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Research Article

Formulation and Evaluation of Gastroretentive Floating Microspheres of TRAMADOL HCl

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Abstract

This study presents the formulation and evaluation of sustained-release microspheres containing Tramadol HCl. The aim was to achieve prolonged drug release for enhanced therapeutic efficacy and improved patient compliance. The microspheres were prepared using a solvent evaporation method with various combinations of polymers Agar and Pectin. The physical appearance, particle size, drug content, and moisture content were assessed for stability over time. Among the formulations, Batch F7 emerged as a standout candidate, displaying excellent buoyancy and sustained drug release characteristics. Comprehensive evaluations included in vitro drug release studies, kinetic data analysis, and stability assessments over 90 days. The study concludes that the combination of Agar and Pectin polymers in Batch F7 holds significant promise for achieving controlled drug release, suggesting its potential for advanced drug delivery systems.

Keywords: Gastroretentive Floating Microspheres, Tramadol HCl, prolonged drug release, patient compliance

INTRODUCTION:

Gastroretentive drug delivery systems have gained significant attention in recent years due to their potential to prolong gastric residence time and achieve site-specific drug release in the upper gastrointestinal tract.1-4 These systems offer numerous advantages, including improved bioavailability, enhanced drug stability, and the ability to target specific sites for localized or systemic effects. Among these drug delivery systems, microspheres have emerged as promising multiparticulate carriers that can provide controlled and prolonged drug release. Tramadol, chemically known as (±) cis-2-[(dimethylamino)methyl]-1-(3-methoxyphenyl) cyclohexanol hydrochloride, is a widely used analgesic, acting as an opioid agonist. Its IUPAC name is (1R,2R)-3-(dimethylamino)-1-[(2R)-2-[(3-methoxyphenyl)cyclohexyl] cyclohexyl] propan-1-ol hydrochloride. 5-6 Tramadol's mechanism of action involves its binding to mu-opioid receptors in the central nervous system, leading to the inhibition of norepinephrine and serotonin reuptake. This dual mechanism results in an analgesic effect, making it an effective option for pain management.

However, Tramadol's short half-life and rapid clearance present challenges in achieving a prolonged therapeutic effect. To address these limitations, a Gastroretentive drug delivery system is required to extend gastric residence time and sustain drug release. 7-10 Formulating Tramadol into Gastroretentive floating microspheres offers a potential solution, as these microspheres can remain in the gastric region for longer periods, continuously releasing the drug over an extended duration. By doing so, this formulation can optimize the therapeutic effect and safety of Tramadol while improving patient convenience and compliance. 10-14 This study aims to develop and evaluate the gastroretentive floating microspheres of Tramadol to enhance its drug delivery efficacy and provide a more effective and convenient pain management option.

MATERIALS AND METHOD

Materials

Tramadol HCl was procured as a gift sample from Mylan Laboratories Limited, Aurangabad, Maharashtra. Agar and Pectin were procured as gift samples from Lab FineChem, Mumbai. All other chemicals used were of analytical grade, and all additional chemicals and reagents used were of pharmaceutical grade.

Method

Preparation of Floating Microspheres - Solvent Evaporation Method:

In the solvent evaporation process, the polymer is dissolved in a suitable water-immiscible solvent, and the medicament is dispersed or dissolved in this polymeric solution. As solvent evaporation occurs, the microspheres harden, resulting in

free-flowing microspheres that can be obtained after suitable filtration and drying. For this study, microspheres containing the drug as a core material were prepared using the non-aqueous solvent evaporation method. Initially, the drug and polymer were mixed in acetone in various ratios to form a slurry. This slurry was then slowly introduced into 35 mL of liquid paraffin while being stirred at 300 rpm using a mechanical stirrer equipped with three-blade propellers at room temperature. The system was continuously stirred for 3 hours to ensure complete evaporation of the solvent, and the microspheres were subsequently collected through filtration. To remove any remaining oil, the collected microspheres were washed repeatedly using petroleum ether until they were free from any residual oil. Finally, the collected microspheres were dried at room temperature and stored in a desiccator for 24 hours to ensure proper storage conditions. The solvent evaporation method proved effective in producing floating microspheres, which hold potential for Gastroretentive drug delivery and prolonged drug release, contributing to improved therapeutic efficacy and patient compliance.

Table 1: Composition ratio of Drug and Polymers

Batch Code	Drug: Polymers TMD HCl : A/P	Stirring Rate (RPM)	Volume of Internal Phase (Acetone)
F-1	1:0.5	300	15 ML
F-2	1:1	300	15ML
F-3	1:1.5	300	15ML
F-4	1:0.5	300	15ML
F-5	1:1.5	300	15ML
F-6	1:1.5	300	15ML
F-7	1:0.5:1	300	15ML
F-8	1:1:1	300	15ML
F-9	1:1:0.5	300	15ML

Characterization of Floating Microspheres:

Preformulation Testing: The solubility of the API (Tramadol HCl) was determined by weighing 10 mg of the compound and adding 10 ml of the solvent. If the compound did not dissolve completely, additional 10 ml of solvent was successively added until complete dissolution was observed visually (Table 3). The melting point of Tramadol HCl was determined using the capillary method (Table 4).

Analytical methodology

Determination of λmax: A solution of Tramadol HCl (100 µg/ml) was prepared in Methanol, and its absorbance was scanned between 200-400 nm to find the maximum wavelength (λmax) at 271 nm, which was used for all subsequent concentration determinations (Figure 1).

Construction of Calibration Curve for Tramadol HCl: Various aliquots of Tramadol Hydrochloride stock solution (100 µg/ml) were pipetted out and transferred to 10 ml volumetric flasks to create solutions of 30 to 150 µg/ml of Tramadol Hydrochloride. These solutions were scanned in the range of 200-400 nm against diluent as blank to construct the calibration curve (Figure 2) (λmax = 271 nm).

Drug Excipient Compatibility Study (FTIR Study): FTIR techniques were used to study the physical and chemical interactions between Tramadol HCl and the excipients. Pellets of drug sample and potassium bromide were formed by compressing the powders at five tons for five minutes on a KBr - press, and the spectra were scanned in the 4000 - 450 cm-1 region. The infrared spectrum of Tramadol HCl was analyzed using FTIR in the range of 600 to 4000 cm-1 (Figure 3, 4, 5, 6).

Evaluation of Gastroretentive Floating Microspheres of Tramadol HCl:

Particle Size:

The particle size of the microspheres was determined using the optical microscopy method. The particle size of all formulated bead batches in a sample was measured with an optical micrometer fitted with a calibrated eyepiece, and readings were expressed as an average of three trials with standard deviation.

Percentage Drug Content:

Drug-loaded microspheres (100 mg) were powdered and suspended in a methanolic water solvent (1:99 v/v). The resultant dispersion was filtered, and the drug content was determined spectrophotometrically at 271 nm using a regression equation derived from the standard graph (UV-1800, Shimadzu).

Micromeritic properties

The evaluation results of various parameters, including Angle of Repose, Bulk Density, Tapped Density, Carr's index, and Hausner's ratio, are shown in Table 6.

Drug Entrapment Efficiency:

The drug entrapment efficiency of Tramadol HCl microspheres was determined as follows: 100 mg of microspheres was accurately weighed and suspended in 100 ml of phosphate buffer (pH 6.8). The suspension was left to stand for 24 hours and then stirred for 15 minutes. Subsequently, it was filtered, and the filtrate was collected. The drug content in the filtrate was analyzed spectrophotometrically at 271 nm using a UV Spectrophotometer to quantify the percentage of drug content in the given sample of microspheres.

This calculation enabled the determination of the percentage of drug entrapped within the microspheres, which is a critical parameter in assessing the effectiveness of the drug delivery system. The drug entrapment efficiency plays a pivotal role in optimizing drug release kinetics and ensuring that the desired therapeutic effect is achieved. The drug entrapment efficiency (DEE) was calculated using the following equation:

$$DEE = (Ads / Tc) \times 100$$

Surface Morphology by Binocular (Motique) Microscope: Morphology in the context of this study refers to the size, shape, and arrangement of the microspheres. To observe the surface morphology of the microspheres, a Binocular Microscope (Motique) was employed, using different magnifying powers such as 10X and 40X (Figure 7).

Buoyancy Assessment:

a) Percentage Buoyancy: The percentage buoyancy of the microspheres was determined by calculating the volume of the microspheres that is submerged in a denser fluid. The displaced volume, which has an equal weight to the object (microspheres), was divided by the volume of the denser fluid (displaced water). The result was multiplied by 100 to obtain the percentage volume of the microspheres that is submerged. Subtracting this value from 100 gives the percentage of microspheres that float (Table 8).

b) Total Floating Time: The total floating time test was

conducted using a pH 1.2 buffer solution without enzymes as the dispersing medium. The microspheres were spread over the surface of 500 mL of the dispersing medium at 37± 0.1°C. The medium was agitated by a paddle rotating at 50 rpm for 12 hours. Afterward, the floating and settled portions of the microspheres were collected separately. The collected microspheres were then dried until a constant weight was achieved. These buoyancy assessments are critical in determining the floating behavior of the microspheres, which is essential for Gastroretentive drug delivery. Understanding the surface morphology and buoyancy characteristics of the microspheres contributes to evaluating their suitability and effectiveness as a drug delivery system. The percentage of floating ability of microspheres was calculated as

$$\% \text{ Floating Ability} = \frac{\text{Weight of Floating Microspheres}}{\text{Total Weight of Microspheres}}$$

In this calculation, the weight of the microspheres that float on the surface of the dispersing medium is divided by the total weight of all the microspheres present in the system. The result is then multiplied by 100 to obtain the percentage of microspheres that are floating. This percentage represents the ability of the microspheres to remain buoyant on the surface of the medium, indicating their potential for Gastroretentive drug delivery. A higher percentage of floating ability suggests better buoyancy and a higher chance of prolonged gastric retention, which is a desirable characteristic for Gastroretentive drug delivery systems.

In Vitro Dissolution Study:

For the in vitro dissolution study, 900 ml of freshly prepared 0.1 M HCl buffer was placed in a dissolution test apparatus type II. An amount of Microspheres equivalent to the therapeutic dose of Tramadol HCl was added to the 900 ml 0.1 M HCl buffer, and the temperature was maintained at 37°C ± 0.5°C. The Paddle was rotated at a speed of 50 rpm. At every 1-hour time interval, a 10 ml sample was withdrawn, filtered, and diluted ten times. The absorbance of the sample solution was then measured in a 1 cm cell on a suitable UV spectrophotometer at 271 nm, using dissolution as a blank. The absorbance readings were used to calculate the percentage of Tramadol HCl dissolved in the 0.1 M HCl buffer (Table 9).

Drug Release Kinetics:

To understand the mechanism and kinetics of drug release, the results of the in vitro dissolution study of the optimized batch were fitted with various kinetic equations (Figure 8, 9, 10). These kinetic models include:

- Zero-order model (% release vs. time)

- First-order model (log % unreleased vs. time)

- Higuchi's model (% release vs. square root of time)

- Pappas Korsmeyer Equation (% release vs. time raised to the power of n)

The value of 'n' in the Korsmeyer-Peppas model is used to determine the drug release mechanism, where:

n = 0.5: Fickian Diffusion

0.5 < n < 1: Non-Fickian Diffusion

n = 1: Case - II Transport

n > 1: Super Case - II Transport

Stability Study:

Stability studies are crucial to assess the quality and shelf life of a pharmaceutical dosage form. These studies examine how the quality of a drug substance or product changes over time due to environmental factors such as temperature, humidity, and light. Regulatory bodies require stability studies as part of the product submission requirements (Table 11).

The samples were tested for various parameters during the stability study, including physical appearance, particle size, drug content, and moisture content. These assessments are essential to ensure the stability and efficacy of the formulated microspheres throughout their shelf life, providing valuable insights into their suitability for commercial use.

RESULTS AND DISCUSSION

Pre-formulation Study

Table 1: Solubility

Solvent	Solubility Description
Distilled Water	Freely Soluble
Methanol	Freely Soluble
Acetone	Slightly soluble
Phosphate Buffer (pH. 6.8)	Soluble

The provided data illustrates the solubility of a substance in various solvents and conditions. It is freely soluble in distilled water and methanol, indicating complete dissolution, while showing slightly lower solubility in acetone, suggesting partial dissolution with possible cloudiness. In a phosphate buffer with pH 6.8, it is described as soluble, implying moderate solubility. These solubility characteristics highlight how different solvents and environmental factors can influence the extent to which the substance dissolves, crucial information for applications ranging from pharmaceuticals to materials science.

Table 2: Melting Point:

Test	Observation
Melting Point	181oC

The recorded melting point is 181°C, which falls within the expected range of 180°C to 181°C. The alignment between the observed melting point on the Gallenkamp Melting Point Apparatus and the established range suggests accurate results.

Table 3: Preformulation Evaluation of Tramadol HCl Microspheres

Batch Code	Angle of Repose	Bulk Density	TappedDensity	Carr's index	Hausner Ratio
F1	26.40±0.2	1.22±0.2	2.10±0.2	10.90	0.901
F2	27.45±0.3	1.74±0.2	2.56±0.3	11.53	0.896
F3	28.00±0.3	2.10±0.3	2.92±0.2	61.45	0.914
F4	30.20±0.4	1.20±0.2	2.11±0.3	8.10	0.925
F5	35.40±0.4	1.26±0.2	2.14±0.3	10.25	0.904
F6	36.10±0.2	1.48±0.3	2.32±0.2	12.12	0.891
F7	**26.10±0.3**	**1.50±0.3**	**2.35±0.2**	**11.11**	**0.900**
F8	27.00±0.3	1.75±0.2	2.66±0.4	5.42	0.948
F9	28.20±0.4	1.85±0.2	2 .60±0.2	15.62	0.864

The preformulation evaluation of Tramadol HCl microspheres has been conducted across different batches labeled as F1 to F9, with each batch undergoing analysis based on key parameters. These parameters include the angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio. Among the batches, F7 appears to align most closely with the ideal preformulation evaluation standards. Notably, F7 exhibits an angle of repose of 26.10±0.3 degrees, a bulk density of 1.50±0.3 g/cm^3, a tapped density of 2.35±0.2 g/cm^3, a Carr's index of 11.11, and a Hausner ratio of 0.900. These values mirror the targeted criteria, suggesting favorable flowability, compressibility, and physical characteristics of the microspheres. Such preformulation assessments are crucial in tailoring the formulation process for enhanced quality, consistent production, and accurate predictions regarding the behavior of the microspheres during various stages of handling and processing.

Table 4: Evaluation of Tramadol HCl Microsphere

Batch Coad	Percentage Drug Content (%)	Drug Entrapment Efficiency	Particle Size (nm)
F1	75.27±0.2	78.90±0.2	42.25±0.2
F2	73.76±0.4	65.55±0.4	40.32±0.2
F3	76.32±0.4	67.59±0.2	44.08±0.3
F4	72.53±0.5	75.55±0.5	35.12±0.5
F5	73.20±0.4	78.08±0.4	34.40±0.2
F6	75.32±0.5	74.12±0.3	36.52±0.2
F7	**78.84±0.5**	**84.02±0.5**	**43.54±0.5**
F8	70.12±0.3	82.14±0.4	43.66±0.3
F9	71.14±0.3	83.32±0.5	45.32±0.5

The evaluation of Tramadol HCl microspheres has been conducted across various batches, each assessed based on key parameters. The results indicate variations in percentage drug content, drug entrapment efficiency, and particle size among the batches. Notably, batch F7 stands out as the ideal batch in this evaluation. It showcases a percentage drug content of 78.84%, which is the highest compared to other batches, indicating efficient drug incorporation. Additionally, the drug entrapment efficiency for this batch is 84.02%, reflecting its effectiveness in retaining the drug within the microspheres. Moreover, the particle size of the ideal batch is 43.54 nm, suggesting a desirable size for the microspheres. These findings underscore the favorable attributes of batch F7 in terms of drug content, drug entrapment, and particle size, making it a noteworthy candidate for further development and application. Such evaluations play a pivotal role in optimizing formulation processes, ensuring consistent quality, and enhancing the performance of drug delivery systems.

Scanning Electron microscopy

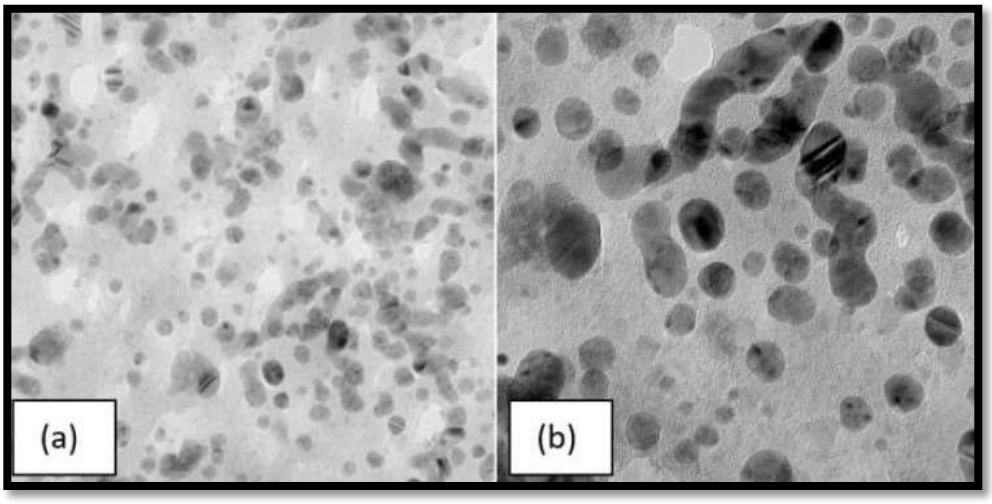

Figure 1: The surface view of ideal batch (a) Scanning Electron microscopy (b) Scanning Electron microscopy.

A buoyancy study has been conducted using a binocular (Motique) apparatus on various batches, labeled as F1 to F9. The study aims to determine the buoyant behavior of the batches in a liquid medium. The percentage of microspheres that remained floating and the total floating time in hours were recorded for each batch. Notably, batch F7 emerged as the ideal batch in this buoyancy study.

Batch F7 demonstrated the highest buoyancy performance, with a percentage of 89.25% of the microspheres remaining afloat, and an extended total floating time of 8.0 hours. This extended floating duration signifies the batch's ability to remain suspended in the liquid medium for an extended period, which aligns well with the study's objective. This buoyancy study, through the meticulous observation of floating behavior and time, provides valuable insights into the microspheres' potential for controlled drug release and prolonged therapeutic effect.

Table 5: Buoyancy Study by Binocular (Motique)

S.N.	Percentage (%)	Total Floating Time in (hr)
F1	56.22 ±05	3.5 hr
F2	59.91±02	3.9 hr
F3	62.23±04	4.5 hr
F4	71.23±02	5.2 hr
F5	78.45±05	5.8 hr
F6	82.41±09	6.4 hr
F7	**89.25±03**	**8.0 hr**
F8	81.26±05	7.4 hr
F9	74.52±02	7.1 hr

Table 6: In Vitro drug Release StudieS

Timein hr.	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	10.88	13.70	14.50	08.10	13.12	13.08	**9.66**	14.12	14.20
2	16.25	21.96	19.86	14.12	20.12	16.56	**17.70**	16.54	15.90
3	21.08	33.76	22.75	16.21	23.15	25.67	**22.63**	21.56	22.45
4	36.66	42.54	31.51	22.45	30.02	30.34	**29.45**	24.85	26.74
5	43.04	51.32	37.33	25.12	35.66	36.44	**35.25**	29.56	30.86
6	53.67	62.03	41.22	26.10	37.05	41.40	**41.12**	32.41	33.96
7	61.02	68.89	48.48	29.45	45.56	48.56	**53.89**	36.42	38.42
8	74.45	72.99	50.21	33.45	47.89	53.89	**61.13**	41.52	42.12
9	-	-	62.18	50.42	54.90	57.23	**69.12**	50.47	48.63
10	-	-	70.12	55.15	58.23	63.12	**78.87**	53.12	52.14
11	-	-	-	64.12	62.03	68.21	**82.12**	58.14	60.23
12	-	-	-	-	70.23	71.78	**89.78**	66.74	70.83

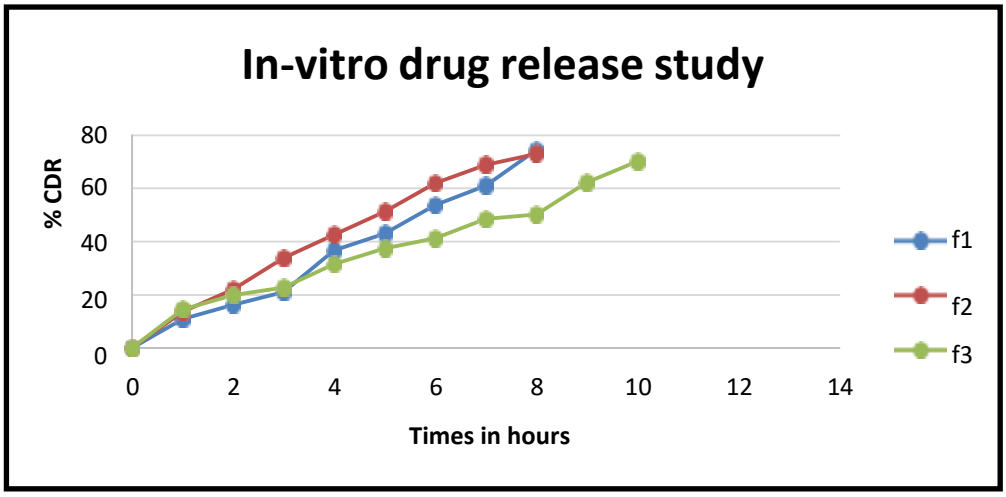

Figure 2: Graph of In Vitro Drug Release Studies of Formulation (F1-F3)

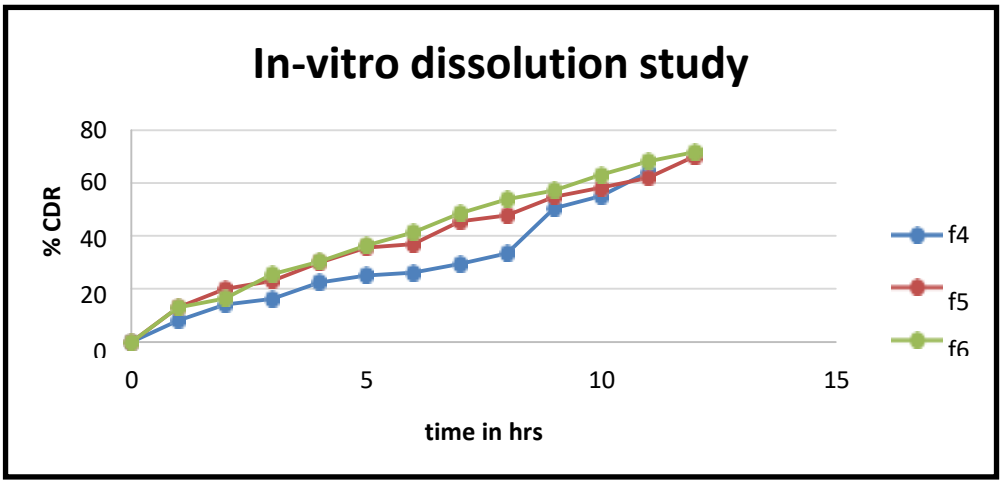

Figure 3: Graph of In Vitro Drug Release Studies of Formulation (F4-F6)

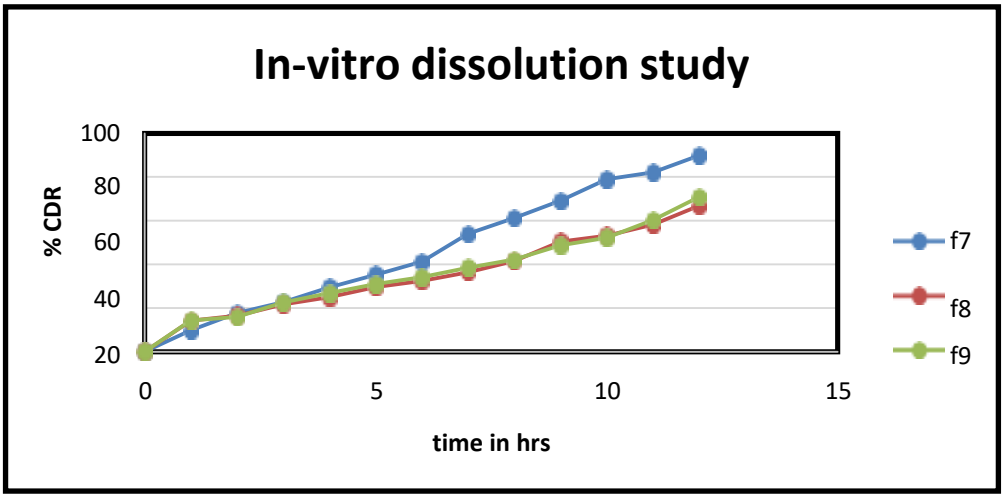

Figure 4: Graph of in Vitro Drug Release Studies of Formulation (F7-F9)

In vitro drug release studies were conducted across different time intervals for various batches denoted as F1 to F9. The study involves tracking the percentage of drug released from the microspheres over time. The data reveals the progressive release patterns for each batch: At 1 hour, batch F1 released 10.88%, F2 released 13.70%, F3 released 14.50%, F4 released 8.10%, F5 released 13.12%, F6 released 13.08%, F7 released 9.66%, F8 released 14.12%, and F9 released 14.20%.

As time progressed: - At 2 hours, there were further releases with batch F1 at 16.25%, F2 at 21.96%, F3 at 19.86%, F4 at 14.12%, F5 at 20.12%, F6 at 16.56%, F7 at 17.70%, F8 at 16.54%, and F9 at 15.90%.

At 3 hours, the percentages increased again: F1 at 21.08%, F2 at 33.76%, F3 at 22.75%, F4 at 16.21%, F5 at 23.15%, F6 at 25.67%, F7 at 22.63%, F8 at 21.56%, and F9 at 22.45%.

This trend continued throughout the study, showcasing varying release rates for each batch as time progressed. Batch

F7 exhibited the most consistent and controlled release pattern over the 12-hour period, ultimately releasing 89.78% of the drug. These in vitro drug release studies provide crucial insights into the release kinetics of the microspheres, informing their potential applications and therapeutic effectiveness based on their controlled drug release profiles over time.

Table 7: Kinetic Data Studies of Tramadol HCl Microspheres

Formulation Code	Zero Order	First Order	Higuci	Hixon CrowellModel	Korsmeyer-Peppas Model
F-7	0.9242	0.9125	0.934	0.9123	0.8667

The kinetic data studies of Tramadol HCl microspheres were conducted to evaluate their drug release behavior based on different kinetic models. Each formulation was assessed using various models to understand the release mechanism. Notably, the ideal batch, F-7, exhibited the following kinetic data results:

Zero Order: The correlation coefficient for the Zero Order model was 0.9242, suggesting that the drug release from the microspheres follows this kinetic model to a significant extent.

First Order: The First Order model yielded a correlation coefficient of 0.9125, indicating that the drug release kinetics can be described by this model with a high degree of accuracy.

Higuchi Model: The Higuchi model showed a correlation coefficient of 0.934, implying that the drug release mechanism follows this model closely.

Hixon Crowell Model: The Hixon Crowell model yielded a correlation coefficient of 0.9123, suggesting that this model can adequately describe the drug release behavior from the microspheres.

Korsmeyer-Peppas Model: The Korsmeyer-Peppas model had a correlation coefficient of 0.8667, indicating that this model can also provide insights into the drug release kinetics of the microspheres.

These kinetic data studies provide valuable information about the release mechanisms and profiles of the drug from the microspheres. The data from the ideal batch (F-7) aligns closely with these kinetic models, indicating a controlled and predictable drug release behavior, which is essential for designing effective drug delivery systems.

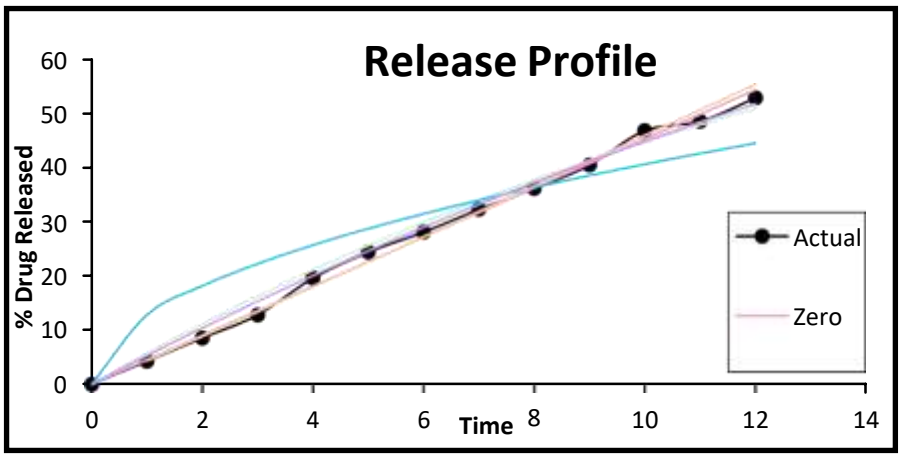

Figure 5: Kinetic Drug Release Data

Stability Study

A stability study was conducted on the microspheres of the ideal batch F7 to assess their performance and attributes over time. The study involved monitoring various parameters at different sampling times:

Initial: The microspheres exhibited a free-flowing powder appearance with a particle size of 43.54±0.5 nm, a drug content of 78.84±0.5%, and a moisture content of 0.15%.

Table 9: Stability study of Microspheres

SamplingTime	Physical Appearance	ParticleSize	Drug Content(%)	Moisture(%w/w)
Initial	Free Flowing Powder	43.54±0.5	78.84±0.5	0.15
30 Day	Free Flowing Powder	43.68±0.2	77.14±0.2	0.13
60 day	Free Flowing Powder	44.21±0.3	75.54±0.3	0.15
90 day	Free Flowing Powder	45.10±0.6	74.35±0.2	0.15

30 Day: Even after 30 days, the microspheres maintained their free-flowing powder appearance. The particle size slightly increased to 43.68±0.2 nm, while the drug content reduced to 77.14±0.2%, and the moisture content decreased to 0.13%.

60 Day: At the 60-day mark, the microspheres still retained their free-flowing powder nature. The particle size slightly increased further to 44.21±0.3 nm, the drug content decreased to 75.54±0.3%, and the moisture content remained stable at 0.15%.

90 Day: After 90 days, the microspheres remained as free-flowing powder. The particle size continued to increase to 45.10±0.6 nm, the drug content decreased to 74.35±0.2%, and the moisture content stayed at 0.15%.

Based on these results, it can be concluded that the ideal batch F7 of microspheres remains stable for a period of 90 days at room temperature. Despite some slight variations in particle size and drug content, the overall physical appearance and attributes of the microspheres were well-maintained throughout the study duration. This stability study provides valuable insights into the shelf-life and potential storage conditions for these microspheres, which is critical for their practical application and long-term use.

DISCUSSION

The development of Tramadol HCl-containing microspheres aimed to achieve a sustained and prolonged drug release, enhancing therapeutic effectiveness while ensuring patient convenience and compliance. By formulating an extended-release product, the balance between therapeutic efficacy and safety can be optimized. The comprehensive approach taken in this study involved the systematic selection of drug and excipients, guided by an extensive literature survey. The stepwise investigation using the Solvent Evaporation Method resulted in the successful creation of effective microspheres with Tramadol HCl.

Through the preformulation study, a thorough understanding of the interactions between the drug and excipients was established using FTIR analysis. The subsequent evaluation of key parameters including bulk density, tapped density, and angle of repose further illuminated the physical characteristics of the microspheres. Notably, the selection of excipients such as Agar and Pectin played a pivotal role in determining the microspheres' performance.

The Solvent Evaporation Method enabled the preparation of microspheres across various ratios and batches, each with its distinct composition. Among these, Batch F7 emerged as a standout, demonstrating desirable drug release characteristics. This batch, through meticulous optimization, showcased a promising drug release profile, indicating the successful achievement of the intended extended-release effect.

The evaluation of the prepared microspheres encompassed a spectrum of parameters, including Percentage Drug Release, Drug Entrapment Efficiency, Particle Size, Scanning Electron Microscopy, In Vitro Drug Release Studies, and Kinetic Data Studies. These comprehensive analyses collectively provided insights into the microspheres' performance, release mechanisms, and potential applications.

CONCLUSION

In conclusion, the synthesis of sustained-release microspheres through the judicious combination of polymers Agar and Pectin has yielded promising results. This study has demonstrated the potential of these polymers as effective drug release retardants, resulting in microspheres with favorable attributes, including high Percentage yield and efficient Drug entrapment. The systematic exploration of various polymer combinations and ratios has unveiled the versatility of these materials in achieving sustained drug release profiles. Notably, the formulation represented by F7 emerged as a standout candidate, displaying excellent buoyancy characteristics compared to other formulations.

The comparison between Agar and Pectin polymers not only shed light on their impact on physical properties but also provided insights into their influence on in vitro drug release kinetics. The significance of these observed effects cannot be overstated, as they play a pivotal role in shaping the design and efficacy of microsphere formulations.

In essence, this study underscores the potential of Agar and Pectin as promising polymer choices for developing sustained-release microspheres. The tailored approach of utilizing different combinations and ratios of these polymers has contributed to the creation of microspheres with desirable drug release characteristics. However, it is important to consider the comprehensive implications of these findings when designing microsphere formulations, accounting for physical properties, drug release behavior, and potential applications. This study's findings not only enrich the field of controlled drug delivery but also provide a stepping stone for further research and development in the pursuit of optimized therapeutic outcomes.

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