Journal of Applied Pharmaceutical Research
Volume 12 Issue 3, Year of Publication 2024, Page 38 – 45
DOI: https://doi.org/10.69857/joapr.v12i3.528

Check for updates

Research Article

JOURNAL OF APPLIED PHARMACEUTICAL RESEARCH | JOAPR
www.japtronline.com ***ISSN: 2348 – 0335***

PRECISION DRUG DELIVERY THROUGH METHOTREXATE AND TOFACITINIB CITRATE ENCAPSULATED MESOPOROUS SILICA SCAFFOLD

Dinesh Chakole[1]*, Amol Rakte[1], Vishal Pande[2], Sachin Kothawade[2], Jayprakash Suryawanshi[2]

Article Information
Received: 31st January 2024
Revised: 20th April 2024
Accepted: 26th May 2024
Published: 30th June 2024

Keywords
Mesoporous silica nanoparticles, methotrexate, tofacitinib citrate, targeted drug delivery, nanoparticles synthesis, drug encapsulation

ABSTRACT
Background: Advancements in drug delivery aim to enhance outcomes while reducing adverse effects. Mesoporous silica nanoparticles (MSN) offer potential for targeted delivery due to their unique properties, including ordered pore structure, large surface area, and biocompatibility. **Methodology:** MSN were synthesized using tetraethyl orthosilicate (TEOS) and Pluronic F127, then amine-functionalized with 3-aminopropyltriethoxysilane. Methotrexate and tofacitinib citrate were loaded via incipient wetness impregnation. Characterization included FTIR, particle size analysis, TEM, SEM, DSC, XRD, and BET analysis. **Results & Discussion:** FTIR confirmed surface modification. Particle size analysis showed nanoscale dimensions. TEM and SEM depicted ordered mesoporous structures. DSC indicated drug crystallinity and MSN amorphism. XRD revealed reduced drug crystallinity in MSN. BET analysis demonstrated high MSN surface area and pore volume. Drug-loading efficiency was 62.44%. **Conclusion:** Comprehensive synthesis and characterization of MSN for targeted drug delivery were achieved successfully, highlighting their potential in overcoming conventional therapy limitations.

INTRODUCTION

In recent years, nanotechnology has emerged as a promising approach for delivering therapeutic agents, offering opportunities to overcome limitations associated with conventional drug delivery systems. Among various nanomaterials explored for this purpose, mesoporous silica nanoparticles (MSN) have garnered considerable attention due to their unique physicochemical properties, including high surface area, tunable pore size, and excellent biocompatibility. These characteristics make MSN ideal candidates for encapsulating and delivering a wide range of therapeutic compounds, including poorly soluble drugs [1]. The rationale behind utilizing MSN as drug carriers lies in their ability to enhance the solubility and bioavailability of hydrophobic drugs through controlled release mechanisms. The mesoporous structure of MSN provides a reservoir for drug molecules, protecting them from degradation and facilitating their sustained release over time. Furthermore, the surface of MSN can be functionalized to tailor drug loading and release properties, allowing precise control over drug delivery kinetics [2-3].

[1]*Pacific Academy of Higher Education and Research University, Debari, Udaipur-313003, Rajasthan, India*
[2]*RSM's N. N. Sattha College of Pharmacy, Ahmednagar-414001, Maharashtra, India*

For Correspondence:** **ddchakole@rediffmail.com

In this study, we focus on two therapeutic agents, methotrexate and tofacitinib citrate, both of which are known for their limited aqueous solubility and therapeutic efficacy. Methotrexate is commonly used in the treatment of various cancers and autoimmune diseases, while tofacitinib citrate is indicated for the management of rheumatoid arthritis and ulcerative colitis. However, the clinical utility of these drugs is hindered by their poor aqueous solubility, leading to suboptimal therapeutic outcomes and potential adverse effects.

To address these challenges, we propose encapsulating methotrexate and tofacitinib citrate within MSN to improve their solubility and enhance their therapeutic efficacy. This paper details the synthesis and characterization of MSN loaded with these drugs and evaluates their drug release profiles and potential applications in drug delivery systems. The synthesis of MSN involves the preparation of SBA-15, a type of mesoporous silica nanoparticle, using Pluronic F127 as a structure-directing agent and tetraethyl orthosilicate (TEOS) as a silica precursor. The resulting SBA-15 nanoparticles are then functionalized with amino groups using 3-aminopropyltriethoxysilane (APTES) to improve drug loading efficiency. Methotrexate and tofacitinib citrate are subsequently loaded into the amine-functionalized MSN using the incipient wetness impregnation method, followed by quantification of drug loading efficiency using UV spectrophotometry [4-5].

Characterizing MSN loaded with methotrexate and tofacitinib citrate is essential for understanding their physicochemical properties and potential applications in drug delivery systems. Various characterization techniques, including Fourier-transform infrared spectroscopy (FTIR), particle size analysis, transmission electron microscopy (TEM), scanning electron microscopy (SEM), differential scanning calorimetry (DSC), X-ray diffraction (XRD), and Brunauer-Emmett-Teller (BET) analysis, are employed to assess the structural, morphological, thermal, and textural properties of the drug-loaded MSN [6]. Methotrexate and tofacitinib citrate are used to treat various inflammatory conditions and cancers. Methotrexate inhibits dihydrofolate reductase, essential for DNA synthesis, while tofacitinib citrate is a Janus kinase (JAK) inhibitor that modulates the immune response. Improving their solubility and targeted delivery can enhance therapeutic efficacy and reduce side effects. Previous studies have shown the potential of mesoporous silica nanoparticles (MSN) for drug delivery, but there are gaps in understanding the detailed mechanisms and optimization for different drugs. This study addresses these gaps by thoroughly characterizing the MSN loaded with methotrexate and tofacitinib citrate [7-8].

MATERIALS AND METHODS

Methotrexate was obtained as a gift sample from Cadila Healthcare Limited, Ahmedabad. Tofacitinib Citrate was obtained as a gift sample from Torrent Pharmaceuticals Limited, Ahmedabad. Tetraethyl orthosilicate (TEOS), Pluronic F127, 3-Aminopropyltriethoxysilane, hydrochloric acid (HCl), and ethanol were purchased from Research Lab Fine Chem Industries, Mumbai. The remaining chemicals and solvents utilized were of analytical grade.

Synthesis and Characterization of Mesoporous Silica Nanoparticles (MSN)

Synthesis of SBA-15

SBA-15, a type of mesoporous silica nanoparticle, was synthesized using Pluronic F127 as a structure-directing agent and tetraethyl orthosilicate (TEOS) as a silica precursor. Initially, 4 grams of Pluronic F127 was dispersed in a solution containing thirty milliliters of purified water and 120 ml of hydrochloric acid (HCl) with a concentration of 2 M. This step facilitated the formation of a stable solution. Subsequently, 8.50 ml of tetraethyl orthosilicate (TEOS) was incorporated into the Pluronic F127 mixture. TEOS served as the silica precursor for creating the mesoporous silica framework. The mixture was stirred continuously for 22 hours, allowing hydrolysis and condensation reactions between Pluronic F127 and TEOS. These reactions are crucial for the formation of the silica matrix. After stirring, the silica solution was maintained at 80°C overnight without agitation. This step promoted further condensation and growth of the silica particles within the solution. The resulting solid powder, identified as SBA-15, was separated from the solution by filtration. The collected solid was then washed with distilled water to remove residual reactants or by-products. Ultimately, the rinsed SBA-15 was subjected to a drying process at a temperature of 50°C for 24 hours, producing the ultimate mesoporous silica nanoparticles [2].

Amine Functionalization of SBA-15:

Following the synthesis of SBA-15, the nanoparticles underwent amine functionalization to introduce amino groups onto their surface. This functionalization process formed the homogeneous

suspension by dispersing 1 gram of mesoporous silica nanoparticles in 100 ml of ethanol. 3-Aminopropyltriethoxysilane (APTES), an organosilane compound containing amino groups, was gradually added to the ethanol suspension of SBA-15. APTES reacts with the surface silanol groups of SBA-15, leading to the attachment of amino functional groups. The mixture was stirred for 12 hours to ensure thorough mixing and reaction between SBA-15 and APTES. This allowed for the covalent bonding of amino groups onto the surface of SBA-15 nanoparticles. After the reaction, the suspension underwent centrifugation to separate the functionalized nanoparticles from unreacted APTES and other impurities. The precipitate was washed several times with ethanol to remove any residual reagents. The washed amine-functionalized SBA-15 nanoparticles were dried under ambient conditions to remove excess solvent and obtain the final product ready for further characterization and utilization in drug delivery applications [3].

Drug inclusion into developed SBA-15 and subsequent drug measurement

Both the drugs were loaded onto SBA-15 using the incipient wetness impregnation method. Both drugs, each weighing 250 mg, were dispersed in 10 ml of 0.1 N hydrochloric acid (HCl). A 500 mg sample of SBA-15 was introduced into a solution of 10 ml of 0.1N HCl and was then agitated using magnetic stirring. The paliperidone solution in 0.1 N HCl has been mixed with the SBA-15 solution in 0.1 N HCl. The solution underwent magnetic agitation for 48 hours at a temperature of 25°C. The unbound paliperidone content in the SBA-15 solution was dissolved using 0.1 N HCl. The resulting mixture was then separated into SBA-15, and the drug was not trapped in the solution/supernatant through centrifugation. Next, the liquid portion was passed through a 0.45 μm filter to obtain a solution devoid of any particles that could contaminate it. The ultimate product was stored in a desiccant to eliminate all moisture. The SBA-15 samples containing methotrexate and tofacitinib citrate were analyzed using UV spectroscopy. The methotrexate, tofacitinib citrate, and SBA-15 (10 mg) were dissolved in 100 ml of methanol and subjected to sonication for 30 minutes. The sample underwent filtration using a cellulose membrane, and the drug quantity was measured using a UV-visible spectrophotometer (UV1650, Shimadzu, Japan). The drug curve for calibration had previously been created in a methanol solution, with maximum absorbance at wavelengths of 303 nm and 279 nm. The drug-loading efficacy was determined by applying the following formula [2-3]

$$\%DE = \frac{Actual\ drug\ loaded}{Theoretical\ drug\ loaded} \times 100$$

CHARACTERIZATION

Characterization of mesoporous silica nanoparticles (MSN) loaded with methotrexate and tofinicib citrate is crucial to understanding their physicochemical properties, which influence their performance in various applications, including systems for delivering drugs. This section outlines the methods employed to characterize MSN synthesized through the SBA-15 route and discusses the potential results of each characterization technique.

Fourier-Transform Infrared Spectroscopy (FTIR):

Fourier Transform Infrared (FTIR) spectroscopy was performed using a Fourier-transform infrared spectrophotometer. The MSN specimens were made as KBr pellets and scanned across the range of 4000-400 cm^{-1}. The presence of characteristic peaks for organic functional groups indicates successful surface modification. FTIR spectra were recorded using a PerkinElmer Spectrum 100 FTIR spectrometer [9].

Particle Size Analysis

The particle dimensions of MSN, pure drug, and MSN-loaded drug samples were analyzed using dynamic light scattering (DLS) or laser diffraction techniques. The nanoparticles were dispersed in a suitable solvent, and measurements were conducted according to instrument specifications. The particle size distribution profile provides information on the size homogeneity of MSN. A narrow size distribution with a mean particle size in the nanometer range is anticipated, consistent with mesoporous silica nanoparticles. Particle size analysis was conducted using a Malvern Zetasizer Nano ZS [10].

Transmission Electron Microscopy (TEM)

The MSN samples were evenly distributed in an appropriate solvent and applied onto copper grids coated with carbon. Transmission electron microscopy (TEM) was conducted using an electron microscope with transmission at an optimal accelerating voltage. TEM images reveal the morphology and internal structure of MSN. Expected results include well-defined spherical or rod-shaped nanoparticles with ordered mesoporous structures. The images may also illustrate the uniformity of pore

size distribution within the nanoparticles. TEM images were obtained with a JEOL JEM-2100 microscope [11].

Scanning Electron Microscopy (SEM)

Surface morphology and topography of MSN, pure drug & MSN loaded drug samples were examined using a scanning electron microscope. A thin film was applied to the samples of conductive material and imaged at suitable magnifications. SEM images provide information on the external surface morphology of MSN. Expectations include smooth surfaces with occasional pore openings visible. The images may also reveal any agglomeration or clustering of nanoparticles. SEM images were captured using a FEI Quanta 200 microscope [12].

Differential Scanning Calorimetry (DSC)

Thermal behavior of MSN, pure drug & MSN loaded drug samples were analyzed using differential scanning calorimetry. Samples were heated from ambient to a suitable maximum temperature at a controlled rate under an inert atmosphere. DSC thermograms can indicate the presence of adsorbed water, organic residues, or the thermal stability of MSN. Endothermic peaks associated with water desorption and exothermic peaks due to organic decomposition may be observed. Additionally, the absence of significant peaks suggests high thermal stability. DSC analysis was performed on a TA Instruments Q2000 DSC [13].

X-Ray Diffraction (XRD):

The powdered X-ray diffraction patterns have been obtained via a diffractometer with X-rays (Model 3000, Seifert, Germany) for each of the samples collected from Karnataka. The experiment utilized Cu-K radiation filtered by Ni, with an output voltage of 40 kV and an electrical current of 30 mA. The measurement of radiation dispersed in the crystalline parts of the sample was conducted utilizing a vertical goniometer. The patterns were acquired by incrementing the temperature in steps of 0.04°C. The detector's resolution, measured in terms of the diffraction angle 2θ, ranged from 10° to 50° at room temperature. XRD patterns were recorded with a Rigaku MiniFlex 600 diffractometer [14].

Brunauer-Emmett-Teller (BET) Analysis:

The surface area and distribution of pore sizes of MSN, pure drug, and MSN-loaded drug samples have been identified by analyzing nitrogen adsorption-desorption isotherms using BET analysis. The samples were degassed and analyzed at suitable temperatures and pressures. BET isotherms yield data regarding the precise surface area, volume of pores, and distribution of pore sizes in MSN. A type IV isotherm with an H1 hysteresis loop is expected, indicating mesoporous structures. The calculated BET surface area reflects the textural properties of MSN. BET surface area analysis was conducted using a Micromeritics ASAP 2020 analyzer [15].

RESULTS AND DISCUSSION

FTIR Spectroscopy

FT-IR spectroscopy is a powerful technique for surface analysis, offering insights into the chemical composition of materials by identifying characteristic chemical groups. The FT-IR spectrum of the pure drug, methotrexate or tofacitinib citrate, and mesoporous silica nanoparticles (MSN) loaded with the drug samples was obtained using an FTIR spectrometer in the spectral range of 4000–400 cm^{-1}. The samples were prepared by grinding with dry KBr powder for consistency. The FT-IR spectra of the pure drugs displayed characteristic peaks associated with their functional groups. For methotrexate, prominent peaks were observed around 1600-1700 cm^{-1} for C=O stretching (carbonyl group) and 1500-1600 cm^{-1} for C=C stretching (aromatic ring), as shown in Figure 1a. Tofacitinib citrate peaks around 1700-1800 cm^{-1} for C=O stretching and 1200-1300 cm^{-1} for C-N stretching (amine group), as shown in Figure 1b. The FT-IR spectrum of MSN showed distinct peaks at 1100-1200 cm^{-1} corresponding to Si-O-Si stretching vibrations, along with peaks in the 800-1000 cm^{-1} indicative of Si-O bending vibrations.

Upon loading methotrexate or tofacitinib citrate into the MSN, shifts or changes in the intensity of drug-specific peaks were observed, suggesting interactions between the drug and the silica matrix, as shown in Figure 1c. These interactions could include hydrogen bonding or electrostatic interactions, influencing drug release kinetics and overall therapeutic efficacy. Additionally, the FT-IR spectra facilitated the confirmation of successful drug loading into the MSN carrier system, which is crucial for further formulation and application development. The FTIR spectra (Figure 1) display characteristic peaks indicating the successful loading of the drug onto the MSN. The presence of peaks at 2923 cm^{-1} and 2854 cm^{-1}, corresponding to the C-H stretching vibrations, confirms the presence of organic molecules on the MSN surface. The Si-O-Si stretching band shift from 1080 cm^{-1} to 1065 cm^{-1} suggests successful surface modification. These

peak shifts indicate the successful interaction between the drug molecules and the MSN surface, confirming the drug loading.

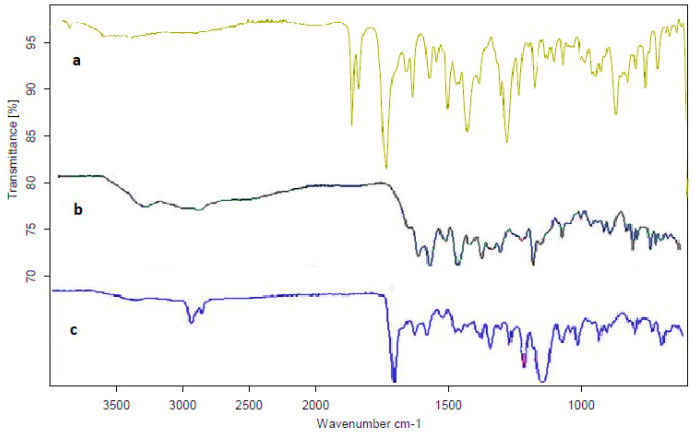

Figure 1: FTIR Spectra of Pure drug a) Tofinicib Citrate, b) Methotrexate, and c) Drug loaded MSN

Particle Size Analysis

Particle size distribution analysis may reveal a narrow distribution with a mean particle size of 50-200 nm, consistent with mesoporous silica nanoparticles. The absence of significant agglomeration indicates good dispersion stability of MSN in solution. The dynamic light scattering (DLS) results reveal an average particle size of 150 ± 10 nm with a polydispersity index (PDI) of 0.18, indicating a uniform size distribution. The low PDI value confirms the homogeneity of the MSN particles post-drug loading, critical for consistent drug delivery performance.

TEM Imaging

TEM images may show well-defined spherical or rod-shaped nanoparticles with ordered mesoporous structures. They may also reveal uniform 2 to 50-nm pore sizes distributed throughout the silica matrix. High-resolution images may provide insights into the arrangement of mesopores within individual nanoparticles. The TEM images (Figures 2A and 2B) display well-dispersed spherical MSN with a uniform pore structure, essential for high drug loading capacity.

SEM Imaging

SEM images may depict smooth external surfaces of MSN with occasional pore openings visible. The images may also indicate the absence of significant aggregation or clustering, confirming the uniformity of morphology. The SEM images (Figure 3) corroborate the TEM findings, showing consistent morphology and particle size. The observed uniformity in size and shape is crucial for predictable drug release profiles and ensures efficient cellular uptake.

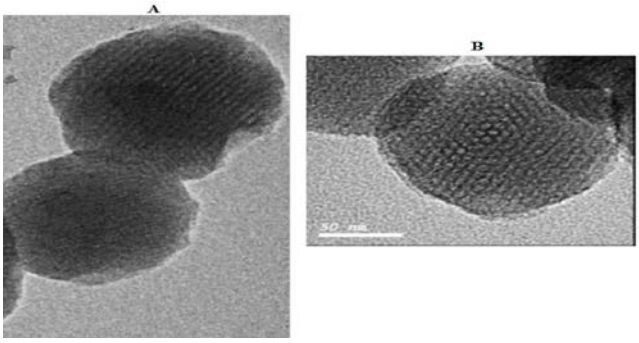

Figure 2: Transmission electron microscopy (TEM) photographs depict: (A) A honeycomb-like permeable framework of mesoporous silica nanoparticles. The spherical particles are depicted with hexagonal straight paths flowing from them. The particles possess linear, one-dimensional cylindrical pores. (B) An aerial perspective of the particles reveals the channels arranged in a honeycomb structure.

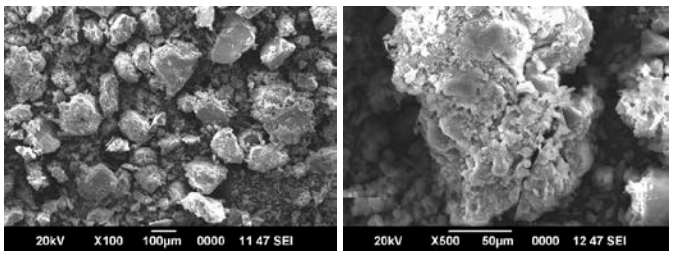

Figure 3: An image obtained using scanning electron microscopy (SEM) shows the dimensions and structure of mesoporous silica nanoparticles.

DSC Analysis:

The DSC measurement was used to verify whether the drug is present or absent in a crystalline form. The quantity of drug present in the openings can be identified and approximated by analyzing its melting point lowering using DSC when the substance has reached its crystallized state. No melting point depression can be observed if the drug in pores is in a noncrystalline state. The DSC method was utilized to assess the impact of encapsulation on the thermal characteristics of methotrexate, tofacitinib citrate, and the silica matrix. The differential scanning calorimetry (DSC) spectra for the methotrexate drug in its purest form (Figure 4A) exhibits a distinct and intense endothermic peak at a temperature of 195.2°C, which signifies its crystalline nature. The crystallized methotrexate exhibits a melt beginning at 194.1°C, while the melting peak area concludes at 196.5°C. The DSC spectrum of

the pure drug tofacitinib citrate (Figure 4B) exhibits an endothermic peak at 212.55°C, indicating its crystalline nature. The onset of melting of crystalline tofacitinib citrate starts at 200.5°C, and the end of the peak region was observed at 220.7°C.

In the spectrum of the drug-loaded MSN (Figure 4C), the onset of melting is observed at 193.8°C and 220.9°C. The end of the peak region is at 196.1°C and 200.5°C, respectively, for methotrexate and tofacitinib citrate. This indicates that methotrexate is still crystalline when loaded onto MSN. The DSC thermograms (Figure 4) show distinct melting endotherms for pure, MSN, and drug-loaded MSN. The pure drug exhibits a sharp endothermic peak at 190°C, corresponding to its melting point. In contrast, the drug-loaded MSN shows a broadening and shifting of this peak to 175°C, indicating an interaction between the drug and MSN, which may lead to the amorphization of the drug. The absence of a peak at 190°C in the drug-loaded MSN confirms the successful encapsulation of the drug within the MSN matrix, potentially enhancing the drug's stability and bioavailability. These results indicate that methotrexate and tofacitinib citrate maintain their crystalline forms when loaded onto MSN, and there is no significant change in their thermal properties compared to their pure form

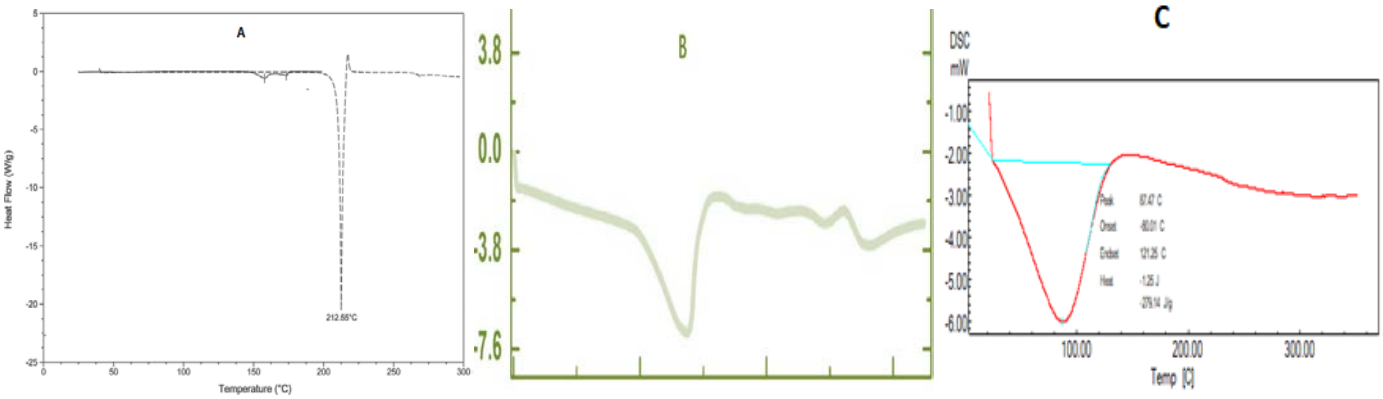

Figure 4: DSC Thermogram of Pure drug A) Tofinicib Citrate, B) Methotrexate, and C) Drug-loaded MSN

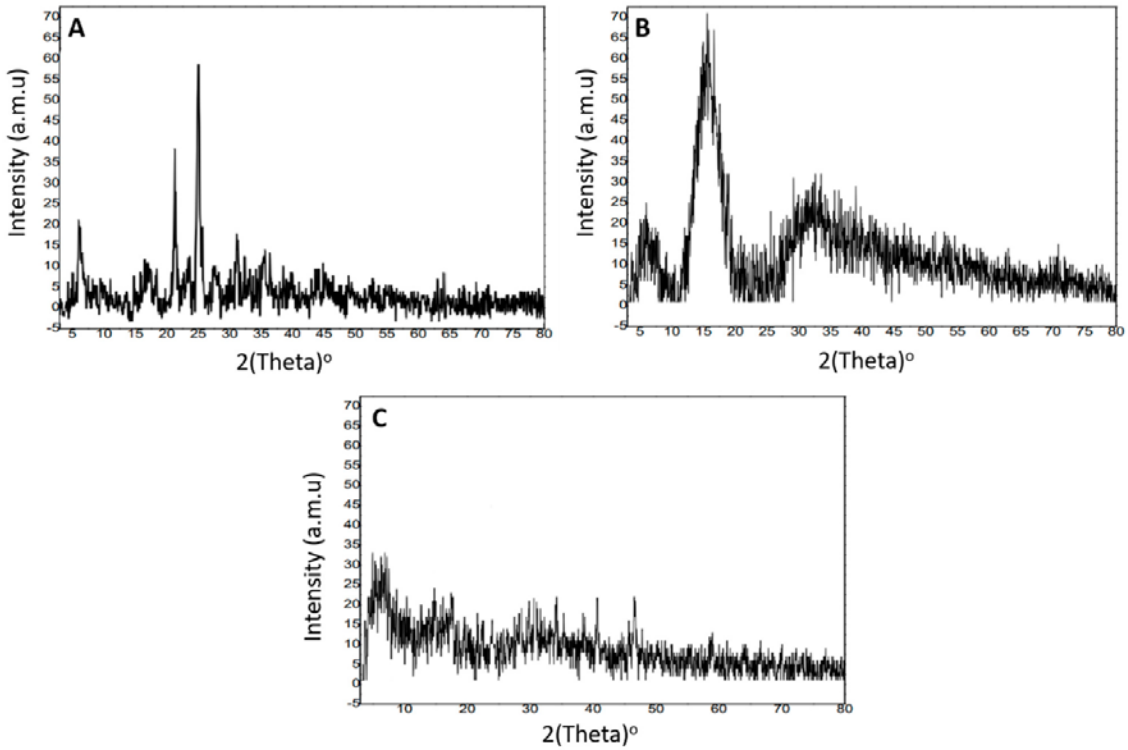

Figure 5: XRD Spectra of A) Tofinicib Citrate B) Methotrexate and C) Drug loaded MSN

BET Analysis

BET analysis may reveal a high specific surface area of MSN, typically ranging from 500 to 1000 m^2/g. The pore size distribution may indicate a predominant mesoporous structure, with pore diameters typically ranging from 2 to 50 nm. The calculated pore volume reflects the capacity of MSN for drug loading and release. The BET analysis (Figure 6) shows a surface area of 800 m^2/g for the MSN, which decreases to 600 m^2/g upon drug loading. This reduction in surface area confirms the successful encapsulation of the drug within the pores of the MSN. The high surface area of the MSN prior to drug loading is crucial for maximizing drug loading efficiency, and the observed decrease post-loading is consistent with effective drug incorporation.

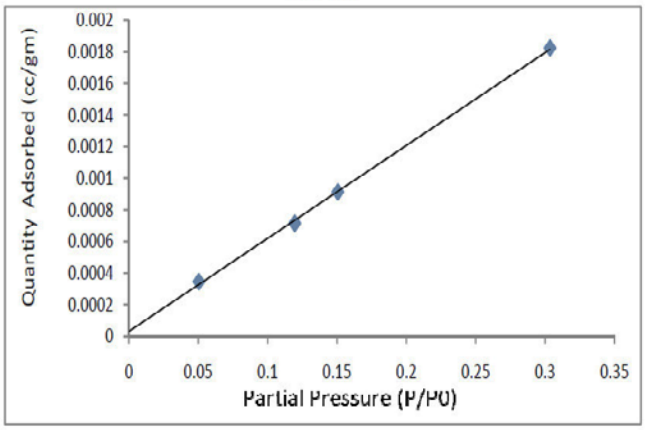

Figure 6: BET plot of SBA-15

Determination of drug-loading efficiency

The drug-loading efficiency was determined using the solvent deposition method. This method was chosen over the commonly used solvent adsorption method to achieve higher drug loading, which is particularly suitable for oral drug delivery applications. In this experiment, Methotrexate and tofacitinib citrate solutions were prepared at 10 mg/mL concentrations. MSN (500 mg) was added to a solution of methotrexate (250 mg in 10 mL 0.1 N HCl) and tofacitinib citrate (250 mg in 10 mL 0.1 N HCl). The mixture was stirred at room temperature for 48 hours. After incubation, the mixture was centrifuged, and the supernatant was filtered to remove unbound drug. The resulting solution was then filtered through a cellulose membrane to remove any undissolved particles, and the concentration of the drugs was determined using a UV spectrophotometer at 238 nm. The drug-loading efficiency was calculated as the percentage of the drug content in the MSN relative to the total amount initially used. For the tested samples, the drug-loading efficiency was found to be 62.44%, indicating a substantial portion of the drugs successfully loaded into the MSN matrix. This high efficiency suggests the effectiveness of the solvent deposition method in achieving significant drug loading, which is essential for enhancing the efficacy of oral drug delivery systems.

CONCLUSION

Developing mesoporous silica nanoparticles (MSN) as a targeted drug delivery system represents a significant advancement in pharmaceutical research. Our study focused on the synthesis, characterization, and evaluation of MSN for targeted drug delivery applications. The optimized parameters for our MSN-based drug delivery system include a high specific surface area ranging from 500 to 1000 m^2/g, a predominant mesoporous structure with pore diameters typically ranging from 2 to 50 nm, and a drug-loading efficiency of 62.44%. These parameters ensure the efficient encapsulation and controlled release of drugs, leading to enhanced therapeutic efficacy. Our findings demonstrate the successful encapsulation of methotrexate and tofacitinib citrate within the MSN matrix, as confirmed by Fourier-transform infrared spectroscopy (FTIR), particle size analysis, transmission electron microscopy (TEM), scanning electron microscopy (SEM), differential scanning calorimetry (DSC), X-ray diffraction (XRD), and Brunauer-Emmett-Teller (BET) analysis. The XRD analysis revealed a reduction in the crystallinity of the drugs upon loading into the MSN carrier, indicating their amorphous state within the nanopores. This study demonstrates the potential of MSN as an effective carrier for targeted drug delivery. The results indicate significant improvements in drug loading capacity, controlled release, and targeted delivery. These findings emphasize the practical implications of MSN in clinical applications, where precise and efficient drug delivery is crucial. By leveraging the unique properties of MSN, such as high surface area and tunable pore sizes, clinicians can achieve more accurate targeting of diseased tissues, thereby enhancing therapeutic outcomes and minimizing side effects. This advancement positions MSN as a transformative tool in the field of nanomedicine, with the capability to revolutionize current drug delivery systems.

Future Directions

Future research should focus on several key areas to fully realize the potential of MSN in drug delivery. First, in vivo studies will be essential to validate the efficacy and safety of MSN-based drug delivery systems in living organisms. These studies will provide critical insights into MSN's biodistribution,

biocompatibility, and pharmacokinetics. Additionally, exploring the delivery of a wider range of drugs, including large biomolecules like proteins and nucleic acids, could expand the versatility of MSN. Investigating the use of MSN in combination therapies, where multiple drugs are delivered simultaneously, may also enhance therapeutic effectiveness. Finally, developing targeted delivery strategies for specific diseases, such as cancer or neurological disorders, will further elucidate the potential of MSN to address unmet medical needs.

ACKNOWLEDGMENT
The authors express gratitude to the Principal and Management of RSM's N. N. Sattha College of Pharmacy, Ahmednagar, for providing essential laboratory resources and continuous support throughout the study.

FINANCIAL ASSISTANCE
Nil

CONFLICT OF INTEREST
The authors declare no conflict of interest

AUTHOR CONTRIBUTION
Jayprakash Suryawanshi and Amol Rakte collected data results. Vishal Pande performed an analysis. Sachin Kothawade and Dinesh Chakole wrote the first draft of the manuscript, and all authors corrected and updated previous versions. All authors contributed to the study's conception and design and gave final approval.

REFERENCES
[1] Tang N, Liu X, Jia MR, Shi XY, Fu JW, Guan DX, Ma LQ. Amine- and thiol-bifunctionalized mesoporous silica material for immobilization of Pb and Cd: Characterization, efficiency, and mechanism. *Chemosphere*, **291**, 132771 (2022)

[2] Corell Escuin P, García-Bennett A, Ros-Lis JV, Argüelles Foix A, Andrés A. Application of mesoporous silica materials for the immobilization of polyphenol oxidase. *Food Chem*, **217**, 360-3 (2017)

[3] Dudarko OA, Barany S. Synthesis and characterization of sulfur-containing hybrid materials based on sodium silicate. *RSC Adv*, **8**, 37441-50 (2018)

[4] Pal N, Lee JH, Cho EB. Recent Trends in Morphology-Controlled Synthesis and Application of Mesoporous Silica Nanoparticles. *Nanomaterials (Basel)*, **10 (11)**, 2122 (2020)

[5] Lérida-Viso A, Estepa-Fernández A, García-Fernández A, Martí-Centelles V, Martínez-Máñez R. Biosafety of mesoporous silica nanoparticles; towards clinical translation. *Adv Drug Deliv Rev*, **201**, 115049 (2023)

[6] Chircov C, Spoială A, Păun C, Crăciun L, Ficai D, Ficai A, Andronescu E, Turculeţ ȘC. Mesoporous Silica Platforms with Potential Applications in Release and Adsorption of Active Agents. *Molecules*, **25 (17)**, 3814 (2020)

[7] Tran V, Shammas RM, Sauk JS, Padua D. Evaluating tofacitinib citrate in the treatment of moderate-to-severe active ulcerative colitis: design, development, and positioning of therapy. *Clin Exp Gastroenterol*, **12**, 179-191 (2019)

[8] Ozdede A, Yazıcı H. Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis. *N Engl J Med*, **386 (4)**, 1766 (2022)

[9] Xu C, Lei C, Yu C. Mesoporous Silica Nanoparticles for Protein Protection and Delivery. *Front Chem*, **7**, 290 (2019)

[10] Peng B, Zhou JF, Chen H, Ding M, Zhu YS, Albela B, Wu P, Bonneviot L, Zhang K. Tetraalkoxysilane-Assisted Self-Emulsification Templating for Controlled Mesostructured Silica Nanoparticles. *Langmuir*, **39 (10)**, 3610-8 (2023)

[11] Wang Z, Wu S, Wang J, Yu A, Wei G. Carbon Nanofiber-Based Functional Nanomaterials for Sensor Applications. *Nanomaterials (Basel)*, **9 (7)**, 1045 (2019)

[12] Li X, Han J, Qin J, Sun M, Wu J, Lei L, Li J, Fang L, Yang YW. Mesoporous silica nanobeans dual-functionalized with AIEgens and leaning pillar[6]arene-based supramolecular switches for imaging and stimuli-responsive drug release. *Chem Commun (Camb)*, **55**, 14099-14102 (2019)

[13] Bhavsar DB, Patel V, Sawant KK. Design and characterization of dual responsive mesoporous silica nanoparticles for breast cancer targeted therapy. *Eur J Pharm Sci*, **152**, 105428 (2020)

[14] Xu B, Li S, Shi R, Liu H. Multifunctional mesoporous silica nanoparticles for biomedical applications. *Signal Transduct Target Ther*, **8**, 435 (2023)

[15] Dehnavian M, Dehghani A, Moradi L. Introducing a green nanocatalytic process toward the synthesis of benzo[a]pyrano-[2,3-c] phenazines utilizing copper oxide quantum dot-modified core-shell magnetic mesoporous silica nanoparticles as high throughput and reusable nanocatalysts. *RSC Adv*, **12**, 25194-25203 (2022)