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Original Research Article

Formulation and Optimization of Ion Exchange Resin Beads of Tolperisone Hydrochloride Using 2^3 Factorial Desing

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Abstract:

Ion exchange resins (IERs) are polymers that can exchange specific ions within a solution with ions that are attached to the resin itself. These resins are widely used in water purification, chemical processing, and various industrial applications for the removal of undesirable ions or the separation of valuable ones. This study aims to develop resin beads containing Tolperisone hydrochloride for controlled release using various cation exchange resins. Due to its brief half-life (1.5 - 2.5 hours) and limited bioavailability, encapsulation with a hydrophobic polymer via solvent evaporation microencapsulation will be used to extend drug release. The goal is to enhance the drug's therapeutic effect in treating muscle spasms by sustaining its release over a longer period. Optimization was done by using 2^3 factorial design and further evaluated for extent of coating, drug content, particle size, micromeritics properties, SEM, in-vitro dissolution investigation.

Keywords: IERs, Tolperisone hydrochloride, bioavailability, encapsulation, hydrophobic polymer, micromeritics properties, SEM, 2^3 factorial design.

Introduction

Ion exchange resins are synthetic polymers capable of exchanging ions from their functional groups with ions in the surrounding solution. They function by reversibly exchanging target ions in liquid solutions without altering the chemical properties of the solution itself. [1] The basic principle of ion exchange is governed by the selectivity of the resin for certain ions, often driven by charge density and ion size. [2]

There are two main types of ion exchange resins:

Cation Exchange Resins:

These resins contain negatively charged functional groups (such as sulfonic acid groups, $-SO_3^-$) and exchange positive ions (cations) like Na^+, Ca^{2+}, or H^+.

Application: Often used in water softening to remove calcium and magnesium ions, which cause hardness in water.

Anion Exchange Resins:

These resins have positively charged functional groups (such as quaternary ammonium groups, $-NR_4^+$) and exchange negative ions (anions) like Cl^-, NO_3^-, or OH^-. [3]

Tolperisone HCl is classified as a BCS class I medication, which means it may be used as a muscle relaxant. The recommended dosage for this medication is to take it three times per day. Tolperisone hydrochloride found brief half-life, which ranges from 1.5 - 2.5 hours. Toxic effects are coupled with

a limited bioavailability and a quick reaction time, which limits its application in the treatment of muscular spasms. [4] The purposes of our study are the work toward the development of resinates beads containing a chosen drug for controlled releases (Tolperisone hydrochloride) by using a variety of cation exchanger resins. The drug's release from the drug's resonate will be further controlled by encapsulating the prepared resinate with an appropriate hydrophobic polymer using solvent evaporation microencapsulation technology. This will allow the drug's release from the complex of drug resin designed in support of a longer stage of time. [5]

Tolperisone hydrochloride resinate bead preparation:

The batch process used to synthesize Tolperisone resin compounds. The previously processed dry resins (1g) were agitated within a 100 ml 1% w/v drug mixture using a magnetic stirrer lasting 5 hours (single batch). The amount of the medication was quantified using a UV spectrophotometer at a wavelength of 261 nm, after the collection of a 0.1 ml sample that was diluted with distilled water and obtained at predetermined intervals throughout the complexation process at room temperature. This was conducted to evaluate the rate at which equilibrium may be achieved. Filtration has been employed to isolate the complexes through the supernatant. Following rinsing with distilled water to remove any uncomplexed medicines, the resultant complex had been dried for 24 hours at 400°C. [6]

Optimization of Tolperisone HCl–resin microcapsules employing a 2^3 factorial design:

We were using the factorial design, a popular statistical method for establishing and optimizing experimental sets. A 2^3 complete factorial design is the one that was employed. A series of experiments were carried out using a variety of independent variables, and the responses were tabulated and analysed. In a trial version of the full factorial factorial design, polynomial equations and statistical analysis were used to find a link between the independent variable and the response variables. The impacts of all the mentioned variables on the response are indicated through coefficient's value X1,X2 and X3. Synergistically influence has been shown by a coefficient values that is positive, whereas an antagonist influence upon this responses is indicated by a number that is negatives. [7]

2^3factorial method has been employed to formulate Tolperisone HCl-resin microcapsules. The 2^3factorial designs are employed to explore overall impact of factors(variables) and experimental situations on each other. In this approach, three factors are investigated, every at two-level, furthermore practical runs are investigated using the entire eight different configurations. Concentration of Eudragit-RS100(X1) was first independent variable, followed by the rotational speed (X2), and finally PEG-400 concentration (X3). As the dependent variables, it was decided to use the microcapsules' extent of coating (Y1), drug released percentage after 1 hour (Y2), drug released percentage after 6 hours (Y3), and drug released percentage after 12 hours (Y4). [8]

Table 1: 2^3Factorial design Run used to optimize the formulation.

Factors (Independent Variables)	**Levels**	
	(-) Low level	**(+)High level**
X1=EudragitRS100 concentrations	5%	20%
X2=Speed of Rotation	500	1500
X3=PEG 400 Concentration	0%	10%

Table 2: Table of Coded variable

Formulation	X_1	X_2	X_3	X_1	X_2	X_3
F1	-	-	-	5	500	0
F2	+	-	-	20	500	0
F3	-	-	+	5	500	10
F4	+	-	+	20	500	10
F5	-	+	-	5	1500	0
F6	+	+	-	20	1500	0
F7	-	+	+	5	1500	10
F8	+	+	+	20	1500	10

Table 3: Formulation table of Microcapsule by O/O Method

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Tolperisone HCl DRC (mg)	365	365	365	365	365	365	365	365
Eudragit RS100 (% w/v)	5	20	5	20	5	20	5	20
PEG-400 (%w/v)	0	0	10	10	0	0	10	10
Span 80 (%w/v)	1	1	1	1	1	1	1	1
Light liquid paraffin (ml)	100	100	100	100	100	100	100	100
Magnesium stearate (%w/v)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Speed (rpm)	500	500	500	500	1500	1500	1500	1500

Results and Discussion

After applying optimization (numerical) by Design expert software, predicted process variables and response variables were obtained. Microcapsules (O1) were prepared using obtained value and were evaluated. The optimal settings of the formulation variables (factors) as predicted by the design expert software as numerical were as follows:

Table 4: Optimized formulation process and response variables

Code	Solution			Response Variables			Error	Desirability
	Process Variables							
	X1	X2	X3		Predicted Value	Observed Value		
O1	5.4	1201.65	6.26	Y1	7.26	7.28	-0.03	1.00
				Y2	8.22	8.26	-0.03	
				Y3	36.46	35.35	1.12	
				Y4	68.24	68.68	-0.45	

Where

X1	Eudragit RS100 Concentration	Y1	% Extent Coating
X2	Speed of Rotation	Y2	Cumulative % drug release after 1 hr
X3	PEG 400 Concentration	Y3	Cumulative % drug release after 6 hr
		Y4	Cumulative % drug release after 12 hr

Determination of extent of coating of optimized formulation:

Extent coating (Y1) was determined by utilizing the methodology developed in the methodology segment and detailed results are demonstrated in table below.

Table 5: Extent Coating of optimized Formulation

Formulation	**Weight of Microacapsules (mg)**	**Weight of dried Tolperisone HCl resinate beads(mg)**	**Weight of extent coating(mg)**	**% extent coating**
O1	500	464.57	35.43	7.34

Extent coating was found to be 7.28%.

Drug content and Microencapsulation efficiency of optimized Formulation:

Amount of drug encapsulated in microcapsules was estimated and the drug content found was reported Microencapsulation efficiency was determined by utilizing the methodology developed in the methodology segment and detailed results are demonstrated in table below.

Table 6: Drug content and % Microencapsulation efficiency

Formulation	**Drug content**		**% Microencapsulation efficiency**
	Theoretical (mg)	**Practical (mg)**	
O1	50	48.87	98.01

The % microencapsulation efficiency of the optimized microcapsules was found to be 98.01%.

Particle Size of the Optimized microcapsules:

A microscopy procedure has been performed to measure the microcapsule's size. Utilizing a calibrated ocular micrometer, we were able to collect measurements concerning the overall distribution of particle sizes and figure out the averaged size. After suspending the microcapsules into paraffin, they were examined using a microscope with a magnification of 10*10X. A calibration factor of 14.28 was employed to calculate the size of the 300 microcapsules randomness. The procured result was demonstrate in tabulated form below.

Table 7: Particle size of the optimized microcapsules

Formulation	Average Particle Size(µm)
O1	199.75

The average particle size of optimized microcapsule is 199.75µm.

Micromeritics properties of Microcapsules:

The Micromeritics rheological properties of drug loaded optimized microcapsules determined by utilizing the methodology developed in the methodology segment and the investigated results demonstrated into the tabulated form below:

Table 8: Micromeritics properties of optimized Microcapsules

Formulation	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratio	Angle of Repose
O1	0.65	0.71	8.02	1.08	15.96

All of the above-mentioned measurements stayed inside the permitted range.

SEM of Optimized microcapsule :

SEM investigation was performed by utilizing the methodology developed in the methodology segment and SEM-Images are demonstrated following. A photomicrograph was obtained at an appropriate magnification after the gold-coated samples had been observed utilizing a scanning-electron microscope. SEM-micrographs of optimized Tolperisone HCl resinate beads encapsulated with RS100-Eudragit were captured.

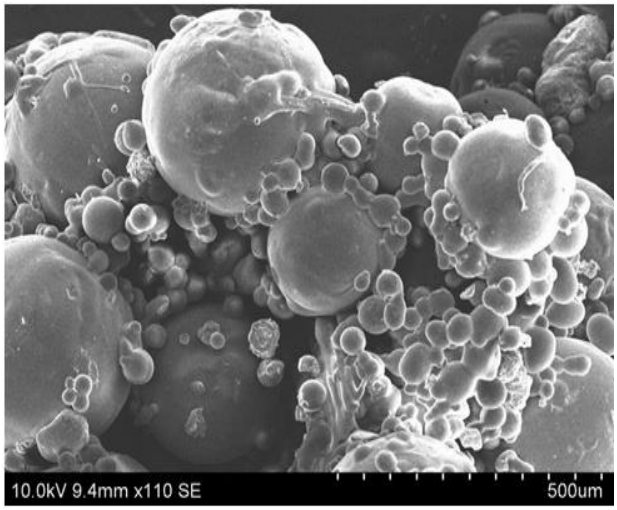

Fig.1: SEM of Optimized microcapsule(O1)

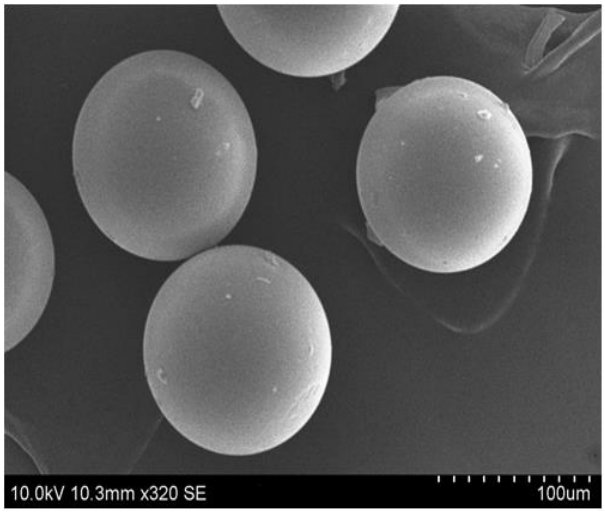

Fig. 2: SEM of Optimized microcapsule (O1)

The scanning electron micrograph (SEM) figure shows the exterior surface of the developed Eudragit RS100 coated Tolperisone HCl-resin microcapsules. It is evident that the formulation's surface seems smooth, regular, and flawless.

In-vitro dissolution investigation of an optimized preparation:

The procedure for releasing the drug from the optimized Tolperisone resinate microcapsules has been conducted utilizing USP-II dissolution unit. 900 millilitres of distill water kept on a temperature 37°±1°C served as the dissolving media. It rotated at a rate of 50 rpm. As the solution is stirred up with the paddle, a specific weight of an Tolperisone hydrochloride resinate microcapsule that is equal to 150 mg of drug (Tolperisone hydrochloride) has been introduced. At suitable intervals, 1ml mixture solution has been taken out and updated by adding fresh solution into it. Using an ultraviolet spectrophotometer set to 261 nm, the absorbance of the sample that was obtained was determined.

The tabulated outcomes of 12 hour in-vitro release study from optimized formulation of microcapsule were calculated and are depicted in table below:

Table 9: Optimized Tolperisone HCl Microcapsule's release studies

Time (Min.)	Cumulative % drug release
0	0
60	8.26
120	12.77
180	19.53
240	24.81
300	30.80
360	35.35
420	42.93
480	48.97
540	54.28
600	60.29
660	64.15
720	67.97

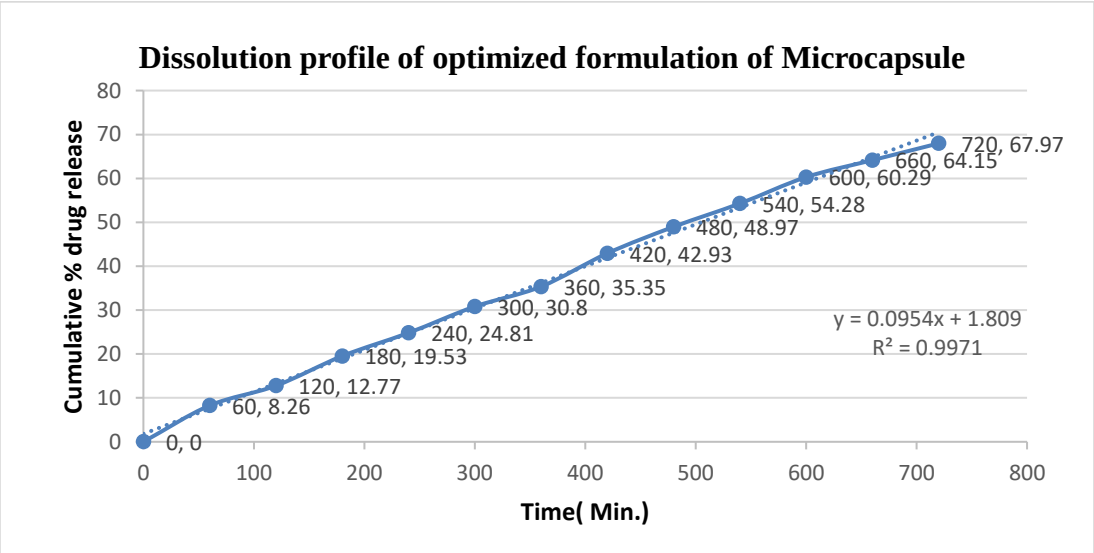

Fig. 3: Optimized microcapsule's (O1) *In-vitro* Tolperisone HCl release

Conclusion

Ion exchange resins play an indispensable role in various industries, with their ability to selectively exchange ions making them versatile for purification and separation applications. Using a variety of cation exchange resins, this research intends to create resin beads bearing Tolperisone hydrochloride for controlled release. Using a 23 factorial design, optimisation was carried out, and the amount of coating, drug content, particle size, micromeritics characteristics, SEM, and in vitro dissolution research were further assessed. The design expert software performed numerical optimisation, and the results showed process factors and response variables that might be anticipated. A variety of microcapsules were developed and tested. After evaluation and preparation, multiple responses have been observed and found to be consistent with expectations.

References

1. Singh V, Bansal M, Gupta R, Sharma A, Preparation and Evaluation of Eperisone Hydrochloride Resinate Beads, International Journal of Health Advancement and Clinical Research (tz) 2023; 1 (1); 12-18.
2. Sharma V, Chauhan C.S, Ion Exchange Resins and Their Applications, Journal of Drug Delivery & Therapeutics; 2014; 4(4): 115-123.
3. Sharma , N., Sharma , V., & Singh , V. An Overview on Ion Exchange Resins. International Journal of Health Advancement and Clinical Research (tz), 2023; 1(4): 80–84.
4. Patait S.S, Formulation Development of Tolperisone Hydrochloride Film Coated Tablet. J Pharmaceutical research,2023; 8(2): 238-247.
5. Butola, M., Badola, A., Nainwal, N., Rana, S., Jakhmola, V., Ale, Y. and Ansori, A.N., 2024. Formulation of Sustained-Release Tablets of Tolperisone HCl Using Different Blends of Hydrophilic and Hydrophobic Polymers. Indian Journal of Pharmaceutical Education and Research, 2024; 58(3s): s872-s879.
6. Sharma V, Singh C, Gupta AK, Yashwant. Development and Optimization of Eperisone Hydrochloride Microcapsule. International Journal of Drug Delivery Technology. 2024;14(1):230-235.
7. Shah, M. and Pathak, K., Development and statistical optimization of solid lipid nanoparticles of simvastatin by using 2 3 full-factorial design. AAPS pharmscitech,2010; 11: 489-496.
8. Prakobvaitayakit M. and Nimmannit U., Optimization of polylactic-co-glycolic acid nanoparticles containing itraconazole using 2 3 factorial design. Aaps Pharmscitech, 2003; 4: 565-573.