Ind. J. Pharm. Edu. Res., 2027; 61:10.5530/ijper.20270252.
https://www.ijper.org

Original Article

COK-19 Mesoporous System for Controlled Bosutinib Release

Anisha, Surender Duhan*

Department of Physics, Deenbandhu Chhotu Ram University of Science and Technology, Murthal, Sonepat, Haryana, INDIA.

ABSTRACT

Objectives: This study aimed to develop and evaluate COK-19 mesoporous silica as a drug-releasing carrier for bosutinib to enhance its dissolution and *in vitro* drug-release characteristics. **Materials and Methods:** COK-19 mesoporous silica was synthesized using a hydrothermal method, and bosutinib was incorporated into the COK-19 matrix by post-impregnation. The drug-loaded mesoporous system was evaluated for drug entrapment efficiency and physicochemical characteristics using Brunauer-Emmett-Teller (BET) nitrogen adsorption-desorption analysis, Fourier-Transform Infrared Spectroscopy (FTIR), Wide-Angle X-ray Diffraction (WAXRD), Small-Angle X-ray Scattering (SAXS), Scanning Electron Microscopy (SEM), and Transmission Electron Microscopy (TEM). *In vitro* drug-release studies were subsequently performed to assess the release behavior of bosutinib. **Results:** Bosutinib-loaded COK-19 demonstrated a high drug entrapment efficiency of 93.56%. Characterization studies confirmed the preservation of the surface morphology and structural properties of both bosutinib and the mesoporous silica matrix. BET, SAXS, SEM, and TEM analyses demonstrated a high surface area, uniform pore structure, and ordered mesoporous architecture. The *in vitro* drug-release study showed an enhanced bosutinib release of 81.85%, indicating improved release characteristics from the COK-19 carrier. **Conclusion:** COK-19 mesoporous silica demonstrated excellent potential as a carrier for bosutinib, providing high drug loading and enhanced *in vitro* drug release. The findings suggest that COK-19-based mesoporous delivery systems may be a promising approach for improving the dissolution and therapeutic performance of poorly water-soluble bosutinib.

Keywords: Bosutinib, Drug loading, Drug releasing, Mesoporous silica, Tyrosine kinase inhibitor.

Correspondence:
Dr. Surender Duhan
Department of Physics, Deenbandhu Chhotu Ram University of Science and Technology, Murthal, Sonepat-131039, Haryana, INDIA.
Email: surender6561@gmail.com

Received: 08-08-2026;
Revised: 20-08-2026;
Accepted: 24-08-2026.

INTRODUCTION

Lung cancer is the third most common cancer and the primary cause of cancer related mortality globally. Among lung cancers, 80-85% of lung cancers are Non-Small Cell Lung Cancer (NSCLC).[1] The identification of certain genetic mutations that promote tumor growth has led to significant advancements in the treatment of NSCLC.[2,3] By targeting these mutations, Tyrosine Kinase Inhibitors (TKIs) have completely changed the way NSCLC is treated.[4,5] TKIs have recently gained widespread popularity in early and late-stage lung cancer treatment.[1] TKIs work by interfering with mutant kinases, which are important for controlling signaling pathways related to cellular development and division. These medications target the aberrant proteins or mutations that cause cancer to progress. Even while TKIs are quite effective, many patients eventually develop resistance to them.[6] Through TKIs and combination tactics, survival rates and quality of life for individuals with NSCLC can be improved.[7,8] TKIs have emerged as one of the most studied drugs for cancer therapy.[9,10] TKIs such as sorafenib, gefitinib, sunitinib and bosutinib are mainly used for the treatment of clear cell renal carcinoma, advanced non-small cell lung cancer metastatic renal cell cancer.[11-13]

Bosutinib, a second generation TKI that has been investigated as a possible treatment for lung cancer by blocking various signaling pathways to control growth, angiogenesis, survival and metastasis of cancer cells.[14] Bosutinib is an orally administered, competitive tyrosine kinase inhibitor that targets both Src and Abl tyrosine kinase.[15] Bosutinib has strong anticancer potential, however its clinical efficacy is limited by issues such as poor aqueous solubility, low oral bioavailability, rapid metabolism and off target toxicity.[16] To overcome these challenges, the development of advanced carrier systems capable of improving drug loading, stability and controlled release is highly desirable.[17] Its molecular weight is 530.45 g mol^{-1} and its chemical formula is $C_{26}H_{29}Cl_2N_5O_3$. Figure 1 depicts the bosutinib's molecular structure.

Mesoporous Silica Nanoparticles (MSNs) showed considerable ability as drug carriers because of their special physicochemical

DOI: 10.5530/ijper.20270252

Copyright Information :
Copyright Author (s) 2027 Distributed under Creative Commons CC-BY 4.0

Publishing Partner : Manuscript Technomedia. [www.mstechnomedia.com]

properties, which include large surface area, huge pore volume, variable pore size and excellent biocompatibility. High drug loading capacity and regulated release behavior are made possible by these characteristics.[18,19] Furthermore, the abundance of silanol groups facilitates easy surface functionalization, which enhances drug-carrier interactions and permits targeted distribution.[19,20] Because MSNs can improve medication stability, solubility, and therapeutic efficacy, they have been extensively investigated for medicinal uses, including cancer therapy.[20] Recent research has demonstrated that by enabling stimuli-responsive and site-specific drug release, mesoporous silica-based systems can overcome major obstacles related to traditional chemotherapy.[21] These devices ensure controlled and targeted drug release at the sick location by reacting to environmental (temperature, light) or internal (pH, enzymes, redox conditions) stimuli. Additionally, MSN's large surface area and porous shape make it easier to encapsulate hydrophobic medications, increasing their rate of dissolution and bioavailability while reducing systemic toxicity.[22]

COK-19 has garnered increasing attention among the many MSNs because of its linked channels, well-ordered pore architecture, and improved structural stability. These characteristics make it a good option for drug delivery applications, especially for anticancer medications like bosutinib that are poorly soluble.[23] Improved dissolving behavior and therapeutic efficacy result from the confinement of drug molecules within the mesoporous structure, which also encourages their stabilization in an amorphous state and prevents recrystallization. Additionally, strong hydrogen bonding and electrostatic interactions can be facilitated by the interaction of bosutinib molecules and the silanol groups on the surface of COK-19, which enhances drug loading efficiency and sustained release properties. In cancer treatment, controlled drug release from mesoporous carriers is very helpful since it lowers dosage frequency and side effects while maintaining therapeutic drug concentrations over long periods of time.[24]

This study synthesized and assessed bosutinib loaded COK-19 as an effective drug delivery system. X-ray Diffraction (XRD), Fourier Transform Infrared Spectroscopy (FTIR), Brunauer Emmett Teller (BET) analysis, field emission scanning electron microscopy (FESEM), and high-Resolution Transmission Electron Microscopy (HRTEM) were used to verify that bosutinib was successfully incorporated into COK-19. The findings of the characterization showed that COK-19's mesoporous structure and morphology were preserved following drug loading, with alterations in surface and textural characteristics verifying drug incorporation within the pores. *In vitro* drug release studies carried out under physiological conditions demonstrated sustained release of bosutinib during the study period, demonstrating COK-19's capacity to regulate drug release and serve as an effective mesoporous drug delivery vehicle.

MATERIALS AND METHODS

Materials required

The precursors used for the synthesis of mesoporous COK-19 materials include Pluronic F127, anhydrous citric acid, trisodium citrate dihydrate and sodium silicate solution purchased from Sigma-Aldrich (Apurva Biotech, Karnal, India). Bosutinib drug and dialysis membrane (molecular weight: 10 kDa) were bought from Sigma-Aldrich (Bangalore, India). In all of the experimental procedures, deionized water is used. All chemicals used were of reagent grade and no additional refinement needed.

Synthesis

In previously published data (2015), 2.6 g of Pluronic F127 is dissolve in 107.5 g of double distilled water from which F127 self assembles to form a micelle which then acts as a template.[25] Buffering agents, citric acid (3.69 g) and trisodium citrate dihydrate (2.55 g) are then added to the homogeneous solution. The solution is then stirred continuously for overnight to obtain a pH-controlled buffer solution. For the silica framework, a separate solution was made using 10.4 g of sodium silicate solution dissolved in 30 g of distilled water and put in dropwise to the buffer solution to form white precipitates, producing milky white suspension. The suspension is aged for 24 hr at 70°C temperature. Then suspension is centrifuged, washed and dried at 80°C. The dried material is then calcined in air at 350°C with a temperature rising rate of 0.5°C min^{-1} for 24 hr. Consequently, a white COK-19 silica material is acquired at the end. Figure 2 is representing the synthesis procedure of COK-19.

Calibration curve of bosutinib drug

A calibration curve was created using the serial dilution method to evaluate bosutinib in subsequent tests. A series of serial dilutions in concentration range 5 to 30 μg mL^{-1} were made by gradually diluting a stock solution with methanol. These solutions were selected to cover the expected concentration range for analytical purposes. UV-visible spectroscopy was used to measure the absorbance of each diluted sample with maximum absorbance wavelength (λ_{max}) of 267 nm using methanol as a blank reference. Each concentration was measured 3 times to make sure accuracy and reproducibility the average absorbance values were used for data analysis. A calibration curve was plotted between the absorbance (A) and concentration (C) is shown in Figure 3. As the resulting data demonstrated a strong linear relationship, the best fit line was identified using linear regression analysis. Regression analysis is depicted by the equation:

$$A = 0.0186C + 0.0171 (1)$$

Where A is absorbance in nm and C is bosutinib's concentration in μg mL^{-1}. This formula was then used to determine the unknown amount of bosutinib concentrations in experimental samples.

Drug loading

The medication bosutinib was loaded into COK-19 at room temperature using the post-impregnation technique, which is an effective method to load bioactive molecules into porous carriers is shown in Figure 4. For drug loading, 100 mg of bosutinib and 200 mg of COK-19 was added to 50 mL of methanol while being continuously stirred at a speed of 500 rpm for 24 hr. After the impregnation procedure, the resulting suspension was centrifuged for 20 min at 3500 rpm to extract the drug-loaded solid from the supernatant's unbound drug. The sample was dried and stored in a sealed container. The amount of bosutinib that was effectively added to the COK-19 matrix was determined by calculating the concentration of unincorporated medicine in the supernatant. UV-visible spectrophotometric measurements were made using bosutinib's maximum absorption wavelength λ_{max} is equal to 267 nm. A calibration curve generated from several standard bosutinib solutions was used to calculate the medication in the supernatant. The drug entrapment efficiency was computed using the following formula:

$$EE\% = \frac{(C_i - C_f)}{Ci} \times 100 \quad (2)$$

Where, C_i=drug's initial concentration in mg mL^{-1} and C_f=drug's final concentration in the supernatant in mg mL^{-1}. These calculations give quantitative understanding of effectiveness of drug loading procedure.

Drug releasing

Bosutinb's *in vitro* release profile was tested at room temperature. First, 50 mg of the drug loaded COK-19 was submerged in 5 mL of phosphate buffer solution for 15 min with gentle stirring. After that, the solution is then transferred into the dialysis cellulose membrane and kept in a 150 mL of phosphate buffered solution of pH 6.8. At certain intervals, about 2 mL of the solution was substituted with fresh buffer solution. Release media was then analyzed using UV-visible spectroscopy at 267 nm. The amount of bosutinib released was then calculated in accordance with standard curve of bosutinib. The release amount experiences targeted drug delivery with a useful structure for future endorsement.

Characterization

The physicochemical, morphological and structural characteristics of mesoporous COK-19 and bosutinib loaded COK-19 were analyzed using a variety of methods. The amount of bosutinib loaded into COK-19 was investigated using UV-visible spectroscopy (UV-1900, Shimadzu, Japan). The structural characteristics of composites were evaluated using wide angle X-ray Diffraction (XRD, Rigaku) at a 2θ range of 10° to 80°. Fourier Transform Infrared Spectroscopy (FTIR, Perkin Elmer FRONTIER) was used to determine the presence of specific chemical bonds in materials. Brunauer Emmett Teller (BET, Microtac BEL Corp) utilized for the measurements of porous properties and specific surface area of the material using nitrogen sorption isotherm at 77 Kelvin. Field emission scanning electron microscopy (SEM-EDX, JSM-7610FPLUS, JEOL) was used to analyse the elemental composition and structural morphology. High resolution transmission electron microscopy (HR-TEM, JEM-ARM200F NEORAM, 200 KeV) was used to analyse high resolution structural image.

RESULTS AND DISCUSSION

WAXRD

Figure 5 displays the WAXRD patterns of the bosutinib, mesoporous COK-19 and bosutinib loaded COK-19 nanomaterials. Figure 5(a), exhibits several sharp and intense diffraction peaks which are indicative of a substance that are highly crystalline.[26] These peaks validate the crystalline nature of the pure medication bosutinib by matching its ordered crystal lattice. The amorphous nature of the mesoporous silica material COK-19 is demonstrated by a huge hump at 22^0 with no sharp peak in Figure 5(c), and long-range order is absent. The diffraction pattern of bosutinib loaded COK-19 is represented in Figure 5(b), which lacks the strong crystalline peaks of bosutinib and closely matches the amorphous pattern of COK-19. This implies that rather than being present as crystalline particles on the surface, bosutinib is successfully contained inside the pores of COK-19 and is present in an amorphous or highly dispersed state. The mesopores of mesoporous silica COK-19 are uniformly loaded with bosutinib.

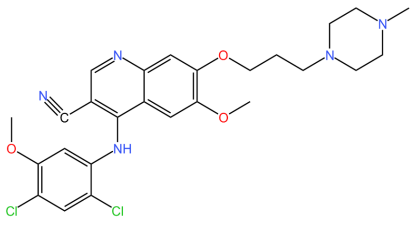


Figure 1: Molecular structure of Bosutinib.

Table 1: Structural characteristics of COK-19 and COK-19 loaded with bosutinib.

Sample	Surface Area ($m^2 g^{-1}$)	Pore Volume ($cm^3 g^{-1}$)	Pore Diameter (nm)
COK-19	1583.81	0.9083	3.1508
Bosutinib-COK-19	215.82	0.1672	2.1543

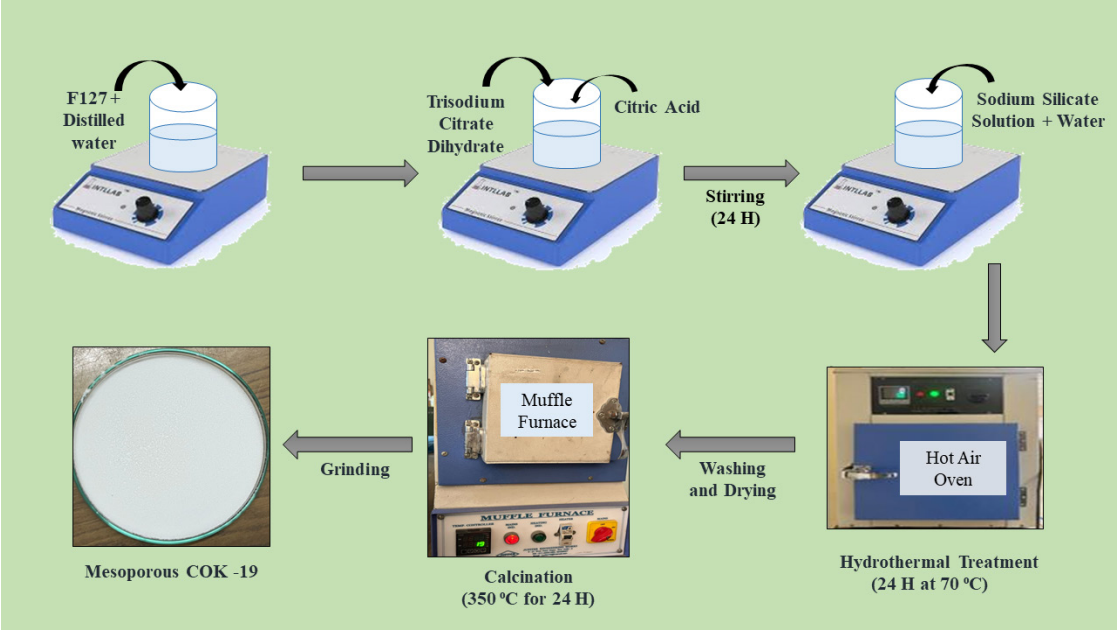


Figure 2: Synthesis of Mesoporous silica COK-19.

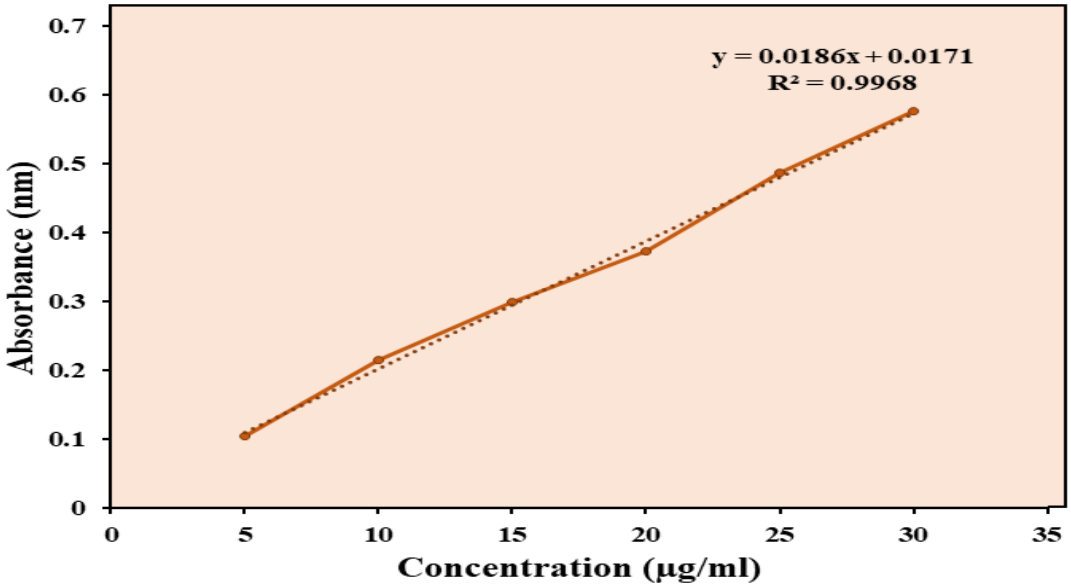


Figure 3: Calibration curve of bosutinib.

FESEM with EDX

FESEM micrographs of COK-19 and COK-19 loaded with bosutinib are shown in Figures 6a and 6b. As shown in Figure 6(b), the morphology of COK-19 does not change after drug entrapment, indicating that the drug is confined in pore channels of the silica matrix.[25] Consequently, it is evident that drug loading had no effect on surface morphology, indicating that drug entrapment had no effect on bare matrix structure. EDX spectra demonstrate that COK-19 is composed of Silicon (Si) and Oxygen (O) as shown in Figure 7(a). The appearance of peaks of carbon (C), Nitrogen (N) and Chlorine (Cl) from Figure 7(b) confirms the bosutinib's loading into the pores of COK-19. The little peaks that represent N, Cl, and C are caused by the presence of bosutinib in the silica matrix COK-19.

HRTEM

The HRTEM pictures of COK-19 and bosutinib loaded COK-19 are displayed in Figure 8(a). These materials have well organized cubic arrays of mesopores.[25] Drug entrapment results in the integration of particles with closely packed structures as seen in Figure 8(b). Furthermore, there were no noticeable drug molecules agglomerates on the surface. After being impregnated with entrapment of drug molecules, COK-19 channels remained

regular and uniform without changing the parent material's framework structure.

BET

The nitrogen sorption isotherms for COK-19 and bosutinib loaded COK-19 are depicted in Figure 9. According to IUPAC classification of sorption isotherms, type IV characteristic curve was observed which is for mesoporous materials.[27,28] A final saturation plateau of varying length, sometimes reduced to a simple inflexion point, is a characteristic of type IV isotherms.[29] Mesoporous silica and drug loaded silica hysteresis loops are similar to the H2 type curve, which is associated with ordered mesoporous materials.[27] Surface area, pore volume and pore diameter are summarized in Table 1 as measured using BET isotherms. All measurements, including specific surface area, pore volume and diameter, show a decrease upon drug loading COK-19 material. This indicates that the pore channels of COK-19 are either fully or partially filled after bosutinib loading. This shows that the bosutinib molecules were successfully incorporated into the COK-19 channels.

FTIR

FTIR spectra of bosutinib, COK-19 and bosutinib loaded COK-19 is shown in Figure 10. Bosutinib's distinctive band, which corresponds to nitrile stretching, was located at 2217 cm^{-1}. Additional peaks were found at 2938 cm^{-1} (alkyl C-H stretching), 2802 cm^{-1} (N-H stretching), 1591 cm^{-1} (NH-bending), 1465 cm^{-1} (methylene group CH-bending), 1421 cm^{-1} (methyl group CH-bending), 1369 cm^{-1} (aromatic amine C-N stretching), 1051 cm^{-1} (C-N stretching), 851 cm^{-1} (C-Cl stretching), and 724

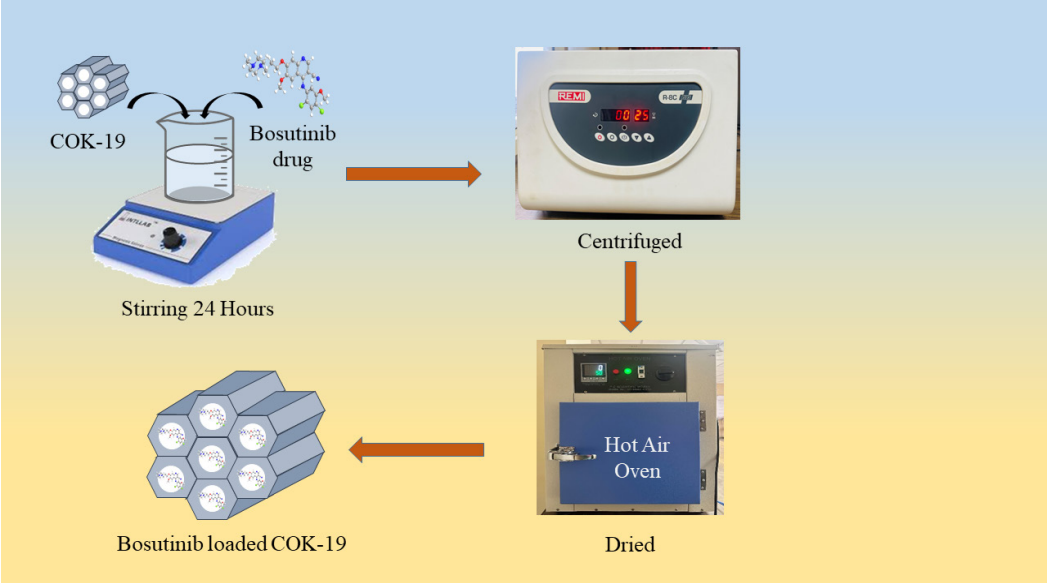


Figure 4: Schematic showing loading of bsutinib into COK-19 using post impregnation method.

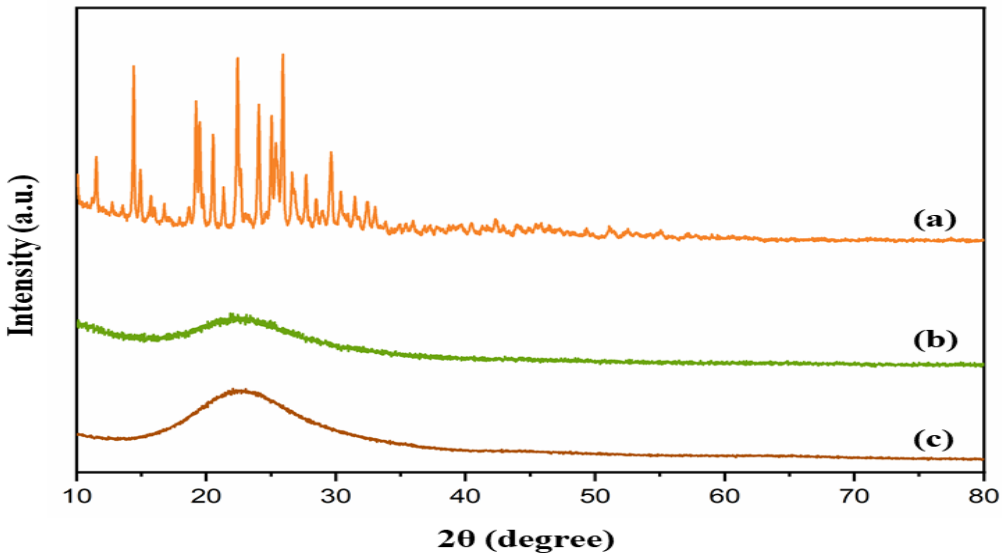
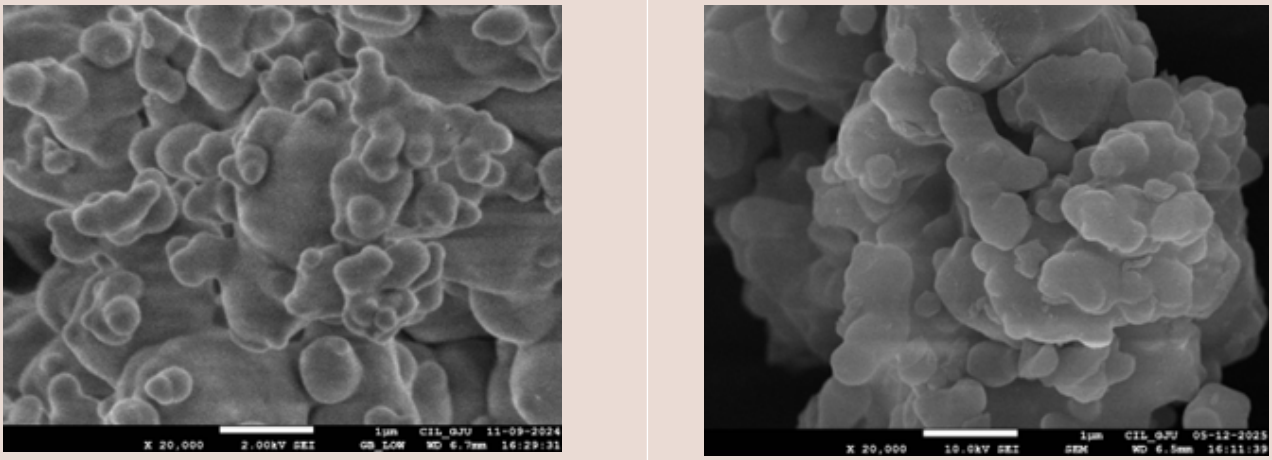
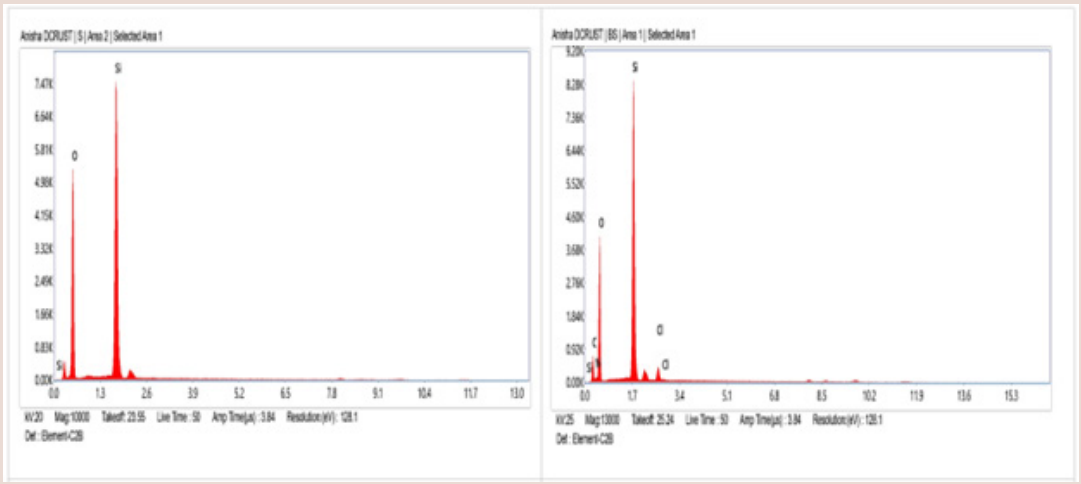


Figure 5: WAXRD pattern of (a) Bosutinib, (b) Bosutinib loaded COK-19 and (c) COK-19.



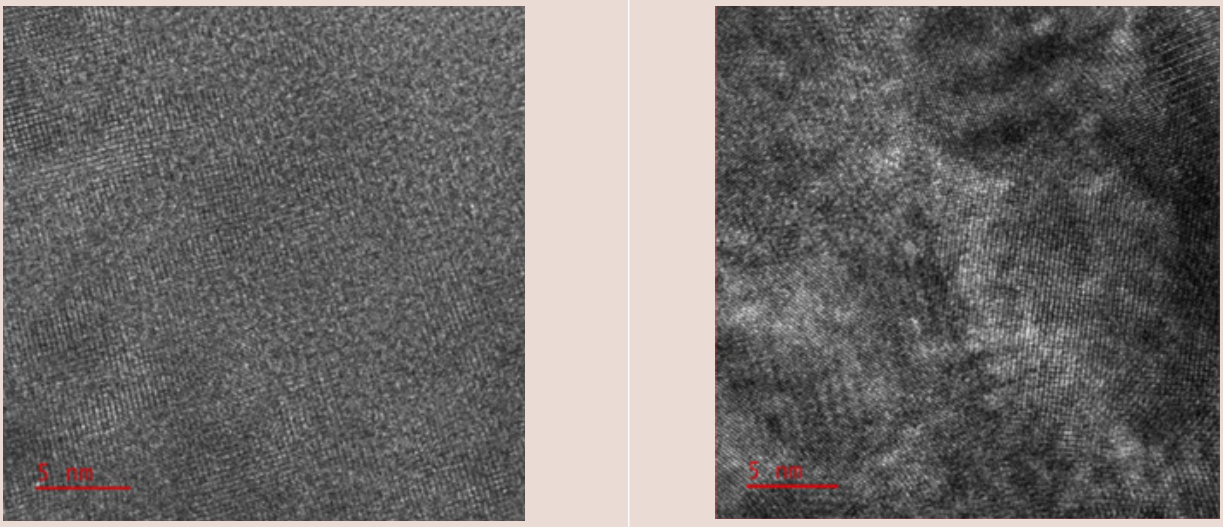
(a) (b)

Figure 6: FESEM pictures of (a) COK-19 and (b) Bosutinib loaded COK-19.



(a) (b)

Figure 7: EDX spectra of (a) COK-19 and (b) Bosutinib loaded COK-19.



(a) (b)

Figure 8: HRTEM pictures of (a) COK-19 and (b) Bosutinib loaded COK-19.

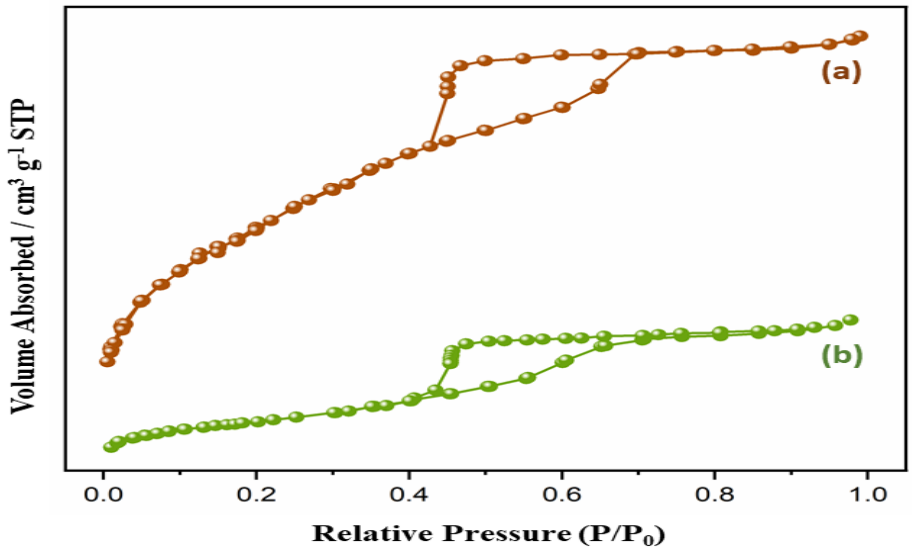


Figure 9: Nitrogen sorption isotherms of (a) COK-19 and (b) Bosutinib loaded COK-19.

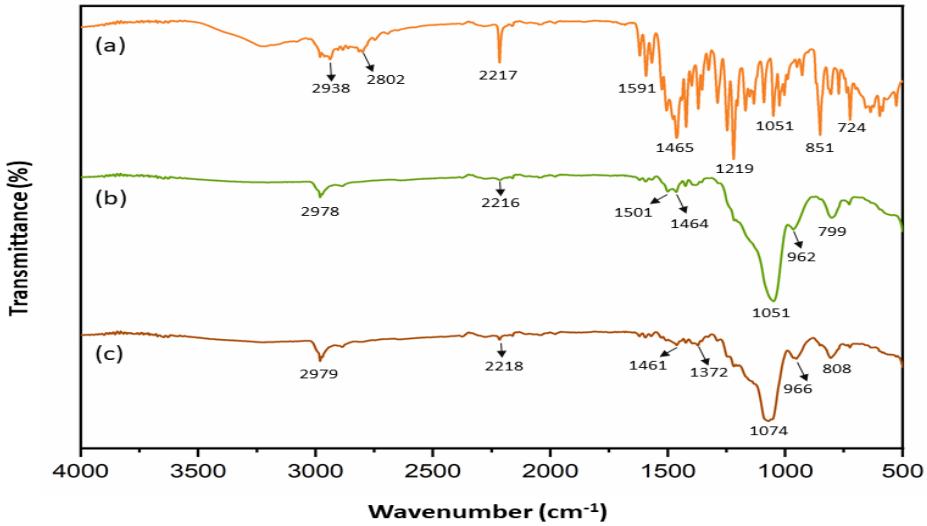


Figure 10: FTIR spectra of (a) Bosutinib, (b) Bosutinib-loaded COK-19 and (c) COK-19.

cm^{-1} (NH wag).[26] The FTIR spectra of COK-19 shows various characteristics bands, the bands at 1074 cm^{-1} and 808 cm^{-1} which are showing symmetric and asymmetric stretching vibrations of siloxane group (Si-O-Si), the band at 1074 cm^{-1} is the mesoporous silica material's major characteristic band. After drug loading, bosutinib loaded COK-19 exhibits band at 1051 cm^{-1} and 799 cm^{-1}, which coincides to the siloxane group. It indicates that there is slightly shift in the bands of siloxane group after drug loading. The FTIR spectra shows a high degree of bosutinib dispersion into the bare COK-19, which is corresponding to the drug entrapment efficiency of bosutinib in mesoporous material.

SAXS

Figure 11(a) depicts the SAXS patterns of COK-19 and bosutinib loaded COK-19 material. The formation of COK-19 is confirmed by the sharp and intense peak at scattering angle of 0.065^0, which shows the ordered mesostructure of mesoporous silica.[23,25] The drug loaded sample still exhibits the peak at 0.065^0, suggesting that loading preserves the structural ordering of COK-19. Additional small peak at 1^0 shows well-ordered mesostructure, but its lower intensity indicates partial ordering. Bosutinib molecules partially fill the mesopores and reduce the electron density difference between the silica walls and the pore voids, which explains the noticeable drop in peak intensity. Reduced peak intensity in Figure 11(b) depicts the successful entrapment of drug bosutinib in mesoporous COK-19.

Drug Release

Figure 12 is showing cumulative drug release profile of bosutinib loaded COK-19, indicates sustained drug release system. In the initial phase, first 12 hr, there was burst release of 42.67% due to the weakly bound drug molecules to the surface of COK-19. In the intermediate phase, 12 to 24 hr, moderate release of 74.23% is observed which shows the diffusion of drug from the mesopores. After 24 hr, a plateau is observed with maximum release of 81.85% in 72 hr. This demonstrates that some drug is

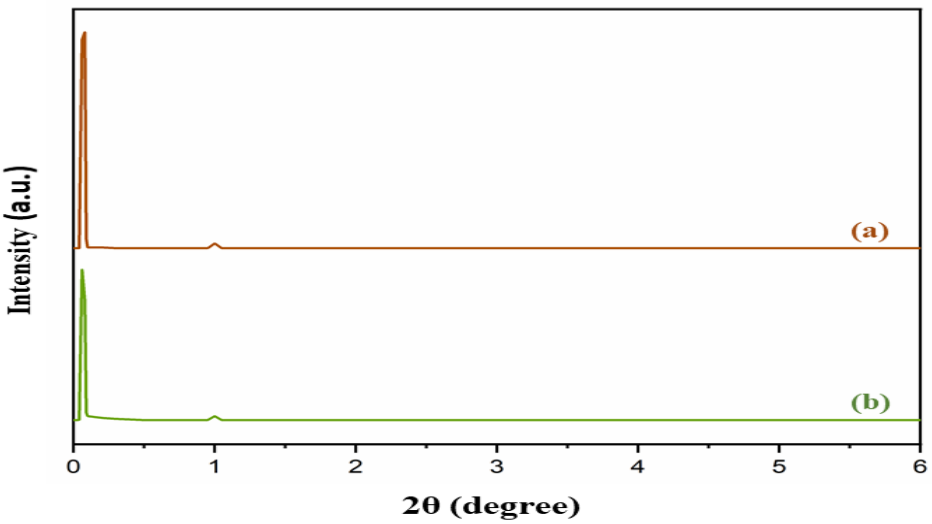


Figure 11: SAXS pattern of (a) COK-19 and (b) Bosutinib loaded COK-19.

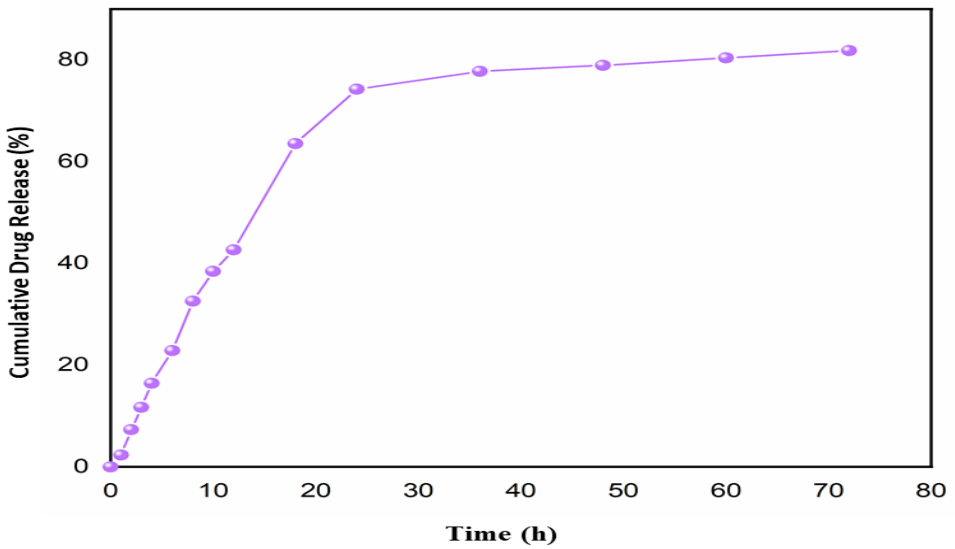


Figure 12: *In vitro* drug release pattern of COK-19 loaded with bosutinib.

deeply trapped inside the pores of mesoporous silica COK-19. This release profile shows the controlled and sustained release of medication, maintaining the therapeutic levels with time and reducing dosing frequency.

CONCLUSION

The hydrothermal approach was used to synthesize the mesoporous silica COK-19, which is ideal for drug delivery applications because of its high surface area, large pore volume and diameter. Bosutinib was loaded into COK-19 using the post impregnation technique, yielding into drug entrapment efficiency of 93.56% without harming the silica framework. BET revealed that COK-19 had a surface area of 1583 $m^2 g^{-1}$ and after bosutinib was loaded into the COK-19 matrix, the area is decreased to 215.82 $m^2 g^{-1}$. Drug release profile shows the 81.85% of drug release in PBS (pH 6.8) after 72 hr study. Initially burst release was observed for 12 hr after that in intermediate stage, moderate release of 74% was observed. Bosutinib loaded COK-19 showed sustained and regulated release which make COK-19 promising material for drug delivery. COK-19's structural characteristics make it a viable drug delivery system for regulated and prolonged drug release, high drug loading, increased therapeutic efficacy and improved drug stability. It is a promising material for advanced pharmaceutical and applications in biomedical as it is suitable for targeted drug administration, which reduces the frequency of doses.

ACKNOWLEDGEMENT

The authors gratefully acknowledge the Department of Science and Technology (DST) provided facilities assistance under the FIST Research Grant, Department of Physics, DCRUST, Murthal.

ABBREVIATIONS

BET: Brunauer Emmett Teller; **FESEM:** Field Emission Scanning Electron Microscopy; **FTIR:** Fourier Transform Infrared Spectroscopy; **HRTEM:** High-Resolution Transmission Electron Microscopy; **NSCLC:** Non-Small Cell Lung Cancer; **SAXS:** Small-Angle X-ray Scattering; **WAXRD:** Wide-Angle X-ray Diffraction; **TKI:** Tyrosine Kinase Inhibitor.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS CONTRIBUTION

Anisha: Writing - original draft, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. Surender Duhan: Writing - review and editing, Validation, Supervision. Acquisition. All authors approved the final manuscript.

DATA AVAILABILITY STATEMENT

Data will be available on request.

REFERENCES

1. Kumar M, Jha A, Bharti K, Manjit, Mishra B. Fucoidan-based Bosutinib nanocrystals for pulmonary drug delivery: solid state characterization and *in vitro* assessment. Chem Phys Impact. 2024;8:100644. doi: 10.1016/j.chphi.2024.100644.
2. Roskoski Jr R. A historical overview of protein kinases and their targeted small molecule inhibitors. Pharmacol Res. 2015;100(1):1-23. doi: 10.1016/j.phrs.2015.07.010, PMID 26207888.
3. Alhazmi HA, Ali Bokar Nasib A, Musleh YA, Hijri KQ, Rehman Z, Khuwaja G, *et al.* Application of drug-metal ion interaction principle in conductometric determination of imatinib, sorafenib, gefitinib and Bosutinib. Open Chem. 2020;18(1):798-807. doi: 10.1515/chem-2020-0123.
4. Attili I, Corvaja C, Spitaleri G, Del Signore E, Trillo Aliaga P, Passaro A, *et al.* New generations of tyrosine kinase inhibitors in treating NSCLC with oncogene addiction: strengths and limitations. Cancers. 2023;15(20):5079. doi: 10.3390/cancers15205079, PMID 37894445.
5. Yuan M, Huang LL, Chen JH, Wu J, Xu Q. The emerging treatment landscape of targeted therapy in non-small-cell lung cancer. Signal Transduct Target Ther. 2019;4(1):61. doi: 10.1038/s41392-019-0099-9, PMID 31871778.
6. Škubník J, Svobodová Pavlíčková V, Ruml T, Rimpelová S. Autophagy in cancer resistance to paclitaxel: development of combination strategies. Biomed Pharmacother. 2023;161:114458. doi: 10.1016/j.biopha.2023.114458, PMID 36889112.
7. Pishvaian MJ, Slack R, Koh EY, Beumer JH, Hartley ML, Cotarla I, *et al.* A Phase I clinical trial of the combination of imatinib and paclitaxel in patients with advanced or metastatic solid tumors refractory to standard therapy. Cancer Chemother Pharmacol. 2012;70(6):843-53. doi: 10.1007/s00280-012-1969-9, PMID 23014737.
8. Xu Y, Ji H, Zhang Y, Xiong L, Han B, Zhong H, *et al.* Combination of EGFR-TKI and chemotherapy versus EGFR-TKI monotherapy as neoadjuvant treatment of stage III-N2 EGFR-mutant non-small cell lung cancer. Oncologist. 2024;29(7):e932-40. doi: 10.1093/oncolo/oyae052, PMID 38529688.
9. Krause DS, Van Etten RA. Tyrosine kinases as targets for cancer therapy. N Engl J Med. 2005;353(2):172-87. doi: 10.1056/NEJMra044389, PMID 16014887.
10. Gergely PA, Murnyák B, Bencze J, Kurucz A, Varjas T, Gombos K, *et al.* Tyrosine kinase inhibitor imatinib mesylate alters DMBA-induced Early Onco/suppressor gene expression with tissue-specificity in mice. BioMed Res Int. 2019;2019(1):8670398. doi: 10.1155/2019/8670398, PMID 30882001.
11. Jackson KD, Durandis R, Vergne MJ. Role of cytochrome P450 enzymes in the metabolic activation of tyrosine kinase inhibitors. Int J Mol Sci. 2018;19(8):2367. doi: 10.3390/ijms19082367, PMID 30103502.
12. Syed YY, McCormack PL, Plosker GL. Bosutinib: a review of its use in patients with Philadelphia chromosome-positive chronic myelogenous leukemia. BioDrugs. 2014;28(1):107-20. doi: 10.1007/s40259-013-0082-x, PMID 24420842.
13. Karim NA, Ullah A, Wang H, Shoukier M, Pulliam S, Khaled A, *et al.* A phase I study of the non-receptor kinase inhibitor Bosutinib in Combination with pemetrexed in patients with selected metastatic solid tumors. Curr Oncol. 2022;29(12):9461-73. doi: 10.3390/curroncol29120744, PMID 36547158.
14. Abbas R, Hug BA, Leister C, Gaaloul ME, Chalon S, Sonnichsen D. A phase I ascending single-dose study of the safety, tolerability, and pharmacokinetics of Bosutinib (SKI-606) in healthy adult subjects. Cancer Chemother Pharmacol. 2012;69(1):221-7. doi: 10.1007/s00280-011-1688-7, PMID 21691746.
15. Budău LV, Pop C, Mogoșan C. Beyond the basics: exploring pharmacokinetic interactions and safety in tyrosine-kinase inhibitor oral therapy for solid tumors. Pharmaceuticals (Basel). 2025;18(7):959. doi: 10.3390/ph18070959, PMID 40732249.
16. Khan MI, Hossain MI, Hossain MK, Rubel MH, Hossain KM, Mahfuz AM, *et al.* Recent progress in nanostructured smart drug delivery systems for cancer therapy: a review. ACS Appl Bio Mater. 2022;5(3):971-1012. doi: 10.1021/acsabm.2c00002, PMID 35226465.
17. Kumari S, Ahuja M, Duhan S. Controlling release and cytotoxicity with berberine-loaded KIT-6. Mater Res Innov. 2024;28(7):528-40. doi: 10.1080/14328917.2024.2341489.
18. Malik P, Kumari S, Kumari P, Ahuja M, Duhan S, Sharma AK, *et al.* Development and assessment of amine-functionalized KIT-6 for *in vitro* drug delivery using juglone as the therapeutic agent. J Porous Mater. 2025;33(2):617-33. doi: 10.1007/s10934-025-01898-4.
19. Kumari S, Ahuja M, Duhan S. Fluconazole adsorption and release study using KIT-6 for targeted and controlled drug delivery system. Mater Res Innov. 2025;29(2):64-74. doi: 10.1080/14328917.2024.2376362.
20. SEHRAWAT S, DUHAN S. Anisha, Sushma Kumari, Aryan BOORA, Bhavna Rohilla, PRIYA malik. Nanomater Synth Appl. 2024; 198.
21. Khalbas AH, Albayati TM, Ali NS, Salih IK. Drug loading methods and kinetic release models using of mesoporous silica nanoparticles as a drug delivery system: a review. S Afr J Chem Eng. 2024;50(1):261-80. doi: 10.1016/j.sajce.2024.08.013.
22. Duhan S, Duhan S. *In vitro* release kinetics of ceftizoxime sodium-loaded COK-19 as an antimicrobial nanocarrier. J Integr Sci Technol. 2026;14(5):1577. doi: 10.62110/sciencein.jist.2026.v14.1577.
23. Senapati S, Mahanta AK, Kumar S, Maiti P. Controlled drug delivery vehicles for cancer treatment and their performance. Signal Transduct Target Ther. 2018;3(1):7. doi: 10.1038/s41392-017-0004-3, PMID 29560283.
24. Kerkhofs S, Willhammar T, Van Den Noortgate H, Kirschhock CE, Breynaert E, Van Tendeloo G, *et al.* Self-assembly of pluronic F127-silica spherical core-shell nanoparticles in cubic close-packed structures. Chem Mater. 2015;27(15):5161-9. doi: 10.1021/acs.chemmater.5b01772, PMID 27293311.
25. Kumar M, Goswami P, Jha A, Dhapte-Pawar V, Koch B, Mishra B. Formulation and evaluation of lipid/soluplus-stabilized nanocrystals of paclitaxel and Bosutinib for a synergistic effect in non-small cell lung cancer therapy. Mol Pharm. 2025;22(2):1061-78. doi: 10.1021/acs.molpharmaceut.4c01334, PMID 39835666.
26. Thommes M, Kaneko K, Neimark AV, Olivier JP, Rodriguez-Reinoso F, Rouquerol J, *et al.* Physisorption of gases, with special reference to the evaluation of surface area and pore size distribution (IUPAC Technical Report). Pure Appl Chem. 2015;87(9-10):1051-69. doi: 10.1515/pac-2014-1117.
27. Sing KSW. Reporting physisorption data for gas/solid systems with special reference to the determination of surface area and porosity (Recommendations 1984). Pure Appl Chem. 1985;57(4):603-19. doi: 10.1351/pac198557040603.
28. Irwansyah FS, Amal AI, Diyanthi EW, Hadisantoso EP, Noviyanti AR, Eddy DR, *et al.* How to read and determine the specific surface area of inorganic materials using the Brunauer-Emmett-Teller (BET) method. Asean J Sci Eng. 2022;4(1):61-70. doi: 10.17509/ajse.v4i1.60748.
29. Levinson NM, Boxer SG. Structural and spectroscopic analysis of the kinase inhibitor Bosutinib and an isomer of Bosutinib binding to the Abl tyrosine kinase domain. PLOS One. 2012;7(4):e29828. doi: 10.1371/journal.pone.0029828, PMID 22493660.

Cite this article: Anisha, Duhan S. COK-19 Mesoporous System for Controlled Bosutinib Release. Indian J of Pharmaceutical Education and Research. 2027;61:10.5530/ijper.20270252.