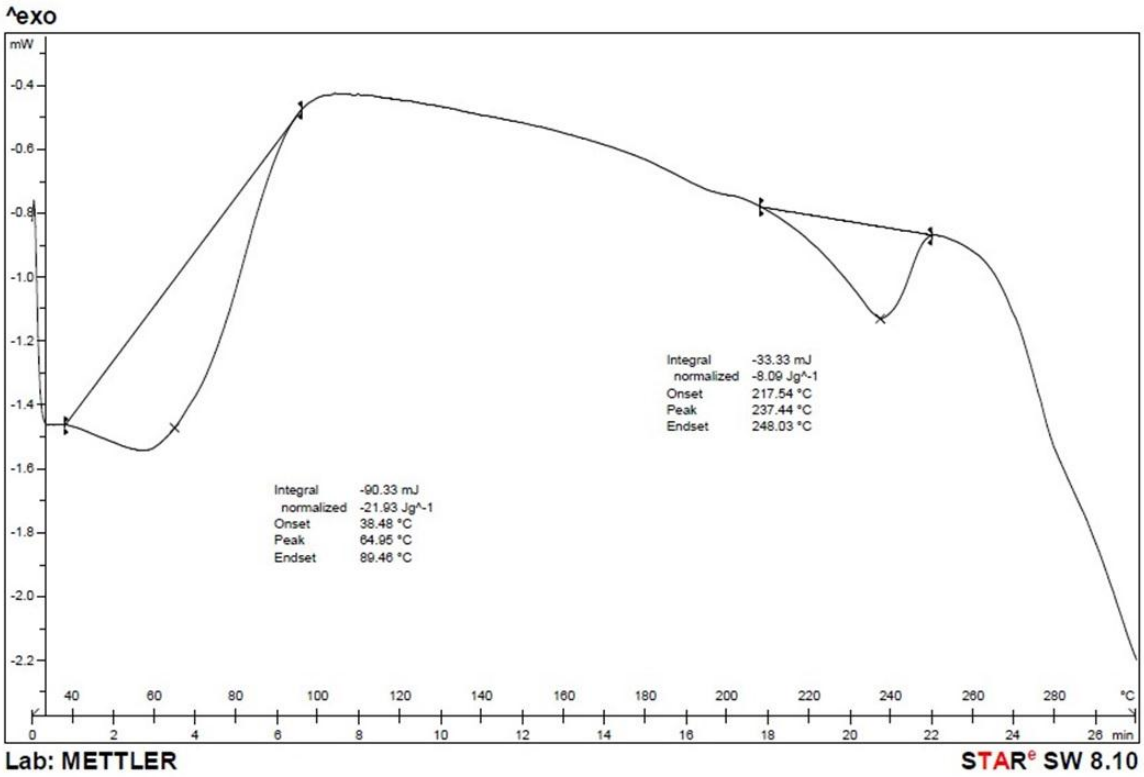

Figure 8: DSC of Perospirone + Gellan Gum.

Table 1: Formulation of microspheres.

Formulation Code	Drug (mg)	Gellan gum (mg)	Polymer ratio (w/w)	External phase
F1	10	10	1:1	0.4%PVA
F2	10	20	1:2	0.4%PVA
F3	10	30	1:3	0.4%PVA
F4	10	40	1:4	0.4%PVA
F5	10	50	1:5	0.4%PVA

Evaluation of microspheres

1. Production yield (%)

Production yield of microspheres was found to be between 39.78% to 52.44%. Due to the loss of material in solvent evaporation method maximum production yield was 52.44%.

Table 2: Production yields of microspheres.

Formulation code	Production yield (% ± SD)
F1	39.78 ± 0.1
F2	52.44 ± 0.2
F3	42.19 ± 0.4
F4	43.11± 0.4
F5	43.82± 0.4

*Values expressed as Mean ± SD

3. Entrapment efficiency (%)

Table 4: Entrapment efficiency of microspheres.

Formulation code	Entrapment efficiency (% ± SD)
F1	62.78 ± 0.4
F2	78.44 ± 0.2
F3	52.19 ± 0.2
F4	53.11± 0.2
F5	52.82± 0.2

* Values expressed as Mean ± S D

Entrapment efficiency of microspheres was found in the range between 52 To 78 %. As the concentration of polymer increased, entrapment efficiency increased both at higher and lower stirring rate. Increase the polymer concentration entrapment efficiency also increases.

4. Particle size analysis

Average particle size of microspheres ranged from 20 µm to 50 µm, Average particle size of microspheres ranged from 35 µm to 60 µm. Particle size mainly depends on the stirring rate; hence, as the stirring rate increased, the particle size decreased irrespective of the concentration of polymer.

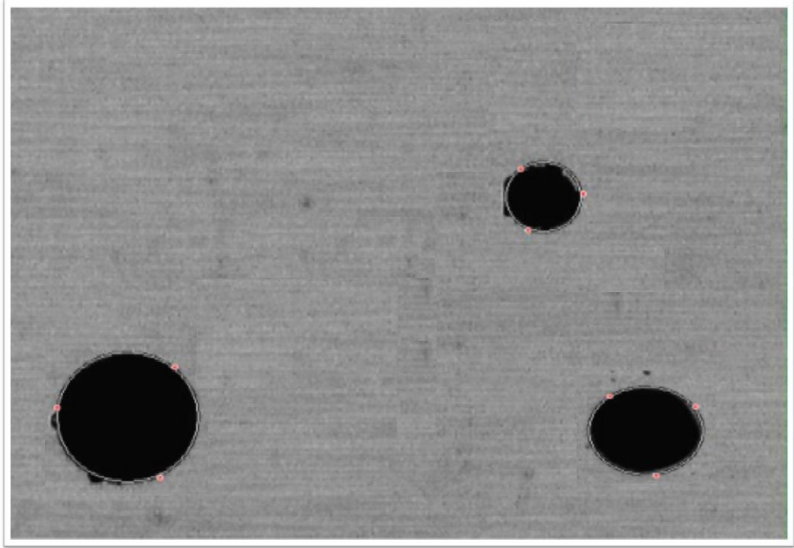

Figure 9: Motic analysis of optimized formulation (F2).

Table 5: Particle size analysis of microspheres.

Formulation Code	Particle size (µm ± SD)
F1	51.7 ± 0.5
F2	35.8 ± 0.4
F3	43.6 ± 0.2
F4	42.9± 0.2
F5	47.9± 0.2

*Values expressed as Mean ± SD, n=100

***In-vitro* drug release study**

% cumulative drug release of batches F1 – F5 is shown From this *in vitro* drug release study, the formulation F2 had highest cumulative drug release of 98.26% as compared to other formulation.

Table 6.

Time	[F1] %CDR	[F2] %CDR	[F3] %CDR	[F4] %CDR	[F5] %CDR
1	4.7	4.35	4.3	4.304	4.69
2	5.48	5.87	5.478	5.086	5.4
3	5.479	6.27	8.23	6.26	7.06
4	7.827	7.45	11.73	9.391	7.826
5	10.18	17.7	17.608	17.608	13.69
6	25.44	39.53	19.956	19.95	25.43
7	46.97	56.97	37.125	37.12	37.12
8	54.85	68.35	44.437	44.43	44.45
9	60.33	80.09	69.117	69.11	69.12
10	68	82.13	76	76.78	76.89
11	75.1	85.22	80.92	80.92	80.93
12	83.7	89.16	84.304	84.30	82.3

Batch F2 which has drug: polymer ratio 1:2 shows highest %CDR 89%. Gallon gum showed lag time in all the formulations from F1 to F5 in the range of 3 to 5 hours. From microsphere formulation F2 batch showed better lag time with controlled drug release than the other formulations.

CONCLUSION

From this study it was concluded that Emulsified Solvent Evaporation technique is suitable for preparation of controlled release microspheres of Perospirone. The present study has been satisfactorily attempted to formulate a controlled release microspheres of Perospirone with a view of increasing rate of absorbtion The controlled release microspheres can retard the drug release in controlled manner and optimum lag time can be developed. % entrapment efficiency was higher for gellan gum based microspheres. The particle size analysis revealed that all formulations gave particles in the range of 35 µm to 60 µm. SEM analysis of the microspheres revealed that all the formulations were smooth and spherical with ideal surface morphology. From all the parameters studied, it can be concluded that gellan gum is better for the formulation of controlled release microspheres of Perospirone.

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CONFLICT OF INTREST: The authors were declare that there were no conflict of interest.

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