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Research Paper

Ticagrelor Solubility and Dissolution Rate Enhancement Using Mesoporous Silica SBA-15

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Abstract
Ticagrelor is a triazolopyrimidine antiplatelet agent with poor water solubility. Ticagrelor was incorporated into mesoporous silica SBA-15 in this study to evaluate its physical stability and improve its solubility and dissolution rate. TEOS was employed as a silica precursor and Pluronic P123 as a template to synthesize SBA-15. Ticagrelor was loaded into SBA-15 at a mass ratio of 1:1. Physicochemical characterization was conducted using nitrogen adsorption-desorption isotherm analysis, powder X-ray diffraction (PXRD), differential scanning calorimetry (DSC), fourier-transform infrared spectroscopy (FT-IR), and scanning electron microscopy (SEM). Ticagrelor solubility and dissolution were tested using distilled water as the medium. To evaluate the physical stability, Ticagrelor-SBA-15 was stored in a climatic chamber at 75% RH and 40°C for a month and analyzed using PXRD. Physicochemical characterization indicated efficient adsorption of ticagrelor into the SBA-15 pores, resulting in an amorphous form of solid material. Meanwhile, solubility and dissolution rate testing showed respective increases of 1.33 times and 1.74 times with significant differences ($p<0.05$) while maintaining its physical stability after storage for one month. Based on this study, it can be concluded that the incorporation of mesoporous SBA-15 significantly enhances ticagrelor's solubility and dissolution rate while maintaining stability.

Keywords
SBA-15, Ticagrelor, Solubility, Dissolution

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1. INTRODUCTION

Ticagrelor, an antiplatelet agent of the triazolopyrimidine class, works by binding to and selectively inhibiting the P2Y12 receptor, blocking prothrombotic effects through its interaction with ADP (Juneja et al., 2013). Ticagrelor is increasingly preferred in the treatment of hypertension due to its rapid onset of action compared to other antiplatelet drugs. However, the solubility of ticagrelor at room temperature is around 10 μg/mL, which classifies it as practically insoluble in aqueous media. It is also classified as a class IV medicine under the Biopharmaceutics Classification System (BCS) due to its low permeability and roughly 35% bioavailability (Bolla et al., 2022; Srivastava et al., 2022;Yuliandra et al., 2020).

Several variables, such as water solubility, drug permeability, dissolution rate, first-pass metabolism, and susceptibility to clearance, influence the bioavailability of medications taken orally. Low bioavailability is usually due to poor solubility and permeability (Bhalani et al., 2022). Drugs taken orally that are poorly soluble in water frequently require large dosages to achieve therapeutic plasma concentrations (Pote et al., 2022). Low water solubility is a significant challenge in the formulation development of new chemical entities and the development of generic drugs. For a drug to be absorbed, it must be dissolved in the biological fluids at the absorption site (Bhairav et al., 2016).

Attempts to enhance solubility have been made using methods such as solid dispersion (Beliatskaya et al., 2019; Chaturvedi et al., 2020; Chen et al., 2020; Febriyenti et al., 2020; Kim et al., 2019; Lutfiyah et al., 2022) and co-grinding (Shane et al., 2017), yet challenges remain. The primary limitation of these methods lies in the instability of the active substance after formulation. However, mesoporous silica materials present a practical approach to improving drug solubility while ensuring stability and shelf life. Silica mesopores offer adjustable pore sizes ranging from 2 to 50 nm and possess a relatively high specific surface area, up to 1500 m^2/g, which enhances their adsorption potential. With large pore volumes reaching 1.5 cm^3/g and surface silanol groups, silica mesopores can be chemically customized to control drug release (Hong et al., 2016). Furthermore, silica mesopores demonstrate superior stability during storage and excellent resistance to change caused by heat, pH variations, mechanical pressure, and hy-

drolysis compared to other polymer materials commonly used for enhancing solubility (McCarthy et al., 2016).

The method of enhancing solubility using silica-based mesopores has been explored by Ambrogi et al. who applied SBA-15 to improve the solubility of furosemide. Classified as a BCS class IV drug, furosemide showed approximately 1.25-fold increased solubility after adsorption within the SBA-15 silica mesopores and the stability of furosemide-SBA-15 was also high, with no detectable drug crystal formation observed after 6 months of storage. Therefore, SBA-15 is a highly promising material for oral delivery of class IV drugs (Ambrogi et al., 2012).

This research aimed to examine the enhancement of solubility and dissolution rate of ticagrelor within SBA-15 silica mesopores, as well as to study the stability of adsorbed ticagrelor. The characterization of the SBA-15 mesopores was conducted using nitrogen adsorption-desorption isotherms, powder X-ray diffraction (PXRD), Fourier-transform infrared spectroscopy (FT-IR), differential scanning calorimetry (DSC), and scanning electron microscopy (SEM). The study then examined ticagrelor's solubility, dissolution rate, and stability within the mesopores under conditions of 75% relative humidity at 40°C for one month.

2. EXPERIMENTAL SECTION

2.1 Materials

Ticagrelor was acquired from MSN Organics Pvt. Ltd. (India). Pluronic P123 and sodium chloride were supplied by Sigma Aldrich (USA). Tetraethyl orthosilicate (TEOS) was acquired from Tokyo Chemical Industry (TCI, Japan). Ethyl acetate and hydrochloric acid were acquired from Merck (Germany).

2.2 Methods

2.2.1 Synthesis of Mesoporous Silica SBA-15

Pluronic P123, distilled water (H_2O), hydrochloric acid (HCl), sodium chloride (NaCl), and tetraethyl orthosilicate (TEOS) were combined in a molar ratio of 1:6:6:166:0.02 to create SBA-15. Initially, Pluronic P123 and NaCl were homogenized, followed by the incremental addition of H_2O and a 2 M HCl solution. For 24 hours at room temperature, the resultant mixture was continuously stirred with a magnetic stirrer set at 300 rpm. The stirring rate was then raised to 700 rpm for three more hours after the introduction of TEOS. Following this, a hydrothermal treatment was carried out by placing the mixture in a Universal Oven Memmert UN55 (Germany) at a temperature of 80°C for 24 hours. The precipitate formed was subsequently isolated through vacuum filtration using filter paper, washed with distilled water to remove unreacted materials, and dried at 50°C for approximately 14 hours. The surfactant was removed through a calcination process conducted at 550°C for four hours, resulting in the production of SBA-15 mesoporous silica powder (Fitriani et al., 2023; Hasanah et al., 2021).

2.2.2 Adsorption of Ticagrelor in SBA-15

Adsorption of ticagrelor on to mesoporous SBA-15 was carried out at a 1:1 weight-to-weight ratio. First, 10 mL of ethyl acetate (p.a.) were used to dissolve 200 mg of ticagrelor. The ticagrelor solution was then added with SBA-15 powder. To create ticagrelor-SBA-15 powder, this mixture was stirred with a magnetic stirrer at 50°C and 300 rpm until the solvent had entirely evaporated. The dried product was stored in a desiccator (Fitriani et al., 2023; Hasanah et al., 2021).

2.2.3 Nitrogen Adsorption-Desorption Isotherm

Nitrogen adsorption-desorption isotherms analysis were conducted on SBA-15 and ticagrelor-loaded SBA-15 samples utilizing a BET surface area and pore-size analyzer (Quantachrome Novatouch LX-4, USA). The analysis was performed at a degassing temperature of 150°C. The results encompassed the P/Po value and the BET transformation value [1/W(P/Po)] to calculate the area (Hasanah et al., 2021).

2.2.4 SEM Analysis

Scanning Electron Microscopy (SEM) was utilized to analyze the samples of ticagrelor, SBA-15, and the ticagrelor-loaded SBA-15 (Hitachi Flexsem-100, Japan). The powder samples were placed in an aluminum holder and coated with a 10 nm gold layer. SEM was operated at 5 kV, and various magnifications were used for the observations (Fitriani et al., 2023).

2.2.5 DSC Analysis

Differential Scanning Calorimetry (DSC) was used to evaluate the thermal characteristics of ticagrelor, SBA-15, and ticagrelor-loaded SBA-15. A Shimadzu DSC-60 Plus (Japan) was used, and the temperature range was adjusted to 25–250°C with a heating rate of 10°C/min (Zaini et al., 2020).

2.2.6 FT-IR Spectroscopy

The samples of ticagrelor, SBA-15, and ticagrelor-loaded SBA-15 were analyzed using FT-IR spectroscopy (Shimadzu IR-Tracer-100–AH, Japan) to identify functional groups. The samples were dispersed on a KBr plate and compressed at high pressure, with the absorption spectrum measured in the range of 4000–500 cm^{-1} (Zaini et al., 2020).

2.2.7 PXRD Analysis

A diffractometer (PAN analytical MPD PW3040/60 type X'Pert Pro, The Netherlands) was employed to conduct powder X-ray diffraction (PXRD) analysis of ticagrelor, SBA-15, and ticagrelor-loaded SBA-15. The generator was set to 40 kV and 30 mA, and the conditions consisted of a 2θ range of 5–50°, a Cu metal target, and a Kα filter (Zaini et al., 2020).

2.2.8 Solubility Test

Solubility studies were conducted on both intact ticagrelor and ticagrelor-loaded SBA-15 samples. 100 mL of CO_2-free distilled water was used to dissolve an excess quantity of each sample. Testing was conducted in an orbital agitator (Memmert Wnb-14, Germany) at room temperature for 16 hours.

The absorption of the filtrate was measured at a wavelength of 221.5 nm using a UV–Vis spectrophotometer (Shimadzu UV-1700, Japan) after it was filtered through a 0.45 μm membrane filter. Triplicates of this examination were administered (Fitriani et al., 2023).

2.2.9 Dissolution Test

The dissolution profile of ticagrelor and ticagrelor-loaded SBA-15 samples was assessed using a type II dissolution apparatus (paddle type) (Hanson SR8-Plus, USA). The dissolution flask was filled with 900 mL of CO_2-free distilled water, and the system was maintained at 37 ± 0.5°C with a stirring speed of 100 rpm. A sample equivalent to 10 mg of ticagrelor was weighed, and 5 mL aliquots were taken at intervals of 5, 10, 15, 30, 45, 60, 90, and 120 minutes. Each sample was analyzed with UV–Vis spectrophotometry (Shimadzu UV-1700, Japan) at 221.5 nm (Fitriani et al., 2023).

2.2.10 Physical Stability Test

For a period of one month, the samples were stored in a climatic chamber (Memmert HPPeco, Germany) at a temperature of 40°C and a relative humidity of 75% in order to execute a physical stability test for ticagrelor–SBA-15. The physical stability was subsequently assessed using PXRD analysis (PAN analytical MPD PW3040/60 type X'Pert Pro, The Netherlands).

2.2.11 Data Analysis

The solubility results underwent statistical analysis with a paired T-test, while the dissolution rates were assessed using one-way ANOVA via SPSS 26 (IBM, USA).

3. RESULTS AND DISCUSSION

The obtained SBA-15 solid appeared as a free-flowing white powder, aligned with previous studies on SBA-15 synthesis (Fitriani et al., 2023). The nitrogen adsorption-desorption isotherm was employed to analyze the pore characteristics of the solid, which confirmed that the white solid possessed pores within the 2-50 nm range, designating it as mesoporous. Other than the pore size, nitrogen adsorption-desorption isotherm tests were implemented to evaluate the surface area and pore volume of the synthesized SBA-15. Figure 1 shows that when applied under pressure, nitrogen gas is increasingly adsorbed following the applied pressure. The curve then rises rapidly when the nitrogen gas enters the pore space and returns to a steady state once the pores of the SBA-15 are saturated. A type IV isotherm curve is indicated by the hysteresis loop depicted in the adsorption-desorption isotherm curves at a relative pressure ranging from 0.4 to 0.8. Porous materials are characterized by a type IV isotherm curve with a hysteresis loop, which remains visible after ticagrelor is adsorbed into the mesopores. This suggests that the mesopores are still present and remain undamaged following the drug's adsorption. Table 1 indicates that the pore size of the mesoporous SBA-15 is between 2 and 50 nm, which is within the mesoporous size range.

Table 1. The Result of Pore Characterization of SBA-15 and Ticagrelor-Loaded SBA-15

Parameter	SBA-15	Ticagrelor - Loaded SBA15
Surface Area (m^2/g)	662.913	236.770
Pore Volume ($\times 10^{-1}$ cm^3/g)	4.504	1.926
Pore Size (d) (nm)	5.0860	4.8870

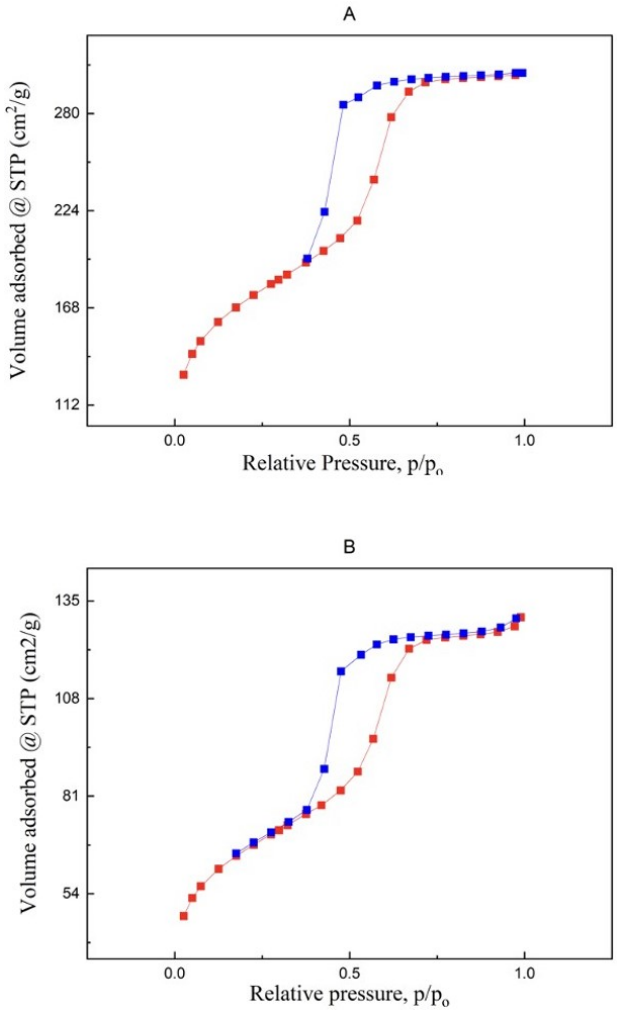

Figure 1. Isothermic Curves of (A) SBA-15 and (B) Ticagrelor-SBA-15

After ticagrelor adsorption, the specific surface area and pore volume of SBA-15 were significantly reduced in comparison to SBA-15, indicating that the pores of SBA-15 are well occupied with ticagrelor. The specific surface area of SBA-15 decreased from 662.91 to 236.77 m^2/g, the pore volume from 4.50×10^{-1} to 1.93×10^{-1} cm^3/g, and the pore size also de-

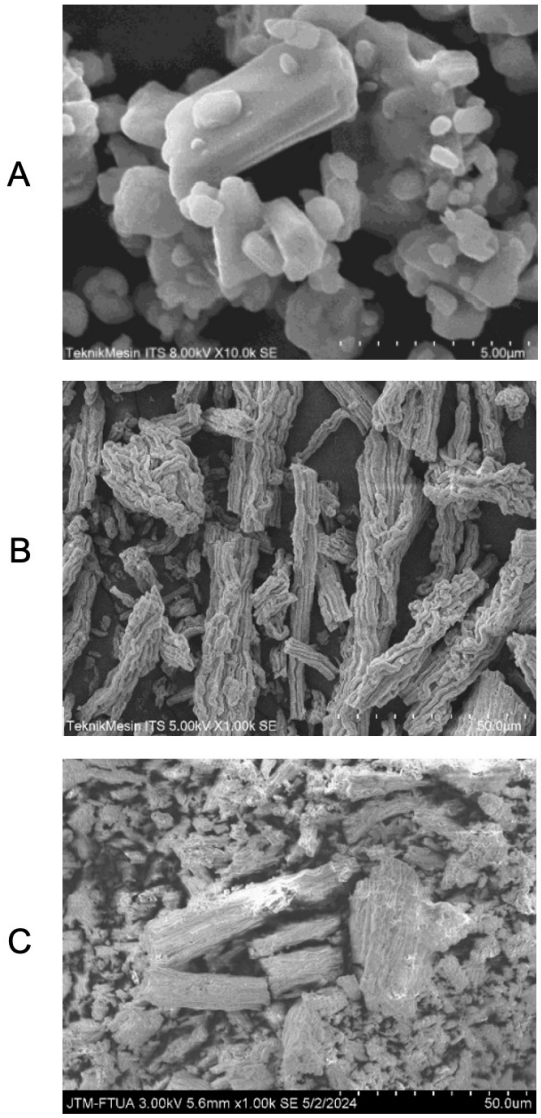

Figure 2. Morphology of (A) Ticagrelor, (B) SBA-15, and (C) Ticagrelor-SBA-15

creased from 5.09 to 4.89 nm. Ticagrelor entering the SBA-15 will cover the pores, thus reducing the specific surface area and pore volume. Although there is a decrease in pore size, the reduction is only by 0.2 nm as ticagrelor adheres to the inner pore walls of SBA-15. These results are in line with the study conducted by Ambrogi et al. (2012) using furosemide, which also showed a decrease in the specific surface area and pore volume of SBA-15 from 791 to 213 m^2/g and from 8.8×10^{-1} to 3.5×10^{-1} cm^3/g, respectively. Similarly, Adrover et al. (2020) observed a decrease in the specific surface area and pore volume of SBA-15 from 387 to 152 m^2/g and from 6.38×10^{-1} to 2.86×10^{-1} cm^3/g after albendazole adsorption.

Regarding the morphology of the materials, SEM micrographs reveal ticagrelor crystal aggregates (Figure 2A) and rod-shaped SBA-15 aggregates (Figure 2B). The morphology of TG-SBA (Figure 2C) resembles that of SBA-15 with ticagrelor crystals adhering to its surface, indicating that, while most of the ticagrelor has been efficiently adsorbed, some ticagrelor particles are still visible. These findings are in accordance with PXRD and DSC results, which indicate the presence of ticagrelor crystals in the TG-SBA sample that possibly form during the solvent drying process using the evaporation method (Shen et al., 2010). While their presence is limited, Figure 2C illustrates that ticagrelor can still be found outside the pores of SBA-15, both on the surface of mesopores and in areas where it has not been adsorbed into the mesopores.

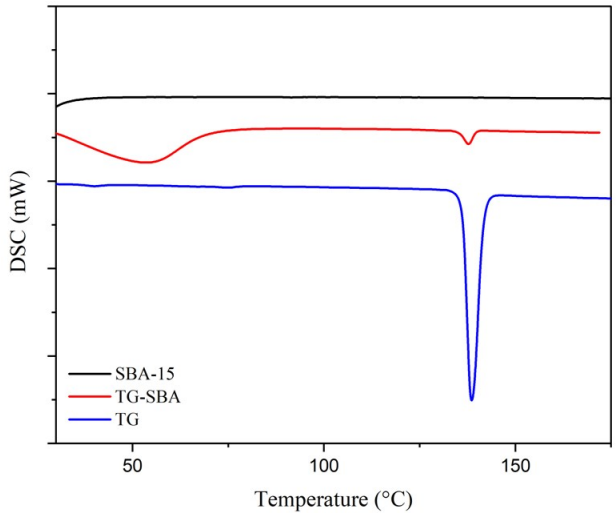

Figure 3. Thermogram of SBA-15, Ticagrelor-SBA-15, and Ticagrelor

In the DSC thermal analysis (Figure 3), ticagrelor exhibits an endothermic peak at 138.61°C indicating a phase transition at this temperature. The thermogram of TG-SBA displays a similar endothermic peak at the same temperature, albeit with lesser intensity, because ticagrelor is not entirely adsorbed into the mesopores of SBA-15. Instead, some remains adhered to the external surface of SBA-15 pores. These findings are consistent with the PXRD analysis results, which reveal the same phenomenon. This outcome was also observed by Ambrogi et al. (2012) in thermal analysis of furosemide-SBA-15. An endothermic peak, although slight and not sharp, indicated that some furosemide crystals were still detectable by DSC, while most of the drug had been adsorbed into the mesopores of SBA-15. Our thermograms indicate that ticagrelor adsorption into SBA-15 is effective. Once adsorbed, the crystallization of ticagrelor within SBA-15 is hindered due to the pre-existing non-crystalline state within the mesopores. The small and confined pore dimensions restrict the formation of crystalline structures by the adsorbed active substance (Speybroeck et al., 2009). The differing characteristics between TG-SBA and pure ticagrelor cause the amorphous crystalline state of ticagrelor within SBA-15.

Ticagrelor is observed to contain functional groups in the

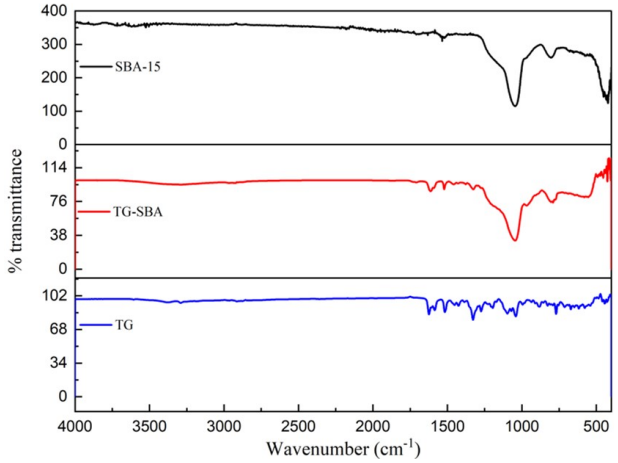

Figure 4. FTIR Spectra of Ticagrelor, Ticagrelor-SBA -15, and SBA-15

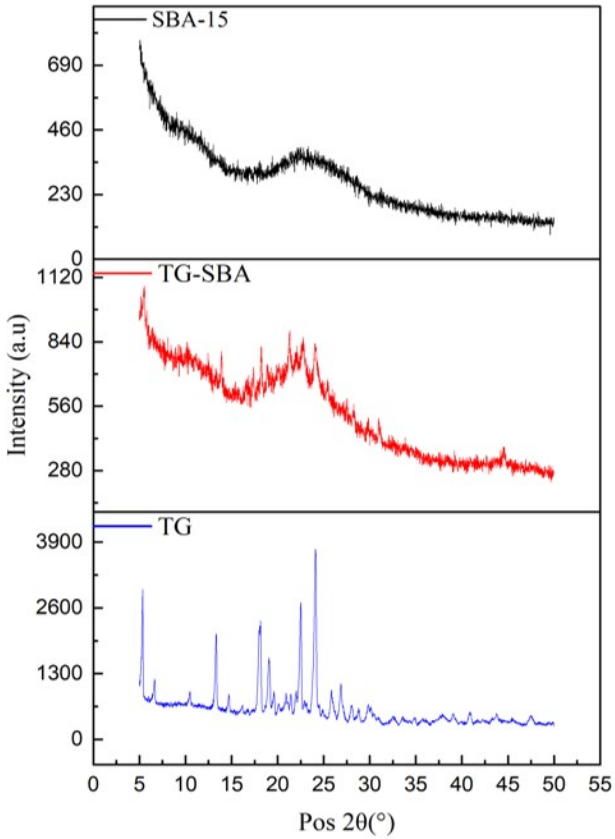

Figure 5. Diffractogram of Ticagrelor-SBA-15, SBA-15, and Ticagrelor

hydrogen stretching region (3600-2700 cm^{-1}) by FTIR (Figure 4), with the O−H functional group exhibiting a band at 3288 cm^{-1}. The C−N and C−O bonds exhibit bands at 1624 and 1452 cm^{-1}, respectively. In the spectrum of SBA-15, the O−H group is described by a band at 3523 cm^{-1}, the Si−O−Si bond by a band at 422 cm^{-1}, asymmetric Si−O−Si at 1045 cm^{-1}, and symmetric Si−O−Si at 804 cm^{-1}. Thahir et al. (2019) found that asymmetric Si−O−Si stretching is detected in the wavenumber range of 1090-1103 cm^{-1}, while symmetric Si−O−Si bonding is detected at 801 cm^{-1}. In the TG-SBA spectrum, a combination of ticagrelor and SBA-15 spectra is observed. The presence of C=C, C=C, C−N, Si−O−Si bending, Si−O−Si asymmetric bending, Si−O−Si symmetric stretching, and O−H groups is indicated at wavenumbers 1614, 1521, 1326, 438, 1045, 790, and 3287 cm^{-1}, respectively. There is a slight shift in wavenumbers due to interactions between ticagrelor and the Si−OH bond in SBA-15. However, overall, there is no damage to the ticagrelor structure after adsorption into SBA-15.

Powder X-ray diffraction (PXRD) analysis (Figure 5) shows the high intensity diffraction peaks of crystalline ticagrelor. In contrast, amorphous mesoporous SBA-15 does not show sharp diffraction peaks. After ticagrelor adsorption into SBA-15, the TG-SBA diffractogram lacks the peak intensity of pure ticagrelor and the diffraction pattern indicates ticagrelor in an amorphous form. The crystallinity index (CI) of Ticagrelor in SBA-15 showed a significant reduction compared to the pure drug, indicating that the encapsulation within the mesoporous structure of SBA-15 effectively decreased the crystalline nature of Ticagrelor. This decrease can be observed at several characteristic peaks of Ticagrelor's diffractogram. Specifically, the CI at 2θ = 13.9° was reduced to 9.0%, at 2θ = 17.3° it dropped to 7%, at 2θ = 22.8° it decreased to 14%, and at 2θ = 24.0° it was reduced to 10%. These four peaks represent the distinctive diffraction signals of crystalline Ticagrelor, and the observed reduction in CI suggests that the drug has become more amorphous after being loaded into SBA-15. This reduction in crystallinity is favorable for enhancing the solubility and dissolution rate, as the amorphous form typically exhibits improved dissolution behavior compared to the crystalline form. However, some crystalline peaks of ticagrelor are still observed, revealing the minor presence of ticagrelor crystals on the surface of SBA-15. The PXRD analysis results are consistent with those in the study by Shen et al. (2010) on ibuprofen, which still showed ibuprofen crystal peaks despite adsorption. Ibuprofen crystals may have formed and adhered to the SBA-15 pores after the solvent evaporation process.

The solubility test results in Table 2 reveal increased solubility of TG-SBA in COa-free distilled water, 1.34-fold higher than pure ticagrelor. The paired t-test results indicate a statistically significant difference in solubility between intact ticagrelor and ticagrelor loaded into SBA-15 (p = 0.003), suggesting that SBA-15 effectively enhances ticagrelor solubility. The solubility of ticagrelor adsorbed into the mesoporous SBA-15 can increase due to its inhibited crystallization. The mesopores of SBA-15 have tube/channel-like spaces whose thickness and rigidity prevent the active ingredient inside from recrystallizing (Letchmanan et al., 2017). The reduction in particle size and hydrogen bonding through silanol groups on the surface of the SBA-15 mesopores also contribute to the increased solubility

of TG-SBA. This increase in ticagrelor solubility is consistent with the study conducted by Ambrogi et al. (2012) using the BCS class IV drug furosemide, which reported a 1.25-fold increase in solubility of furosemide adsorbed in SBA-15 compared to pure furosemide.

Table 2. Solubility Data of Ticagrelor and Ticagrelor-SBA-15

Sample	Solubility ± SD (mg/L)	Solubility Enhancement
Intact Ticagrelor	8.556 ± 0.448	-
Ticagrelor-SBA-15	11.349 ± 0.384	1.337 times

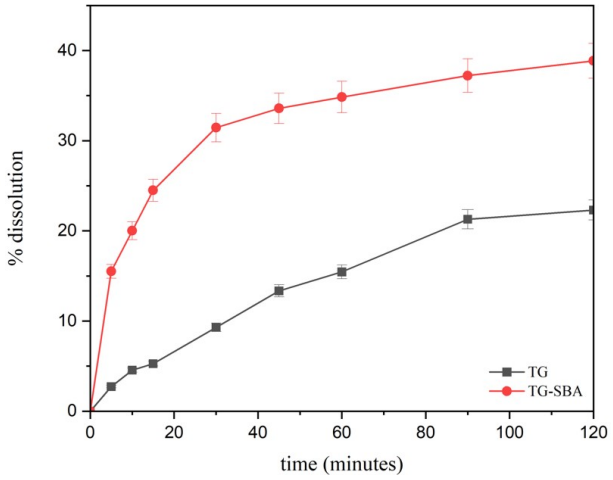

Figure 6. Dissolution Rates Profile of Ticagrelor and Ticagrelor-SBA-15

The dissolution profile analysis using one-way ANOVA revealed a highly significant difference among the samples ($p = 0.000$), indicating that ticagrelor loaded into SBA-15 exhibits a markedly enhanced dissolution rate compared to intact ticagrelor. Within the first 5 minutes, TG-SBA dissolved by 15.5%, whereas pure ticagrelor only dissolved by 2.7%. The dissolution percentage continued to increase up to the 120th minute, when TG-SBA reached 38.9%, 1.74-fold higher than pure ticagrelor at 22.3%. Although the increase is significant ($p < 0.05$), the TG-SBA sample did not reach 80% dissolution after 120 minutes. However, based on the dissolution profile graph (Figure 6) that continues to show an upward trend, it can be assumed that the dissolution percentage of TG-SBA will continue to rise over time. From these results, it can be concluded that TG-SBA has a higher dissolution rate than pure ticagrelor. These results are consistent with those of Fitriani et al. (2023), which showed that pure curcumin only dissolved by 18.0% after 60 minutes of testing, while curcumin in SBA-15 dissolved by 57.8% in the same time frame.

The physical stability of ticagrelor in TG-SBA was tested to evaluate the influence of humidity and temperature on the solid form of the drug (Figure 7). Ticagrelor-SBA-15 largely retained its amorphous form during the 1-month stability test, although shifts in position and an increase in the intensity of the crystal peaks can be observed, indicating that the stored sample may experience some change in solid form. However, the patterns before and after storage are not significantly different, suggesting that the sample remains relatively stable. This result coincides with that of Fitriani et al. (2023) for usnic acid-SBA-15, which maintained an amorphous form after storage in a climatic chamber for two weeks but showed some increase in intensity of crystalline peaks.

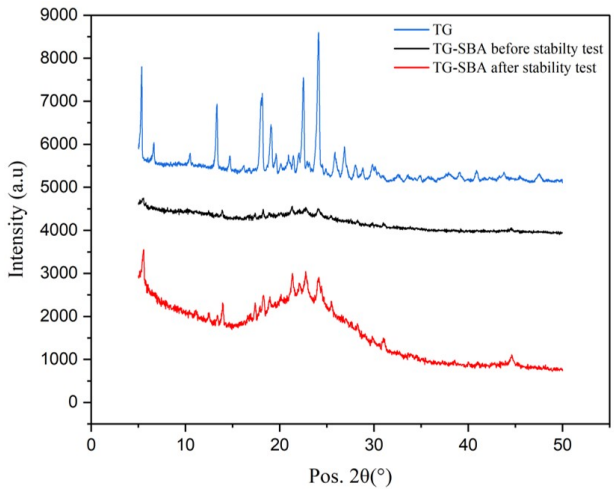

Figure 7. Diffractogram of Ticagrelor-SBA-15 and Ticagrelor -SBA-15 at 75% RH and 40°C

4. CONCLUSIONS

The adsorption of ticagrelor into the pores of mesoporous silica SBA-15 increased its solubility 1.34-fold and its dissolution rate within 120 minutes 1.74-fold. Ticagrelor-SBA-15 was also relatively stable under storage at 75% RH at 40°C for 1 month.

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REFERENCES

Adrover, M. E., M. Pedernera, M. Bonne, B. Lebeau, V. Bucala, and L. Gallo (2020). Synthesis and Characterization of Mesoporous SBA-15 and SBA-16 as Carriers to Improve Albendazole Dissolution Rate. *Saudi Pharmaceutical Journal*, **28**(1); 15–24

Ambrogi, V., L. Perioli, C. Pagano, F. Marmottini, M. Ricci, A. Sagnella, and C. Rossi (2012). Use of SBA-15 for

Furosemide Oral Delivery Enhancement. *European Journal of Pharmaceutical Sciences*, **46**(1–2); 43–48

Beliatskaya, A. V., I. I. Krasnyuk, I. I. Krasnyuk, O. I. Stepanova, Z. A. Abgaryan, T. P. Kudinova, and I. S. Nesterenko (2019). Study on the Solubility of Ketoprofen From Solid Dispersions with Polyvinylpyrrolidone. *Moscow University Chemistry Bulletin*, **74**(2); 93–99

Bhairav, B. A., J. K. Bachhav, and R. B. Saudagar (2016). Review on Solubility Enhancement Techniques. *Asian Journal of Pharmaceutical Research*, **6**(3); 175

Bhalani, D. V., B. Nutan, A. Kumar, and A. K. S. Chandel (2022). Bioavailability Enhancement Techniques for Poorly Aqueous Soluble Drugs and Therapeutics. *Biomedicines*, **10**(9); 2055

Bolla, G., B. Sarma, and A. K. Nangia (2022). Crystal Engineering of Pharmaceutical Cocrystals in the Discovery and Development of Improved Drugs. *Chemical Reviews*, **122**(13); 11514–11603

Chaturvedi, K., H. S. Shah, K. Nahar, R. Dave, and K. R. Morris (2020). Contribution of Crystal Lattice Energy on the Dissolution Behavior of Eutectic Solid Dispersions. *ACS Omega*, **5**(17); 9690–9701

Chen, X., I. Partheniadis, I. Nikolakakis, and H. Al-Obaidi (2020). Solubility Improvement of Progesterone From Solid Dispersions Prepared by Solvent Evaporation and Co-Milling. *Polymers*, **12**(4); 854

Febriyenti, P. Indra, E. Zaini, F. Ismed, and H. Lucida (2020). Preparation and Characterization of Quercetin-Polyvinylpyrrolidone K-30 Spray Dried Solid Dispersion. *Journal of Pharmacy & Pharmacognosy Research*, **8**(2); 127–134

Fitriani, L., H. Azizah, U. Hasanah, and E. Zaini (2023). Enhancement of Curcumin Solubility and Dissolution by Adsorption in Mesoporous SBA-15. *International Journal of Applied Pharmaceutics*, **15**(Special Issue 1); 61–67

Hasanah, U., S. Wikarsa, and S. Asyarie (2021). Various Chloride Salt Addition in Mesoporous Material (SBA-15) Synthesis and Potential as Carrier for Dissolution Enhancer. In *Proceedings of the 2nd International Conference on Contemporary Science and Clinical Pharmacy 2021 (ICCSCP 2021)*, volume 40. pages 343–349

Hong, S., S. Shen, D. C. T. Tan, W. K. Ng, X. Liu, L. S. O. Chia, and R. Gokhale (2016). High Drug Load, Stable, Manufacturable and Bioavailable Fenofibrate Formulations in Mesoporous Silica: A Comparison of Spray Drying Versus Solvent Impregnation Methods. *Drug Delivery*, **23**(1); 316–327

Juneja, S., K. Gupta, and S. Kaushal (2013). Ticagrelor: An Emerging Oral Antiplatelet Agent. *Journal of Pharmacology and Pharmacotherapeutics*, **4**(1); 78–80

Kim, S. J., H. K. Lee, Y. G. Na, K. H. Bang, H. J. Lee, M. Wang, and C. W. Cho (2019). A Novel Composition of Ticagrelor by Solid Dispersion Technique for Increasing Solubility and Intestinal Permeability. *International Journal of Pharmaceutics*, **555**; 11–18

Letchmanan, K., S.-C. Shen, W. K. Ng, and R. B. H. Tan (2017). Dissolution and Physicochemical Stability Enhancement of Artemisinin and Mefloquine Co-Formulation via Nano-Confinement with Mesoporous SBA-15. *Colloids and Surfaces B: Biointerfaces*, **155**; 560–568

Lutfiyah, D. S., L. Fitriani, M. Taher, and E. Zaini (2022). Crystal Engineering Approach in Physicochemical Properties Modifications of Phytochemical. *Science and Technology Indonesia*, **7**(3); 353–371

McCarthy, C. A., R. J. Ahern, R. Dontireddy, K. B. Ryan, and A. M. Crean (2016). Mesoporous Silica Formulation Strategies for Drug Dissolution Enhancement: A Review. *Expert Opinion on Drug Delivery*, **13**(1); 93–108

Pote, S. V., K. Bavaskar, and A. Jain (2022). Solubility Enhancement of Poorly Soluble Drug by Using Different Techniques. *Research Journal of Pharmaceutical Dosage Forms and Technology*, **14**(4); 315–323

Shane, N. L. J., A. H. Chamle, A. Vasantharaju, A. Pai, G. Pai, and M. B. Sathyanarayana (2017). Fabrication and Solid State Characterization of Ticagrelor Co-Crystals with Improved Solubility and Dissolution. *International Journal of Pharmaceutical Quality Assurance*, **8**(1); 1–8

Shen, S. C., W. K. Ng, L. Chia, Y. C. Dong, and R. B. H. Tan (2010). Stabilized Amorphous State of Ibuprofen by Co-Spray Drying with Mesoporous SBA-15 to Enhance Dissolution Properties. *Journal of Pharmaceutical Sciences*, **99**(4); 1997–2007

Speybroeck, M. V., V. Barillaro, *T. Do*, R. Mellaerts, J. Martens, J. V. Humbeeck, and P. Augustijns (2009). Ordered Mesoporous Silica Material SBA-15: A Broad-Spectrum Formulation Platform for Poorly Soluble Drugs. *Journal of Pharmaceutical Sciences*, **98**(8); 2648–2658

Srivastava, A., M. A. Khan, S. Bedi, and U. Bhandari (2022). A Review on Different Solubility Enhancement Techniques of Ticagrelor. *International Journal of Pharmaceutical Investigation*, **13**(1); 01–06

Thahir, R., A. W. Wahid, N. La Nafie, and I. Raya (2019). Synthesis of Mesoporous Silica SBA-15 through Surfactant Set-Up and Hydrothermal Process. *Rasāyan Journal of Chemistry*, **12**(3); 1117–1126

Yuliandra, Y., L. Fitriani, R. Kurniawan, F. Yasardi, and E. Zaini (2020). Solid Dispersions of Famotidine: Physicochemical Properties and In Vivo Comparative Study on the Inhibition of Hyperacidity. *ChemistrySelect*, **5**(29); 9218–9225

Zaini, E., D. Riska, M. D. Oktavia, F. Ismed, and L. Fitriani (2020). Improving Dissolution Rate of Piperine by Multicomponent Crystal Formation with Saccharin. *Research Journal of Pharmacy and Technology*, **13**(4); 1926–1930

