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Original Article

Formulation and Characterization of Tizanidine HCl Loaded Controlled Release Mesoporous Silica Nanoparticles (MSNs)

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ABSTRACT

Introduction: Spasticity is a disorder in which continuous contraction of certain muscles leads to muscle stiffness. Tizanidine, a frequently prescribed skeletal muscle relaxant for spasticity treatment, exhibits a short elimination half-life and limited oral bioavailability. The aim of current study is to prepare controlled-release microparticles incorporating tizanidine-loaded Mesoporous Silica Nanoparticles (MSNs) for enhancing the bioavailability, to treat spasticity. **Materials and Methods:** The MSNs were synthesized via a sol-gel technique with slight modification, with drug loading using the solvent impregnation method. Design expert software was used and box-behnken design was selected for the optimization of MSNs. The effect of TEOS (silica precursor), CTAB (surfactant), and NaOH (base catalyst) was analyzed on response variables. For controlling the release of tizanidine from MSNs, the tizanidine-loaded MSNs were incorporated in polymeric microparticles. **Results:** The optimized batch of MSNs exhibited a mean particle size of 131.7 nm, a Polydispersity Index (PDI) of 0.202, a Zeta Potential (Z.P.) of 30.6 mV, and an Entrapment Efficiency (EE%) of 51.18%. Additionally, the optimized MSN formulation underwent SEM, DSC, and XRD analyses. The polymeric microparticles containing tizanidine-loaded MSNs were evaluated for particle size, microscopic evaluation, and *in vitro* drug release. The microparticles demonstrated 12% initial rapid release followed by a sustained release pattern for 10 hr and exhibited the Higuchi Model with a regression coefficient (R^2) of 0.9682. **Conclusion:** The developed polymeric microparticles, incorporating tizanidine-loaded mesoporous silica nanoparticles, exhibited a controlled drug release profile, facilitating the enhancement of the drug's oral bioavailability. Consequently, a reduction in dosing frequency is anticipated, leading to improved patient compliance.

Keywords: Tizanidine, MSN, Spasticity, Controlled release, Sol-Gel Method, Box-Behnken design.

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INTRODUCTION

Spasticity is a condition characterized by persistent muscle contractions, resulting in muscle stiffness. Spasticity is described as a motor disorder marked by heightened muscle tone that increases with the speed of movement and involves pronounced tendon jerks due to hyperactive stretch reflexes, a key feature of the upper motor neuron syndrome. Some common reasons which may give rise to spasticity are cerebral palsy, traumatic brain injury, multiple sclerosis, and spinal cord damage.[1,2] Spasticity affects over 12 million people worldwide including 80% of people with cerebral palsy and 80% of those with multiple sclerosis. There are various treatment approaches for spasticity ranging from physical therapy to surgery, but oral drug delivery is preferred among them. Tizanidine, one of the most commonly prescribed skeletal muscle relaxants, is utilized for treating various conditions including back pain, chronic headaches, and postoperative pain, owing to its agonistic action on the α2-adrenergic receptor. The therapeutic dosage typically ranges from 2 to 6 mg every 4 to 6 hr, with a maximum daily intake of 36 mg. Tizanidine belongs to a BCS class II drug (i.e., the drug with low solubility and high permeability). Due to its poor dissolution profile and high first-pass metabolism, its bioavailability is affected which results in low therapeutic action, its mean elimination half-life is approximately 2.5 hr, which necessitates patients to take high doses to get the same therapeutic action this may increase the chances of side effects. This problem can be resolved by forming a controlled-release formulation, which results in reduced dosing frequency, enhanced therapeutic efficacy, and reduced drug toxicity.[3-7] MSNs are promising carriers to enhance the solubility of poorly soluble drugs by changing the drug from crystalline form to amorphous form. MSNs are inorganic-based nanomaterials prepared in the presence of a silica source and surfactant, having unique characteristics of substantial pore volume, large surface area, and tunable pore size distribution. These have resistance to heat, pH, and chemical degradation such as hydrolysis. The large surface area and pore volume facilitate the efficient absorption

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of significant amounts of active substances. Due to these unique characteristics, MSNs have emerged as a prominent candidate for nanotech-based drug delivery systems.[8-13]

The aim of present research work was to improve the bioavailability of tizanidine by preparing controlled-release microparticles incorporating tizanidine-loaded MSNs. Design expert software was used to analyze the effect of different variables on MSNs. For controlled release, the optimized tizanidine-loaded MSNs were incorporated in microparticles by using the double emulsification solvent evaporation method. The optimized drug-loaded MSNs were characterized by SEM, DSC, XRD, Particle size, PDI, and Zeta Potential, and further, to determine the controlled release pattern of polymeric microparticles containing drug-loaded MSNs *in vitro* drug release study was performed.

MATERIALS AND METHODS

Methods

Synthesis of MSNs

The synthesis of MSNs was carried out using a sol-gel process with minor adjustments. This process involves, hydrolysis and condensation of the silica source occurring on the surface of micelles.[14-20] In this process, CTAB (surfactant) was dissolved in Milli-Q water, and the pH of the solution was adjusted to 10 using 2M NaOH and heated to 80°C for 30 min. To the above solution TEOS (silica source) was added dropwise with continuous stirring for 2 hr at 80°C to form a nanoparticle suspension. The suspension was centrifuged at 4000 rpm for 15 min and washed three time with milli-Q water and two time with ethanol to remove surfactant. The residual powder was dried in an oven and calcinated at 550°C for 6 hr in a muffle furnace.[21]

Drug loading into MSNs

Drug loading into MSNs was done by using the solvent impregnation method with slight modifications.[22-24] Before drug loading, these MSNs were preheated in a hot air oven at 120°C for 1 hr. Then, these preheated MSNs were dipped into a drug solution of concentration 3.5 mg/mL with continuous shaking. The dispersion was vortexed on a cyclone mixer for 30 min and kept aside for 24 hr. After 24 hr the dispersion was filtered and washed with a small amount of distilled water to get the drug loaded MSNs. Then the filtrate was collected and dried in a vacuum desiccator.

Optimization of MSNs

The optimization of MSN parameters was conducted using the Box-Behnken design with the aid of Design Expert software. This experimental approach involved the selection of three key factors-TEOS, CTAB, and NaOH 2M and four responses corresponding to these factors, namely particle size, Polydispersity Index (PDI), Zeta Potential (Z.P.) and Entrapment Efficiency% (EE%) (As illustrated in Table 1). The Box-Behnken design recommended 15 batches, incorporating 3 center points, to comprehensively explore the parameter space (as illustrated in Table 2).[25]

Synthesis of polymeric microparticles of drug-loaded MSNs

Polymeric microparticles incorporating drug-loaded MSNs were fabricated via the double emulsification solvent evaporation technique. Initially, ethyl cellulose was dissolved in dichloromethane to create a polymer solution, into which the drug-loaded MSNs were dispersed, forming a polymeric suspension as per the quantities mentioned in Table 3. Subsequently, this suspension was gradually added dropwise into a Polyvinyl Alcohol (PVA) solution (0.2% w/v) under homogenization to generate an emulsion. Further, Dichloromethane (DCM) was allowed to evaporate by stirring the mixture overnight on a magnetic stirrer. Then, the resulting mixture was centrifuged and washed three times for 15 min at 3000 rpm to remove PVA and to separate the microparticles. The pellet of the microparticles were lyophilized and collected in a glass vial and under refrigerated conditions for subsequent analyses.[26,27]

Evaluation

Evaluation of MSNs

The morphological evaluations of MSNs were done using FE-SEM and a light microscope. A range of parameters including particle size, Polydispersity Index (PDI), zeta potential, entrapment efficiency, and analyses using Differential Scanning Calorimeter (DSC) and X-ray Diffraction analysis (XRD) were employed to thoroughly characterize the attributes of MSNs.

Particle size, PDI, and zeta potential determination

The particle size, PDI, and zeta potential of prepared MSNs were analyzed the particle size analyzer (Horiba SZ-100) using dynamic light scattering method. The scattering angle was kept at 90° and the holder temperature was 25°C. The zeta potential was determined since it serves as an indicator for the stability of nanoparticle suspension. The graphical representation illustrating the relationship between particle size and zeta potential is depicted in Figure 1a, while corresponding observations are documented in Table 2.

Morphology of MSNs

The morphology of MSNs was examined using both a light microscope (Leica) and Scanning Electron Microscopy (SEM) conducted with a JSM-IT200 instrument. For microscopic analysis the MSNs were subjected to light microscope under an oil immersion lens with a magnification of 100 X. For SEM analysis, the MSNs were mounted onto a pin stub using adhesive tape and then subjected to gold vapor coating before observation. SEM

analysis was conducted at an accelerated voltage of 10 kV. The resulting images are depicted in Figures 1b and c, respectively.

Differential Scanning Calorimetry of MSNs

The DSC analysis of tizanidine-loaded MSN, MSN, physical mixture (CTAB+tizanidine), CTAB, and tizanidine was performed. These experiments were carried out using differential scanning calorimetry (Perkin Elmer DSC 6000). 3-5 mg sample was weighed and transferred in an aluminum pan and an aluminum cap was placed in it and crimped. The samples were analyzed at the scanning rate of 20°C/min and the temperature range was 50°C-325°C. The thermogram is shown in Figure 1d.

X-ray Diffraction Pattern of MSNs

XRD pattern of tizanidine HCl, physical mixture, and optimized Tizanidine HCl-loaded MSN was done by using Bruker-D8 advanced diffractometer. The X-rays were generated by a sealed tube at a wavelength of 0.154 nm (Cu K-alpha) using a Bruker Lynx Eye detector. The XRD analysis was performed to determine the polymorphic nature of the drug present in MSN. The XRD diffractogram is depicted in the Figure 1e.

Entrapment Efficiency % of MSNs

The Entrapment Efficiency (EE %) of the drug-loaded MSNs was assessed by dispersing them in 10 mL of water, followed by vortexing for 15 min and subsequent incubation for 24 hr. After this incubation period, the dispersion underwent centrifugation, and the supernatant was examined using UV spectroscopy at 320 nm. The entrapment efficiency was then determined using the formula provided below

$$entrapment\ efficiency\ \% = \frac{actual\ drug\ content}{theoretical\ drug\ content} \times 100$$

Evaluation of microparticles

Particle size determination

The particle size of prepared microparticles was determined by Malvern Mastersizer. The laser diffraction technique was used for the analysis of particle size. For the analysis, these microparticles were dispersed in water and then this dispersion was added into the sample compartment.

Morphology of microparticles

The structure of the microparticles was analyzed utilizing a light microscope (Leica) with an oil immersion lens. Observation of the image reveals that the microparticles encapsulating tizanidine-loaded MSNs display a sleek surface texture. This representation is presented in Figure 1f.

In vitro drug release studies of microparticles

The investigation of drug release from the polymeric microparticles was carried out through the Sample and Separate (SS) technique *in vitro*. A specific amount of polymeric microparticles was introduced into a beaker containing the release media (phosphate buffer pH 6.8) and kept under constant stirring at 75 rpm. At predetermined time points, 5 mL portions of samples were withdrawn and substituted with an equivalent volume of fresh medium. The withdrawn samples were than centrifuged, and the resulting supernatant was assessed using a UV spectrophotometer at 320 nm.

RESULTS AND DISCUSSION

Optimization of MSNs

The optimization process involved the selection of various independent variables and corresponding response variables for evaluation. Experimental trials were conducted and the collected data underwent statistical analysis (as presented in Table 2), utilizing the Design Expert software. Based on the desired characteristics (As illustrated in Table 4), the software proposed 57 potential solutions. Among these solutions, the one with the highest desirability score, 0.833, was identified as the optimized batch, and tizanidine-loaded MSNs were prepared accordingly. The experimental design confirmed that particle size, zeta potential, PDI, and entrapment efficiency followed a linear model. A polynomial equation was derived to establish the relationship between independent variables, as depicted in Table 2. Additionally, the desirability contour and response surface plot,

Table 1: Selection of independent variable and response variable for optimization in Box-Behnken design.

Sl. No.	Independent variable	Unit	Lower limit	Upper limit
1.	TEOS (Silica source)	mL	2	5
2.	CTAB (Surfactant)	mg	250	500
3.	NaOH (Base Catalyst)	µL	150	450
Response variable for optimization in Box-Behnken design				
Sl. No.	Response Variable	Unit	Constraints	
1.	Particle size	nm	Minimum	
2.	PDI	mV	Minimum	
3.	Zeta Potential	-	Minimum	
4.	Entrapment Efficiency	%	Maximum	

Table 2: Box-Behnken design for optimization and evaluation of batches of tizanidine HCl-loaded MSNs.

Batch code	TEOS (mL)	CTAB (mg)	NaOH 2M (µL)	Particlesize	PDI	Zetapotential	EntrapmentEfficiency %
MSN-01	3.5	375	300	202.9	0.275	36.6	55.06
MSN-02	3.5	250	150	180.3	0.245	27.1	35.94
MSN-03	2	500	300	200.9	0.272	38.0	55.80
MSN-04	3.5	500	450	274.3	0.375	42.0	42.30
MSN-05	3.5	375	450	280.1	0.381	35.2	55.06
MSN-06	5	375	150	290.6	0.395	39.3	38.12
MSN-07	2	375	450	150.1	0.204	32.9	60.16
MSN-08	5	375	450	210.8	0.286	36.3	46.26
MSN-09	5	500	300	280.3	0.381	40.9	58.76
MSN-10	3.5	250	450	160.5	0.219	32.9	43.83
MSN-11	2	250	300	139.5	0.19	27.7	43.62
MSN-12	3.5	375	300	206.9	0.281	35.2	56.06
MSN-13	2	375	150	230.9	0.313	35.3	46.48
MSN-14	5	250	300	240.6	0.327	29.8	34.89
MSN-15	3.5	500	150	300.4	0.409	42.8	56.03
Statistical summary of response variables							
Response variable	**Y1: Particle Size**		**Y2: PDI**		**Y3: Zeta Potential**		**Y4: Entrapment Efficiency (%)**
Suggested Model	Linear		Linear		Linear		Linear
Suggested p-Value	0.0029		0.0031		0.0001		0.0434
Suggested F-Value	8.83		8.69		26.83		3.79
Lack of Fit	0.0647		0.0708		0.3913		0.0769
R^2	0.7065		0.7033		0.8798		0.5082
Adjusted R^2	0.6265		0.6224		0.8470		0.3741
Predicted R^2	0.4938		0.4875		0.7525		0.0991
Adequate Precision	9.4923		9.4337		15.0288		5.8723
Polynomial equation	224.39+37.61A+ 41.87B-16.75C		0.3050+0.0512A+ 0.0570B-0.0224C		35.47+1.54A+ 5.79B-0.0809C		48.39-3.50A+ 6.83B+2.52C

illustrating the prediction of the optimized batch with maximum desirability, are presented in Figure 2a.

Figures 2b-2m of the response surface graph illustrate that increasing the concentrations of CTAB and TEOS leads to an increase in the particle size of MSNs, while an increase in the amount of NaOH results in a decrease in particle size. As the concentration of CTAB increases, it is believed that particle size will be reduced as CTAB prevents the agglomeration of particles by forming a protective layer around them. However, at certain elevated concentrations, this protective layer becomes too thick, leading to an increase in particle size. Similarly, increasing the concentration of TEOS accelerates nucleation rates, resulting in the formation of larger particles. The Polydispersity Index (PDI) serves as an indicator of particle size distribution, with smaller PDI values indicating monodispersity of particles. Therefore, as particle size increases, the PDI value tends to increase accordingly. Zeta potential serves as an indicator of nanoparticle suspension stability, and it is a measure of charge, on increasing CTAB concentration leads to an increase in zeta potential due to its positive charge, while higher concentrations of TEOS and NaOH lead to a decrease in zeta potential owing to their negative charge. This observation suggests that the prepared nanoparticle suspension exhibits stability. Entrapment efficiency, a critical parameter for effective tizanidine delivery, Higher concentrations of CTAB facilitate the formation of micelles with larger surface areas, thereby enhancing drug entrapment within the pores of Mesoporous Silica Nanoparticles (MSNs). Conversely, increasing TEOS concentration results in the formation of thicker walls around micelles, reducing available surface area for drug entrapment and consequently lowering entrapment efficiency.

Prediction of an optimized batch of MSNs

The Design Expert software identified a solution with a maximum desirability of 0.833, comprising 2 mL of TEOS, 283.88 mg of CTAB, and 450 µL of NaOH 2M, as the optimized batch. Subsequently, this batch underwent evaluation for particle size, zeta potential, PDI, and entrapment efficiency. The experimental outcomes were then compared with the predicted results, as outlined in Table 4.

Particle size, PDI, and zetapotential

The optimized batch of MSNs exhibited a particle size of 131.7 nm and a PDI of 0.202. Additionally, the zeta potential of the optimized batch was measured at 30.6, confirming the stability of the formulation.

Microscopy of MSNs

The morphology of the optimized batch of MSNs was examined using a light microscope (Leica), revealing small spherical porous particles. Additionally, the FE-SEM image displayed an ordered circular structure in the formulated optimized batch of MSNs.

Entrapment Efficiency % of MSNs

The entrapment efficiency of the optimized batch of tizanidine-loaded MSN was 51.18% and the drug loading was 45 mg (approx.) in 1 g of MSNs.

Differential Scanning Calorimetry of MSNs

The DSC analysis of the optimized batch of tizanidine-loaded MSN, MSN, physical mixture, CTAB, and tizanidine was performed to determine the polymorphic nature. The DSC thermogram of tizanidine shows a peak at 296.75°C which confirms that the drug

Table 3: Excipients used in the preparation of different batches of polymeric microparticles.

Batch code	Amount of excipients	
	Ethyl cellulose (mg)	0.2% PVA solution (mL)
DL MSN-1	150	200
DL MSN-1	200	200
DL MSN-1	250	200
DL MSN-1	300	200

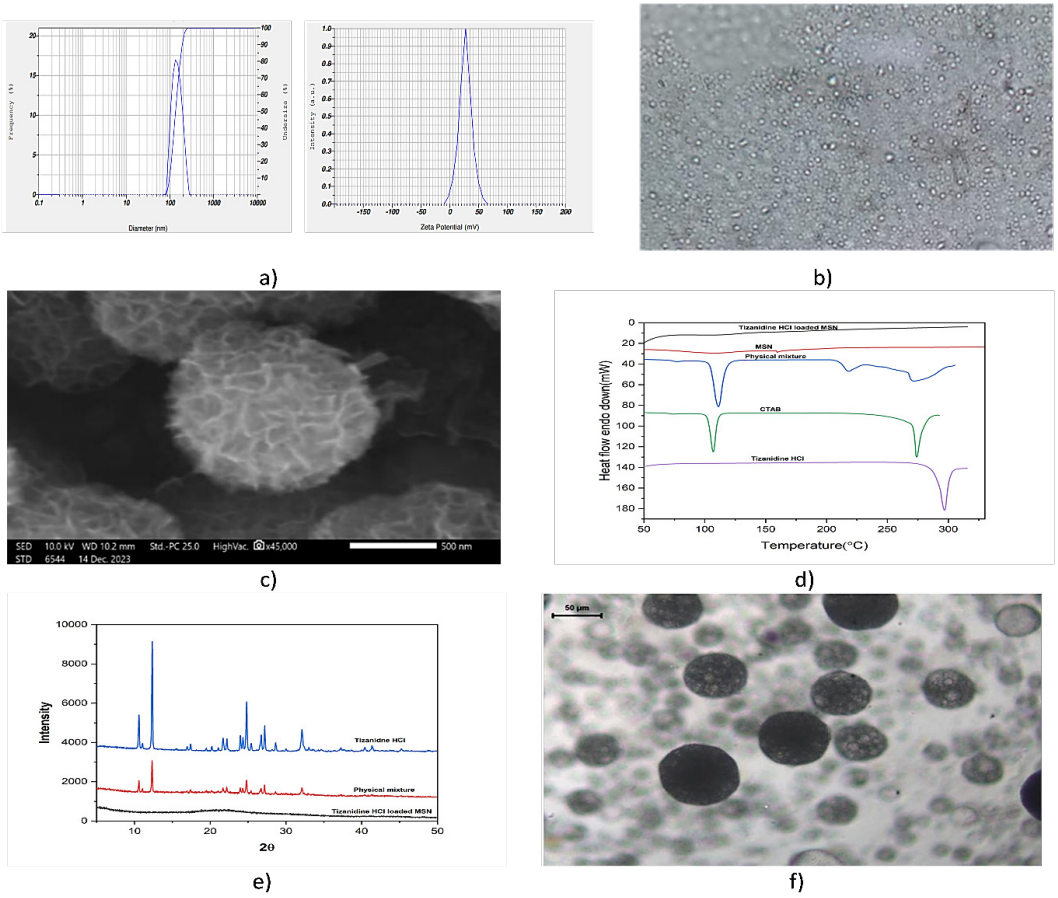


Figure 1: a) Particle size distribution and zeta potential of MSNs, b) Microscopic image of optimized MSNs, c) FE-SEM image of optimized MSNs, d) DSC thermogram of tizanidine-loaded MSN, MSN, CTAB, and tizanidine, e) XRD pattern of tizanidine, physical mixture, and tizanidine-loaded MSNs, f) Microscopic image of polymeric microparticles.

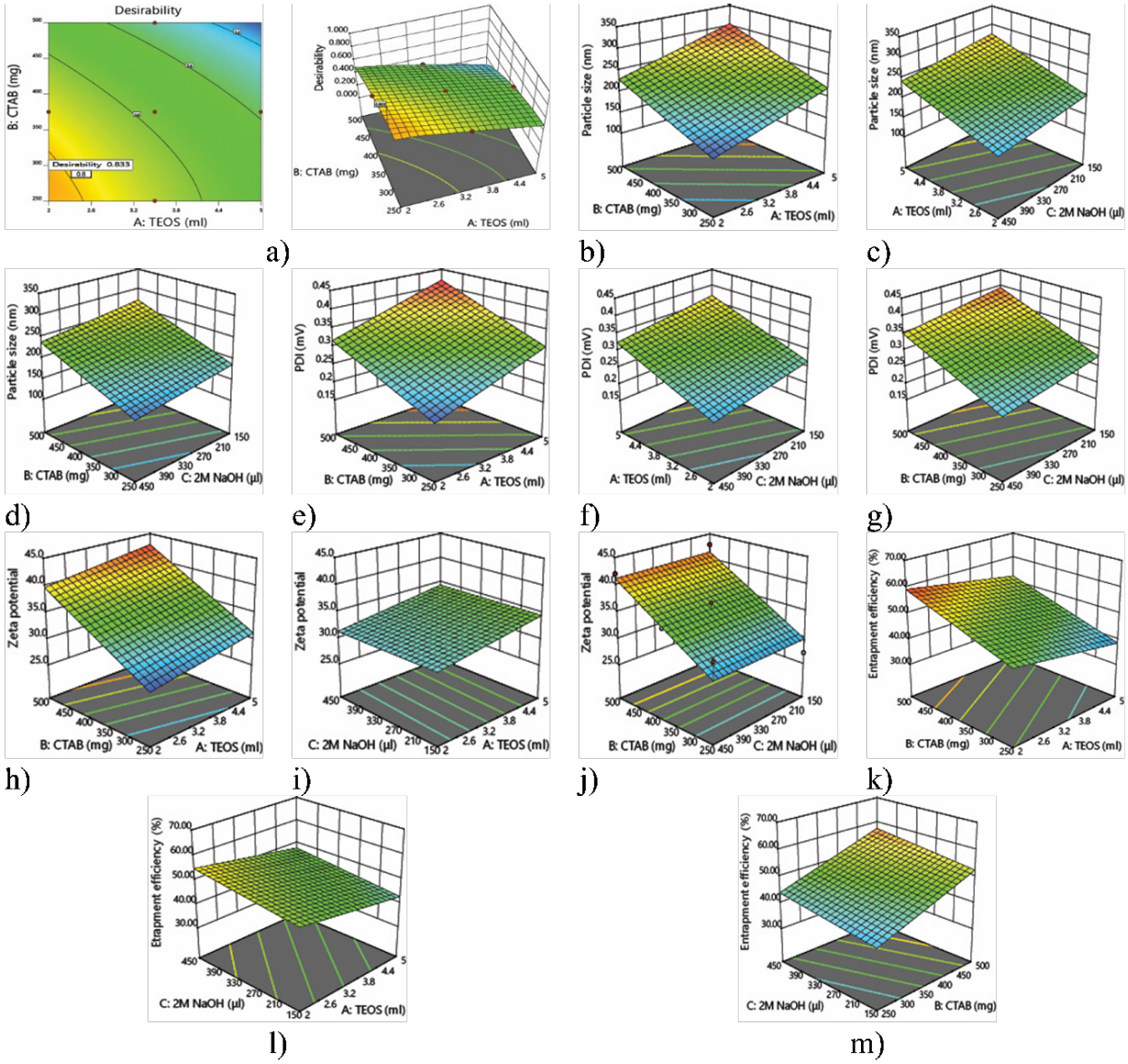


Figure 2: a) Response surface and contour plot showing maximum desirability of MSNs, b) Effect of TEOS and CTAB on Particle size, c) Effect of TEOS and 2M NaOH on Particle size, d) Effect of CTAB and 2M NaOH on Particle size, e) Effect of TEOS and CTAB on PDI, f) Effect of TEOS and 2M NaOH on PDI, g) Effect of CTAB and 2M NaOH on PDI, h) Effect of TEOS and CTAB on Zeta Potential, i) Effect of TEOS and 2M NaOH on Zeta Potential, j) Effect of CTAB and 2M NaOH on Zeta Potential, k) Effect of TEOS and CTAB on Entrapment efficiency %, l) Effect of TEOS and 2M NaOH on Entrapment efficiency %, m) Effect of CTAB and 2M NaOH on Entrapment efficiency %.

Table 4: Experimental plan obtained through Design Expert software for designing MSNs.

Components		Quantity	
TEOS (mL)		2 mL	
CTAB (mg)		283.88 mg	
NaOH 2 M (µL)		450 µL	
Evaluation parameter	**Predicted value**	**Practically observed value**	**Relative error**
Particle size	139.49	131.7	5.58
PDI	0.189	0.202	6.88
Zeta Potential	29.6	30.6	3.37
Entrapment efficiency	49.43	51.18	3.54

is in the crystalline state. Similarly, CTAB and physical mixture exhibited distinct peaks, but the tizanidine-loaded MSN does not show any peak, which confirms that the drug is entrapped into the MSN and drug has been transformed from crystalline form to amorphous form.

X-ray Diffraction Pattern of MSNs

XRD analysis was conducted on the optimized batch of tizanidine-loaded MSN, physical mixture, and tizanidine to ascertain their physical states. The X-ray diffractogram of tizanidine exhibited sharp, distinct peaks at 10.58º, 12.34º, 24.80º, 27.19º, and 32.10º on 2Θ, indicative of its crystalline nature. Similarly, the X-ray diffractogram of the physical mixture displayed distinct peaks. However, the X-ray diffractogram of the tizanidine-loaded MSN revealed no discernible peaks, suggesting that tizanidine is entrapped within the MSN in an amorphous form.

Table 5: Particle size of different batches of polymeric microparticles.

Batch Code	Particle size (µm)
DL MSN-1	35.508
DL MSN-2	40.109
DL MSN-3	54.567
DL MSN-4	61.168

Particle size determination

The particle size analysis of the prepared batches of polymeric microparticles was conducted using Malvern Mastersizer, revealing sizes ranging from 35 µm to 65 µm. The particle size of the polymeric microparticles exhibits a direct correlation with the amount of ethyl cellulose. As the amount of ethyl cellulose increases, the thickness of the polymeric coating layer also increases, leading to larger-sized polymeric microparticles. The particle size of prepared batches of polymeric microparticles is mentioned in the Table 5.

Morphology of microparticles

The morphology of the polymeric microparticles was assessed using a light microscope (Leica), revealing a smooth surface without any observed crystals. This observation confirms the complete incorporation of the optimized batch of tizanidine-loaded MSN into the polymeric microparticles.

In vitro drug release studies of microparticles

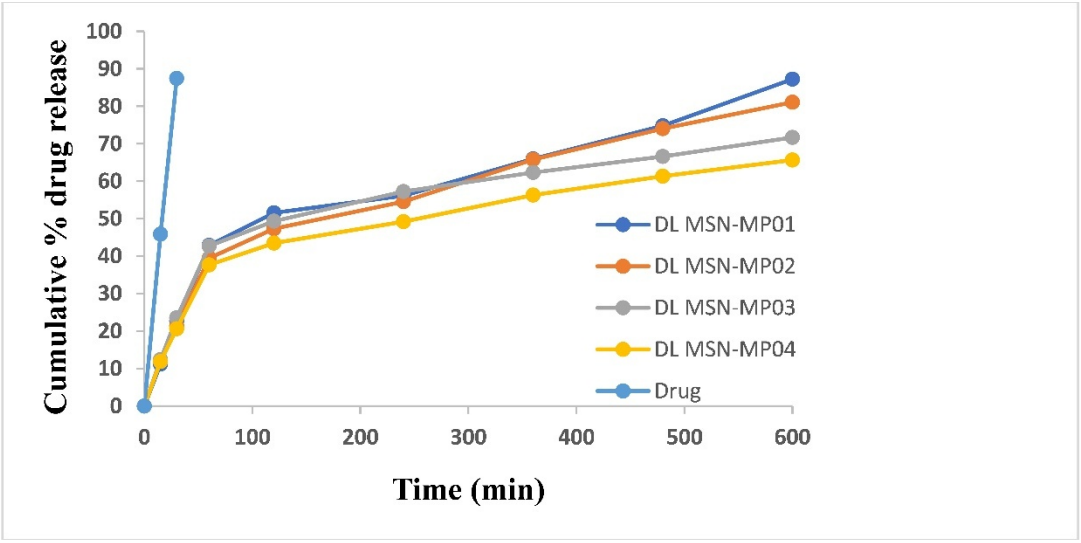
The drug release behaviour of the polymeric microparticles was evaluated *in vitro* utilizing phosphate buffer at pH 6.8. The drug release from the polymeric microparticles was found to be influenced by the concentration of ethyl cellulose. The cumulative drug release of different batches of microparticles was found to be 87.35%, 81.17%, 71.75%, and 66.99%, respectively. The release of drug from polymeric microparticles has an inverse relation with the concentration of ethyl cellulose. Observations

Table 6: Drug release from polymeric microparticles.

Sl. No.	Time (min)	Pure drug sample	CDR (DL MSN-1)	CDR (DL MSN-2)	CDR (DL MSN-3)	CDR (DL MSN-4)
1.	0	0	0.00	0.00	0.00	0.00
2	15	45.86	11.20	12.38	12.38	11.88
3.	30	87.43	22.85	21.23	23.58	20.87
4.	60	-	42.95	39.40	42.71	37.68
5.	120	-	51.57	47.33	49.29	43.34
6.	240	-	56.14	54.56	57.44	49.20
7.	360	-	65.87	65.74	62.53	57.44
8.	480	-	74.77	74.77	67.91	63.80
9.	600	-	87.35	81.17	71.75	66.99

Table 7: Drug release kinetic models of polymeric microparticles.

Sl. No.	Drug Release Kinetic Model	Equation	K	R^2
1.	Zero-order	Q_0-Q_t=K_0t	0.1171 mol/min	0.8491
2.	First order	log Q=log Q_0-kt/2.303	-0.0011 mol/min	0.9625
3.	Higuchi	Q_0-Q_t=$Kt^{1/2}$	3.2373 mol/min	0.9682
4.	Korsemeyer-Peppas	Log (Q_0-Q_t)=log k-nlog t	0.6561 mol/min	0.9427
5.	Hixson-Crowell	$Q_0^{1/3}$ - $Q_t^{1/3}$=Kt	-0.0003 mol/min	0.9349



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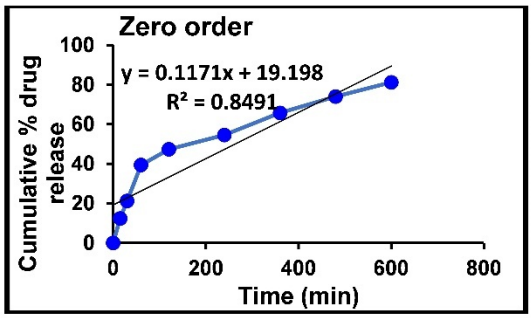

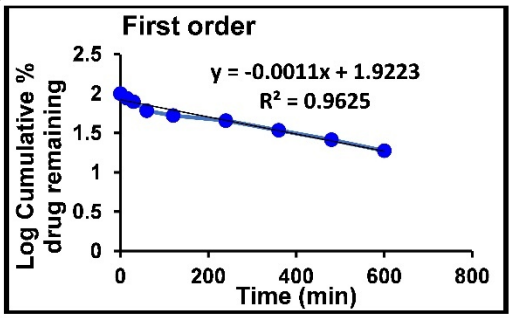

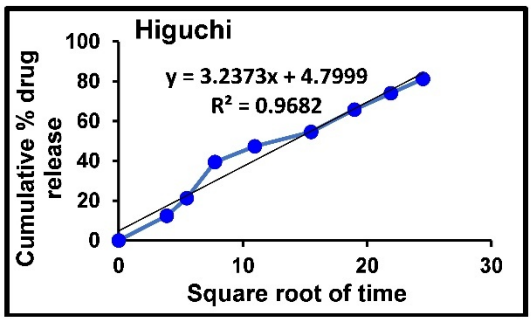

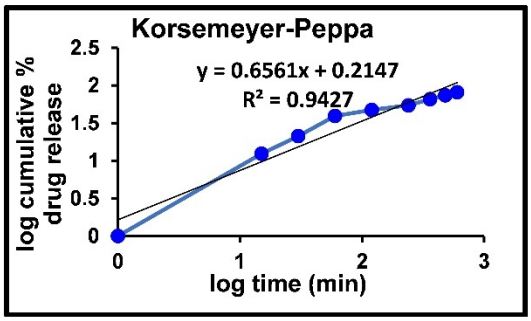

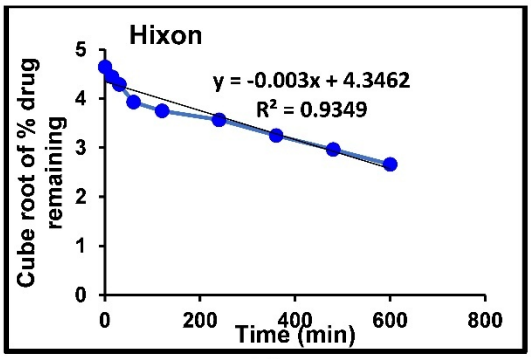

b)

Figure 3: a) *In vitro* drug release of polymeric microparticles, b) Drug release kinetic models of polymeric microparticles.

of particle size variations across different batches of polymeric microparticles, ranging from DL MSN-1 to DL MSN-4, reveal a corresponding decrease in release rate over time. The *in vitro* drug release profiles of polymeric microparticles containing tizanidine-loaded MSNs are presented in Table 6 and Figure 3a. Subsequently, the obtained data were fitted to various mathematical models including zero order, first order, Higuchi, Korsmeyer-Peppas, and Hixson-Crowell, as summarized in Table 7. Graphical analysis of the drug release kinetics for the prepared microparticles is depicted in Figure 3b. DL MSN-2 demonstrated the most substantial regression coefficient (R^2) of 0.9682 when matched with the Higuchi model, suggesting an initial rapid release succeeded by a sustained release pattern, which was consistent across all observed release kinetics.

CONCLUSION

MSNs have gained substantial prominence as a leading candidate for drug delivery due to their distinctive properties. These nanoparticles are primarily composed of a surfactant, a silica precursor, and a catalyst (acid or base). Tizanidine-loaded controlled-release MSNs were prepared to control the release pattern and improve the low oral bioavailability of tizanidine. To regulate the drug's release rate, drug-loaded MSNs were incorporated into polymeric microparticles. Design Expert software, employing Box Behnken design, facilitated the optimization of MSNs characteristics. The optimized MSN batch exhibited specific attributes: a mean particle size of 131.7 nm, a Polydispersity Index (PDI) of 0.202, a Zeta Potential (Z.P.) of 30.6, and an Entrapment Efficiency (EE %) of 51.18%. Afterwards, the optimized batch of MSNs underwent assessment via SEM, DSC, and XRD analyses. The SEM imaging demonstrated the MSNs spherical morphology, while the DSC thermogram of the optimized tizanidine batch revealed an absence of peaks, indicating complete entrapment of the drug within the MSNs. Subsequently, polymeric microparticles containing tizanidine-loaded MSNs were formulated using ethyl cellulose and PVA. The polymeric microparticles (DL MSN-2) demonstrated the most substantial regression coefficient (R^2) of 0.9682 when matched with the Higuchi model, suggesting an initial rapid release succeeded by a sustained release pattern. So, it can be concluded that a tizanidine-loaded controlled release MSN has been prepared, the oral bioavailability of tizanidine will be improved and the drug will be released in a controlled pattern hence dosing frequency will be reduced ultimately resulting in patient compliance.

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ABBREVIATIONS

MSN: Mesoporous Silica Nanoparticles; **CTAB:** Cetyltrimethylammonium Bromide; **TEOS:** Tetraethyl Orthosilicate.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

The primary objective of this research was to enhance the efficacy of tizanidine in treating spasticity by utilizing controlled-release Mesoporous Silica Nanoparticles (MSNs). MSNs were synthesized and optimized using Design Expert software, with parameters including TEOS, CTAB, and NaOH analyzed. The optimized MSNs had a mean size of 131.7 nm, PDI of 0.202, Z.P. of 30.6 mV, and EE% of 51.18%. Incorporating these MSNs into polymeric microparticles showed controlled drug release over 10 hr, with potential for enhanced oral bioavailability and reduced dosing frequency, promoting patient compliance.

REFERENCES

1. Boyd RN, Ada L. Physiotherapy management of spasticity. In: Barnes MP, Johnson GR, editors. Upper motor neurone syndrome and spasticity. Cambridge: Cambridge University Press; 2008. p. 79-98. doi: 10.1017/CBO9780511544866.005.
2. Mohsen AM, El-Hashemy HA, Salama A, Darwish AB. Formulation of tizanidine hydrochloride–loaded provesicular system for improved oral delivery and therapeutic activity employing a 23 full factorial design. Drug Deliv Transl Res. 2023;13(2):580-92. doi: 10.1007/s13346-022-01217-3, PMID 35927549.
3. Wagstaff AJ, Bryson HM. Tizanidine. A review of its pharmacology, clinical efficacy and tolerability in the management of spasticity associated with cerebral and spinal disorders. Drugs. 1997;53(3):435-52. doi: 10.2165/00003495-199753030-00007, PMID 9074844.
4. Granfors MT, Backman JT, Laitila J, Neuvonen PJ. Tizanidine is mainly metabolized by cytochrome P450 1A2 *in vitro*. Br J Clin Pharmacol. 2004;57(3):349-53. doi: 10.1046/j.1365-2125.2003.02028.x, PMID 14998432.
5. Fogelholm R, Murros K. Tizanidine in chronic tension-type headache: a placebo controlled double-blind cross-over study. Headache. 1992;32(10):509-13. doi:10.1111/j.1526-4610.1992.hed3210509.x, PMID 1468911.
6. Jagdale S, Brahmane S, Chabukswar A. Optimization of Microemulgel for tizanidine hydrochloride. Antiinflamm Antiallergy Agents Med Chem. 2020;19(2):158-79. doi: 10.2174/1871523018666190308123100, PMID 30854978.
7. Berry H, Hutchinson DR. Tizanidine and ibuprofen in acute low-back pain: results of a double-blind multicentre study in general practice. J Int Med Res. 1988;16(2):83-91. doi: 10.1177/030006058801600202, PMID 2967781.
8. Li Z, Zhang Y, Feng N. Mesoporous silica nanoparticles: synthesis, classification, drug loading, pharmacokinetics, biocompatibility, and application in drug delivery. Expert Opin Drug Deliv. 2019;16(3):219-37. doi: 10.1080/17425247.2019.1575806, PMID 30686075.
9. Farjadian F, Roointan A, Mohammadi-Samani S, Hosseini M. *Mesoporous silica* nanoparticles: synthesis, pharmaceutical applications, biodistribution, and biosafety assessment. Chem Eng J. 2019;359:684-705. doi: 10.1016/j.cej.2018.11.156.
10. Cecilia JA, Moreno Tost R, Retuerto Millán M. Mesoporous materials: from synthesis to applications. Int J Mol Sci. 2019;20(13):3213. doi: 10.3390/ijms20133213, PMID 31261983.
11. Giraldo LF, López BL, Pérez L, Urrego S, Sierra L, Mesa M, editors. *Mesoporous silica* applications. Macromol Symp. 2007;258(1):129-41. doi: 10.1002/masy.200751215.
12. McCarthy CA, Ahern RJ, Dontireddy R, Ryan KB, Crean AM. *Mesoporous silica* formulation strategies for drug dissolution enhancement: a review. Expert Opin Drug Deliv. 2016;13(1):93-108. doi: 10.1517/17425247.2016.1100165, PMID 26549623.
13. Narayan R, Nayak UY, Raichur AM, Garg S. *Mesoporous silica* nanoparticles: A comprehensive review on synthesis and recent advances. Pharmaceutics. 2018;10(3):118. doi: 10.3390/pharmaceutics10030118, PMID 30082647.
14. Appaturi JN, Adam F. ImX-MCM-41 (X= Cl, Br and I): active catalysts for the solvent free synthesis of phenyl glycidyl carbonate. Surf Interfaces. 2019;14:305-13. doi: 10.1016/j.surfin.2019.01.006.

15. Chircov C, Spoială A, Păun C, Crăciun L, Ficai D, Ficai A, *et al.* Mesoporous silica platforms with potential applications in release and adsorption of active agents. Molecules. 2020;25(17):3814. doi: 10.3390/molecules25173814, PMID 32825791.
16. Jaramillo LY, Henao WA, Pabón-Gelves E. Synthesis of SBA-15/MCM-41 bimodal *mesoporous silica*. MRS Proc. 2016;1817. doi: 10.1557/opl.2016.47.
17. Martínez-Edo G, Balmori A, Pontón I, Martí del Rio A, Sánchez-García D. Functionalized ordered *mesoporous silicas* (MCM-41): synthesis and applications in catalysis. Catalysts. 2018;8(12):617. doi: 10.3390/catal8120617.
18. Mokri NA, Oh PC, Chew TL, Mukhtar H. Synthesis of siliceous mesoporous Mcm-48 via single and binary surfactant system. Process engineering and advanced materials. Amsterdam, The Netherlands: Elsevier Limited. 2016.
19. Pirez C, Morin JC, Manayil JC, Lee AF, Wilson K. Sol-gel synthesis of SBA-15: impact of HCl on surface chemistry. Micropor Mesopor Mater. 2018;271:196-202. doi: 10.1016/j.micromeso.2018.05.043.
20. Renuka NK, Anas K, Aniz CU. Synthesis, characterisation and activity of SBA-16 supported oxidation catalysts for CO conversion. Chin J Catal. 2015;36(8):1237-41. doi: 10.1016/S1872-2067(15)60894-4.
21. Uhlig H, Muenster T, Kloess G, Ebbinghaus SG, Einicke WD, Gläser R, *et al.* Synthesis of MCM-48 granules with bimodal pore systems via pseudomorphic transformation of porous glass. Micropor Mesopor Mater. 2018;257:185-92. doi: 10.1016/j.micromeso.2017.08.033.
22. Seljak KB, Kocbek P, Gašperlin M. *Mesoporous silica* nanoparticles as delivery carriers: an overview of drug loading techniques. J Drug Deliv Sci Technol. 2020;59:101906. doi: 10.1016/j.jddst.2020.101906.
23. Charnay C, Bégu S, Tourné-Péteilh C, Nicole L, Lerner DA, Devoisselle JM. Inclusion of ibuprofen in mesoporous templated silica: drug loading and release property. Eur J Pharm Biopharm. 2004;57(3):533-40. doi: 10.1016/j.ejpb.2003.12.007, PMID 15093603.
24. Popova T, Voycheva C, Tzankov B. Study on the influence of technological factors on drug loading of poorly water-soluble drug on MCM-41 mesoporous carrier. Pharmacia. 2020;67(4):351-6. doi: 10.3897/pharmacia.67.e47528.
25. Kim MK, Ki DH, Na YG, Lee HS, Baek JS, Lee JY, *et al.* Optimization of mesoporous silica nanoparticles through statistical design of experiment and the application for the anticancer drug. Pharmaceutics. 2021;13(2):184. doi: 10.3390/pharmaceutics13020184, PMID 33572523.
26. Freiberg S, Zhu XX. Polymer microspheres for controlled drug release. Int J Pharm. 2004;282(1-2):1-18. doi: 10.1016/j.ijpharm.2004.04.013, PMID 15336378.
27. Iqbal M, Zafar N, Fessi H, Elaissari A. Double emulsion solvent evaporation techniques used for drug encapsulation. Int J Pharm. 2015;496(2):173-90. doi: 10.1016/j.ijpharm.2015.10.057, PMID 26522982.

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