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# *Synthesis of Vinyl Modified Silica as a High-Performance Liquid Chromatography Stationary Phase*

Ardine Zada Alzena, Handajaya Rusli*, Anita Alni, Muhamad Bachri Amran
Program Study of Chemistry, Faculty of Mathematics and Natural Science, Bandung Institute of Technology, Indonesia
*E-mail: handajaya@itb.ac.id.com

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## Abstract

Silica can be produced through hydrolysis in alkaline conditions via the Stober process and has two main functional groups, namely siloxane (Si-O-Si) and silanol (Si-OH). Vinyl modified silica can be produced from the hydrolysis of tetraethyl orthosilicate (TEOS) and vinyl trimethoxysilane (VTMS) with 25%(v/v) ammonia. VTMS is used as a silica surface modifying agent. The resulting silica-vinyl modification is then used as a stationary phase to fill a High Performance Liquid Chromatography (HPLC) column. The aim of this research is to synthesize vinyl-modified silica as a HPLC stationary phase and test its performance. Silica-vinyl modification is carried out by first synthesizing silica from TEOS and then modifying the surface using VTMS. Characterization was carried out using a Scanning Electron Microscope (SEM) and Fourier Transform Infrared Spectroscopy (FTIR). SEM characterization gave a spherical shape and a diameter of 1.73-2.02 µm. FTIR identification gave good results with the identification of siloxane signals (Si-O-Si) at 1,097 $cm^{-1}$ on silica and 2,850 $cm^{-1}$ and 2,922 $cm^{-1}$ which were C-H vibrations on silica-vinyl. Qualitative identification carried out by the addition of alkenes with $I_2$ also shows the binding of vinyl groups to the silica surface. The modified silica is then loaded into a 50 mm x 4.6 mm column. The performance test was carried out by separating caffeine and paracetamol compounds. Optimum separation of MeOH:HOH 1:99 eluent with a flow rate of 1 mL/min. The resulting resolution is 1,80 and selectivity is 1.52. The resulting calibration curve has an $R^2$ value of 0.99156 for caffeine and 0.99431 for paracetamol.

**Keywords:** Alkene, HPLC, Modification, Silica, VTMS

## 1 Introduction

One method to separate an analyte from its components is using High-Performance Liquid Chromatography (HPLC). HPLC is a separation method and can determine the level of a component based on the peak area produced. The advantages of HPLC over other methods are fast, efficient separation and high resolution [1]. In the separation, the analyte and mobile phase are flowed into a column containing a stationary phase. The separation that occurs is based on the interaction of the analyte with the stationary phase and its mobile phase. The stationary phase commonly used in HPLC is divinyl benzene polymer with styrene and often used is silica, either modified or not [2].

Silica can be produced from the hydrolysis of tetraethyl orthosilicate (TEOS) in an alkaline atmosphere through the Stober process [3]. Silica is a chemical that has high stability and is the most widely utilized semiconductor material in the biomedical field, rubber, and plastic industry, and as an absorbent. Silica is widely used because of its harmlessness to the body, high hardness, corrosion resistance, and many more [4], [5], [6].

The resulting silica can be further modified with various functional groups for various applications. Surface modification of silica is then increasingly developed and functioned to change the physical and chemical properties of the silica surface to strengthen its performance [7]. Examples of silica modification applications are as a filler material in the manufacture of polymer nanocomposites, aerogel-modified silica utilized as a drying material for industry, and mesoporous silica nanoparticles (MSNs) as an application for drug delivery and biomedicine [8], [9], [10]. In addition, silica can also be utilized as a stationary

phase for HPLC column fillers. C18-modified silica has been synthesized as a stationary phase filler for HPLC columns and used to separate $Pb^{2+}$, $Hg^{2+}$, and $Cd^{2+}$ analytes [11]. 9-methylacridine-modified silica has also been synthesized to separate aromatic compounds [12]. Poly(ethyleneimine)-N-acetyl-L-phenylalanine-modified silica was synthesized and used to separate nitrogenous bases [13]. In addition, $NH_2$-modified silica has also been used to separate food coloring [14].

Vinyl trimethoxysilane (VTMS) is one of the silica surface modifying agents that has broad potential. Modification of silica using VTMS is growing because it has alkene groups that are quite reactive and can be further modified. Surface modification of silica using VTMS has the potential for superior hydrophobicity properties based on previous studies. In 2010, silica was synthesized using VTMS as a silica surface modifying agent to increase the affinity of inorganic particles with polymers through a two-stage synthesis [15]. FDU-VTMS mesoporous silica was successfully synthesized and used for immobilization of cellulase enzymes with an activity reaching 80% [16]. One of the uses of vinyl-modified silica has been to make superhydrophobic composites [7]. Silica modification using VTMS has also been done to test and evaluate the effect of organo-chain hydrophilicity on the silica surface using a water contact angle [17]. The selection of vinyl groups in this study is because they are hydrophobic so the modification of the silica surface using vinyl groups will produce a non-polar stationary phase. The vinyl-modified silica will then be used as a stationary phase to fill the HPLC column to separate the caffeine and paracetamol mixture. A mixture of caffeine and paracetamol is often found in drug samples, so to know the exact levels, vinyl will be used as a modifier of the silica surface as a stationary phase for HPLC column fillers.

In this study, vinyl-modified silica will be synthesized. The modified silica can be characterized using a Scanning Electron Microscope (SEM) to determine the surface morphology and Fourier Transform Infrared Spectroscopy (FTIR) to determine the functional groups formed. Various synthesis techniques will be tried to get the best results. The successfully synthesized vinyl-modified silica was then applied to the HPLC column to test its performance.

## 2 Method

The research was conducted at the Analytical Chemistry Laboratory, Chemistry Study Program, Faculty of Natural Sciences, Bandung Institute of Technology. The synthesis of vinyl-modified silica was carried out by first synthesizing silica by mixing solution A containing 7.5 mL of 25% (v/v) ammonia; 76.5 mL ethanol; 16 mL mineral-free water; and 0,036 grams of KCl solids in a 250 mL duran bottle. Then, solution B was prepared in a 50 mL beaker by mixing 5.5 mL of Triethyl Orthosilicate (TEOS) into 44.5 mL of ethanol. Solution B was then put into a 50 mL syringe and injected into solution A with the help of a syringe pump at a rate of 9.4 mL/hour while stirring using a magnetic stirrer at room temperature [18]. After solution B had been injected completely, the mixture of solution A and B in the duran bottle was continued to stir for 20 hours. Then, a modified solution was prepared by mixing 0.5 mL of VTMS with 2 mL of isopropyl alcohol. A mixture of 2.5 mL of the solution was then inserted into a 3 mL syringe and injected into the mix of solutions A and B every hour. This repetition was done for 5 hours. Furthermore, the mixture in a 250 mL bottle was rotated for 12 hours transferred to a centrifuge tube and centrifuged at 6,000 rpm for 15 minutes to precipitate the solids. The use of a speed of 6,000 rpm was carried out with the aim of better sedimentation, because if the speed used is smaller, sedimentation will be difficult and take longer. The solid obtained was then washed using ethanol three times and dried in a vacuum oven at 50$^{o}$C for 8 hours. The dried modified silica solids were then yielded and further characterized. Separation in this study was carried out using an Agilent 1260 Infinity II HPLC equipped with a Diode Array Detector (DAD).

## 3 Result and Discussion

The synthesis of vinyl-modified silica was carried out using TEOS as a precursor. The successfully synthesized silica was then modified using VTMS. Silica synthesis using TEOS precursor was carried out by injecting TEOS in ethanol solvent into a duran bottle containing a mixture of KCl, aqua dm, ammonia 25% (v/v), and ethanol solvent on a hotplate while stirring. TEOS in ethanol solvent was injected using a syringe pump with an injection speed of 9.4 mL/min. A syringe pump tool aims to make the resulting silica have a spheric and homogeneous shape. Ammonia acts as a catalyst and KCl serves to provoke core formation. The solvent used in this method has been optimized previously, using the same

method, the use of methanol, ethanol, and isopropanol solvents gives different morphological results and silica size. Based on **Fig. 1** the use of solvents affects the size of the resulting silica particles. SEM characterization results show that the use of ethanol solvents results in more homogeneous silica particles that has the largest size.

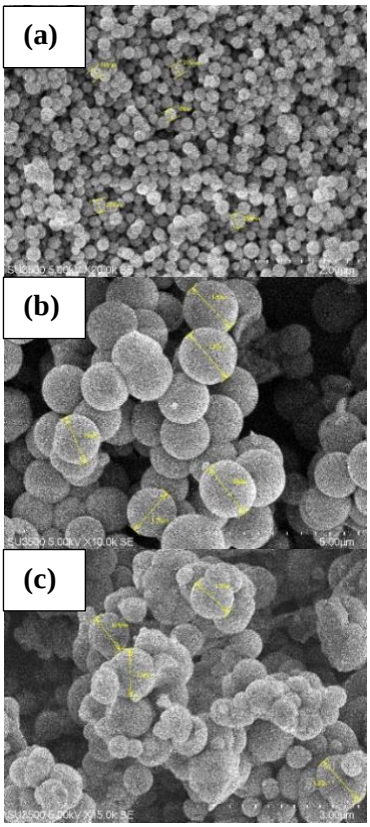


**Figure 1** SEM results of silica using solvents (a) methanol with a magnification of 20,000 times, (b) ethanol with a magnification of 10,000 times, and (c) isopropanol with a magnification of 15,000 times

According to SEM results, the use of methanol solvent for silica synthesis gives silica diameter size of 181 nm-254 nm; 1.73 µm-2.02 µm for the use of ethanol solvent; and 0.944 µm-1.02 µm for the use of isopropanol solvent. Thus, in this study, ethanol solvent was used to synthesize silica from TEOS precursor because it produces silica particles that have the largest and most homogeneous size. The use of methanol will create more nuclei due to the lack of steric hindrance between molecules. In the use of ethanol, ethanol has a larger size than methanol molecules so that there will be greater steric hindrance and create fewer nuclei. The addition of monomers will create a larger size. However, in the use of eluents that have longer chains, there will be a pile of nuclei due to greater steric hindrance, so that the particles are not spherical.

The reaction mechanism of silica formation begins with the hydrolysis of TEOS with the help of ammonia and water to form silanol monomers (Si-OH) by releasing several ethoxy groups ($-OC_2H_5$). Based on **Fig. 2**, the SN1 reaction occurs, namely $OH^-$ ions as nucleophiles will attack the Si center atom which has electrophilic properties to form less stable intermediate compounds. Thus, it will release the ethoxy group to form a silanol group.

The reaction will then proceed to the condensation stage to form a siloxane group (Si-O-Si) by releasing some water. Based on **Fig. 3**, the $Si-O^-$ group will act as a nucleophile and will attack other Si atoms that are electrophilic. Thus, a Si-O-Si bond will be formed.

After 20 hours of stirring, VTMS was added as a silica surface modifying agent. The vinyl group on VTMS will attach to the silica surface and produce hydrophobic silica. The reaction that occurs in this method is shown in **Fig. 4**.

Silica and vinyl-modified silica that have been obtained were characterized using FTIR and SEM. The results of characterization using FTIR are shown in **Fig. 5**. This characterization aims to see the functional groups of the resulting compounds.

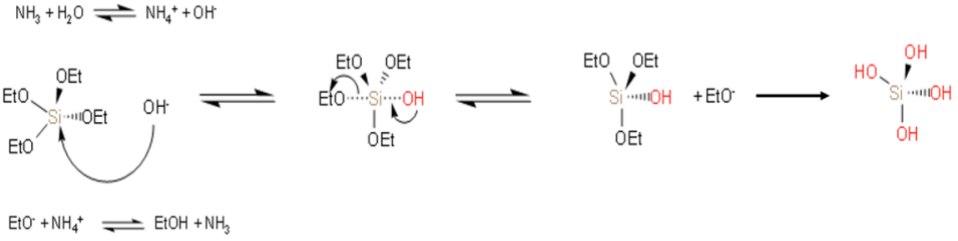


**Figure 2** Mechanism of silica-vinyl hydrolysis

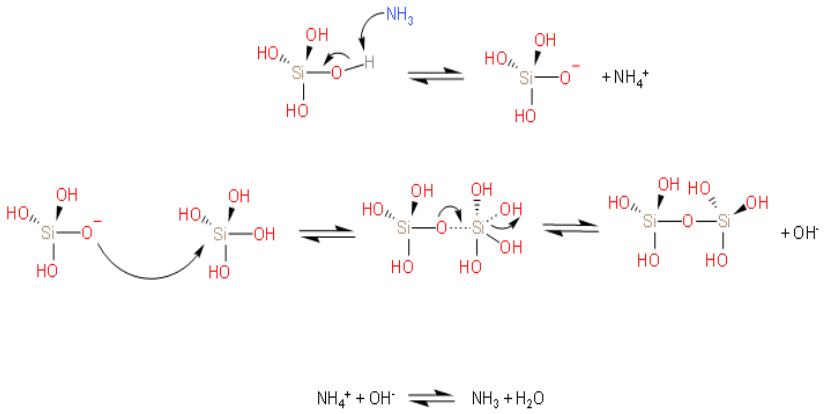


**Figure 3** Mechanism of silica-vinyl condensation

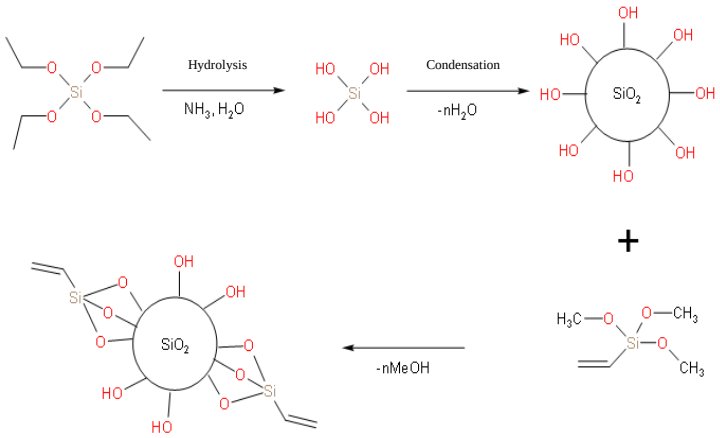


**Figure 4** Silica-vinyl synthesis reaction

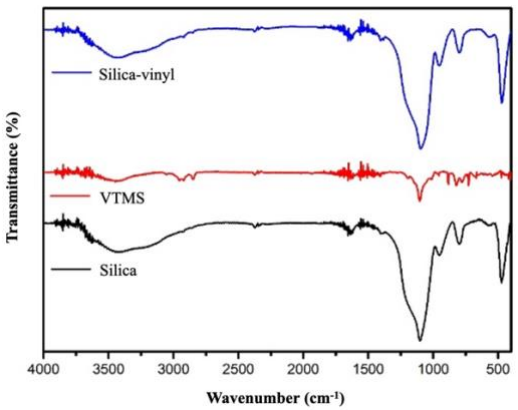


**Figure 5** FTIR spectrum of silica-vinyl

The results of characterization using FTIR gave good results, the synthesis of silica was successfully carried out with the appearance of the absorption peak (Si-O-Si) at a wave number of 1,095 $cm^{-1}$ which means that the condensation runs perfectly. The absorption of silanol groups (Si-OH) on the silica surface was also detected at 3,298 $cm^{-1}$ [19]. The synthesis of vinyl-modified silica was also successfully carried out with the appearance of C-H vibrations at wave numbers 2,850 $cm^{-1}$ and 2,922 $cm^{-1}$ in the silica-vinyl spectrum.

Qualitative tests were also carried out to prove the presence of vinyl attached to silica. Qualitative tests were carried out using an iodine solution added to silica and vinyl-modified silica. The negative sign in **Fig. 6** is an iodine solution added to unmodified silica. Meanwhile, the positive sign is an iodine solution added to vinyl-modified silica.

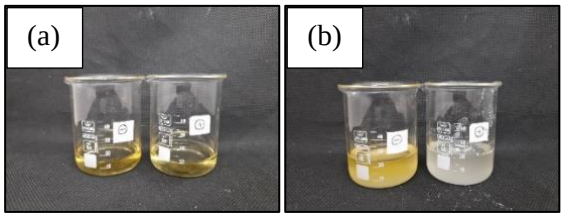


**Figure 6** Qualitative test using iodine solution, (a) iodine solution before treatment, (b) iodine solution after treatment

The solution to which vinyl-modified silica is added changes color from yellow to colorless. Based on the qualitative test using an iodine solution, the color change proves the presence of vinyl groups attached to the surface of the silica. Color change that occurs proves the presence of vinyl groups attached to the surface of the silica surface. The reaction of vinyl with iodine solution is shown in **Fig. 7**.

The successfully synthesized vinyl-modified silica is a white powder solid shown in **Fig. 8**. In addition to being characterized using FTIR, the resulting silica solids were also characterized using SEM. SEM characterization was carried out to determine the morphology and diameter of the resulting silica.

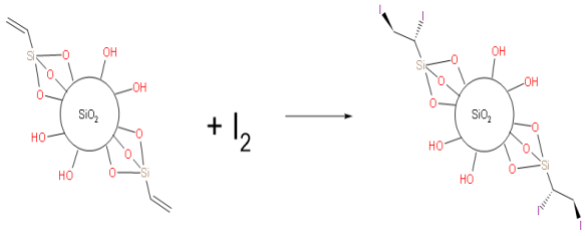


**Figure 7** Reaction of silica-vinyl with iodine solution

**Figure 8** Silica-vinyl

The results of silica characterization using SEM are shown in **Fig. 9** using a magnification of 5.000 times to 50.000 times. The resulting silica has a spheric shape and is quite homogeneous. In addition, the diameter of the silica is 1.73 µm to 2.02 µm. The size obtained in this method still does not reach the target size, which is around 4 µm to 6 µm like commercial silica.

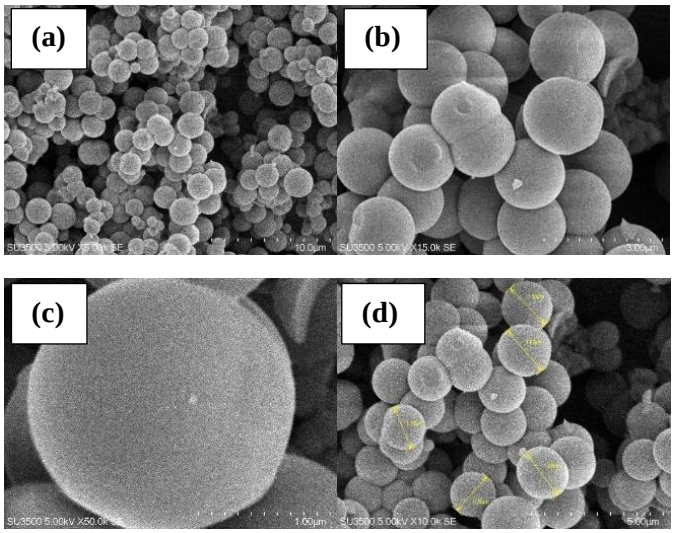


**Figure 9** SEM results of silica with (a) 5,000 times magnification, (b) 15,000 times magnification, (c) 50,000 times magnification, and (d) silica diameter size of 1.73 µm to 2.02 µm using 10,000 times magnification

The column used in this study is 50 mm x 4.6 mm. For loading a 50 mm x 4.6 mm column, approximately 2-3 grams of silica solids are needed. Silica solids before being included in the column were sonicated for 15 minutes first in methanol solvent. The purpose of this sonication is to break the solid into its smallest particles. After that, the silica was put into the column and pressurized to 30 MPa while flowing methanol. The purpose of this high pressure is so that the silica is put into a solid column and there are no gaps. In addition, in the use of a pressure of 30 MPa we consider that if the use of pressure below 30 MPa can cause cavities in the column because the pressure given is too small, while if the pressure given is too large it can cause the column

to expand. After the volume of methanol wasted reaches 100 mL. Loading is stopped, with methanol residues that have reached 100 mL, it is expected that the column has been filled with silica. Silica that was successfully packed in the column was then tested for performance using HPLC.

Testing of vinyl-modified silica columns was carried out using High-Performance Liquid Chromatography (HPLC) with a DAD detector. The selection of this detector was based on the compounds to be separated. Column performance tests were carried out by separating a mixture of

A 50 mm x 4.6 mm vinyl-modified silica column was tested. The eluents used were methanol, water, and a methanol-water mixture. **Fig. 10** shows the chromatogram results of the paracetamol-caffeine mixture using several eluent comparisons and a flow rate of 1 mL/min.

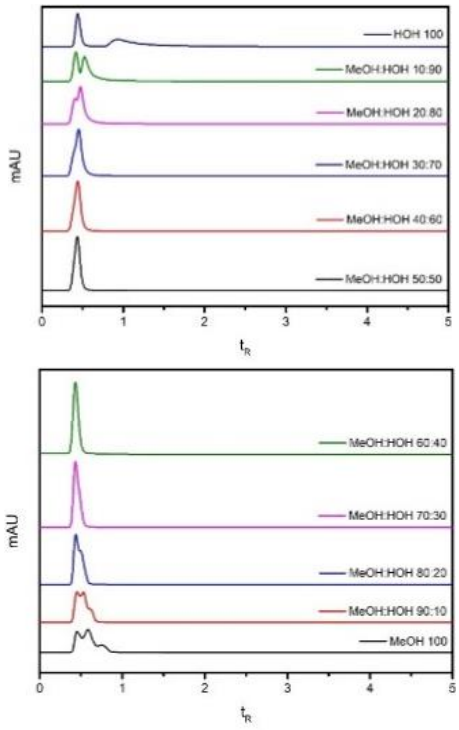


**Figure 10** HPLC chromatogram of caffeine-paracetamol mixture on 50 mm x 4.6 mm column; MeOH-HOH eluent; flow rate 1 mL/min; DAD detector; = 274nm

The chromatogram results obtained using a flow rate of 1 mL/min showed the separation of caffeine and paracetamol mixture peaks in the eluent methanol:water 20:80. At 100% water eluent, the peaks were completely separated. To determine the peaks of paracetamol and caffeine separately, a standard solution was tested using 100% water eluent, a flow rate of 1 mL/min, and a paracetamol and caffeine. Both compounds have chromophore groups which means they can absorb UV light. The DAD detector is based on the absorption of UV light by the sample. The sample injected was 20 µL. Tests were conducted at 274 nm and 246 nm which are the wavelengths for paracetamol and caffeine. Column testing and optimization were performed with eluent variation, eluent composition variation, and flow rate variation. Vinyl-modified silica used as a stationary phase for chromatography column filler is non-polar. Non-polar compounds will be strongly retained in the stationary phase.
column size of 50 mm x 4.6 mm. The results of the standard and mixed chromatograms are shown in **Fig. 11**.

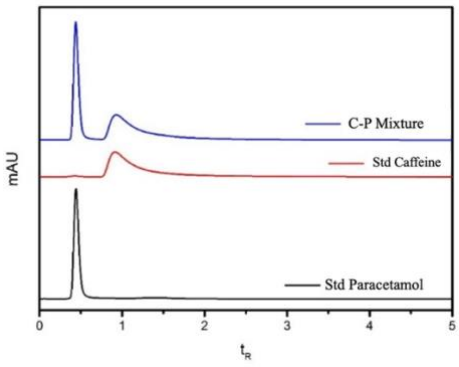


**Figure 11** HPLC chromatogram of caffeine-paracetamol mixture and standards on a 50 mm x 4.6 mm column; 100% HOH eluent; flow rate 1 mL/min; DAD detector; λ = 274nm

Paracetamol will be retained first compared to caffeine, this is because paracetamol has a more polar structure compared to caffeine. In this case, caffeine will be more retained in the column because caffeine has a more non-polar structure. Based on the chromatogram results obtained, caffeine gives a tailing peak. This is because the non-polar caffeine interacts quite strongly with the stationary phase used. So, to overcome this, optimization of the composition of the eluent and the flow rate used is carried out. However, the flow rate used in this study is the result of optimization between the particle size and the stationary phase that has been used.

Eluent optimization was carried out using 100% water and with the addition of a little methanol. The addition of methanol in this case aims to wet the column. A chromatogram of optimization results using eluent composition comparison is shown in **Fig. 12**. Based on the chromatogram that has been obtained, calculations are made to evaluate the performance of the column shown in **Table 1** and **Table 2**.

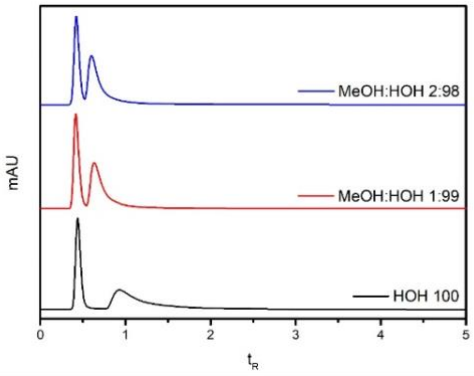


**Figure 12** Eluent optimization chromatogram for caffeine-paracetamol mixture; flow rate 1 mL/min; column size 50 mm x 4.6 mm; DAD detector; λ = 274 nm

**Table 1** Performance evaluation calculations using ω for various eluents

| Eluent | Resolution | N paracetamol | N caffeine | Selectivity |
|---|---|---|---|---|
| HOH 100 | 2.20 | 727.59 | 95.38 | 2.12 |
| MeOH:HOH 1:99 | 1.80 | 596.42 | 216.96 | 1.52 |
| MeOH:HOH 2:98 | 1.57 | 632.08 | 226.32 | 1.42 |

**Table 2** Performance evaluation calculations using $\omega_{1/2}$ for various eluents

| Eluent | Resolution | N paracetamol | N caffeine | Selectivity |
|---|---|---|---|---|
| HOH 100 | 2.20 | 1,007.71 | 132.10 | 2.12 |
| MeOH:HOH 1:99 | 1.80 | 826.04 | 300.49 | 1.52 |
| MeOH:HOH 2:98 | 1.57 | 875.43 | 313.45 | 1.42 |

The calculation results were obtained using ω and $\omega_{1/2}$, the calculation using $\omega_{1/2}$ gives better results. This is due to the presence of tailing peaks in caffeine, causing the value of ω to increase. The selection of the use of $\omega_{1/2}$ because the resulting caffeine peak looks like there is tailing which causes a broadening of the base peak. So to get a better parameter value, the calculation is done using $\omega_{1/2}$. Based on the calculation using $\omega_{1/2}$, the methanol:water 1:99 eluent gave the best result. This is because in 100% water eluent, good resolution, and selectivity values are produced. However, the ω value or peak width of caffeine produced was very wide, causing the number of theoretical plates for caffeine to be very small. Therefore, 1:99 methanol:water eluent was used which gave better results with a resolution value of 1.80; and selectivity of 1.52; in addition, the number of theoretical plates for paracetamol and caffeine was 826.04 and 300.49. HETP values were also calculated using $\omega_{1/2}$ for each analyte, the HETP value for paracetamol was 0.060 mm and 0.166 mm for caffeine.

Further optimization was carried out using flow rate variations. The flow rates used were 1 mL/min; 0.7 mL/min; and 0.5 mL/min. The chromatogram results obtained for the mixture of caffeine and paracetamol are shown in **Fig. 13** with the eluent used methanol:water 1:99 and column size 50 mm x 4.6 mm. The results of calculations to evaluate column performance are also shown in **Table 3** and **Table 4**.

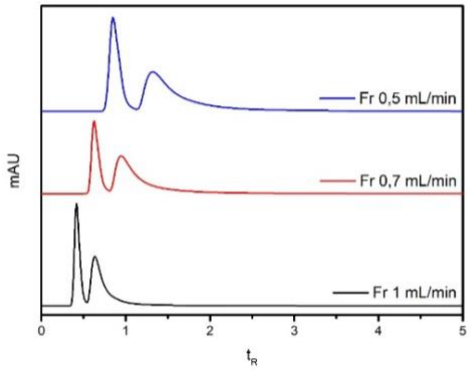


**Figure 13** Eluent optimization chromatogram for caffeine-paracetamol mixture; eluent methanol:water 1:99; column size 50 mm x 4.6 mm; DAD detector; λ = 274 nm

**Table 3** Performance evaluation calculations using ω for various flow rates

| Eluent | Resolution | N paracetamol | N caffeine | Selectivity |
|---|---|---|---|---|
| 1 mL/min | 1.80 | 596.42 | 216.96 | 1.52 |
| 0.7 mL/min | 1.62 | 762.35 | 153.9 | 1.51 |
| 0.5 mL/min | 1.45 | 662.63 | 138.30 | 1.47 |

**Table 4** Performance evaluation calculations using $\omega_{1/2}$ for various flow rates

| Eluent | Resolution | N paracetamol | N caffeine | Selectivity |
|---|---|---|---|---|
| 1 mL/min | 1.80 | 826.04 | 300.49 | 1.52 |
| 0.7 mL/min | 1.62 | 1,055.85 | 213.15 | 1.51 |
| 0.5 mL/min | 1.45 | 917.75 | 191.56 | 1.47 |

The calculation results were obtained using ω and $\omega_{1/2}$, the calculation using $\omega_{1/2}$ gives better results. This is because the slower the flow rate used, the peak width (ω) for caffeine widens, so the number of theoretical plates for caffeine decreases. Based on the calculation results, the use of a flow rate of 1 mL/min gives the best results. This is because the use of a flow rate of 1 mL/min provides the greatest resolution and selectivity values. In addition, the number of theoretical plates for caffeine gave the greatest results when using a flow rate of 1 mL/min. The resolution value of the separation of the caffeine and paracetamol mixture using a flow rate of 1 mL/min was 1.80 and the selectivity value was 1.52. The theoretical number of plates for paracetamol using $\omega_{1/2}$ calculation was 826.04 and for caffeine was 300.49. Based on the calculation of the number of theoretical plates, the HETP value for paracetamol is 0.060 mm for paracetamol and 0.166 mm for caffeine.

The results of optimization calculations that have been carried out can be seen in Appendix B, which obtained the optimum situation in the eluent methanol: water 1: 99 with a flow rate of 1 mL/min. The column used was 50 mm x 4.6 mm with the use of a DAD detector and the wavelength used was 274 nm. Thus, standard measurements were carried out using a mixed solution of paracetamol and caffeine with a concentration of 20 ppm to 100 ppm, the chromatogram obtained is shown in **Fig. 14**.

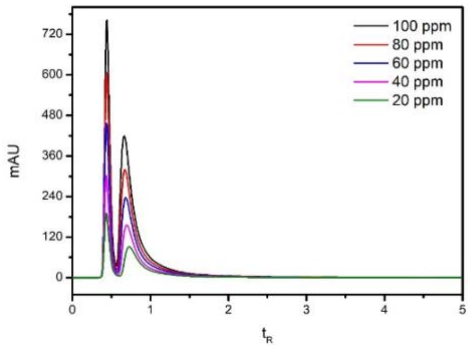


**Figure 14** Standard chromatogram for caffeine-paracetamol mixture; flow rate 1 mL/min; eluent methanol:water 1:99; column size 50 mm x 4.6 mm; DAD detector; λ = 274 nm

In addition, a standard calibration curve was determined by plotting the area value against the standard concentration. The resulting area is proportional to the concentration of the analyte used. An $R^2$ value of 0.99431 for paracetamol and 0.99156 for caffeine was obtained. The resulting calibration curve is shown in **Fig. 15**. **Table 5** is a comparison of the results of research that has been conducted with previous research.

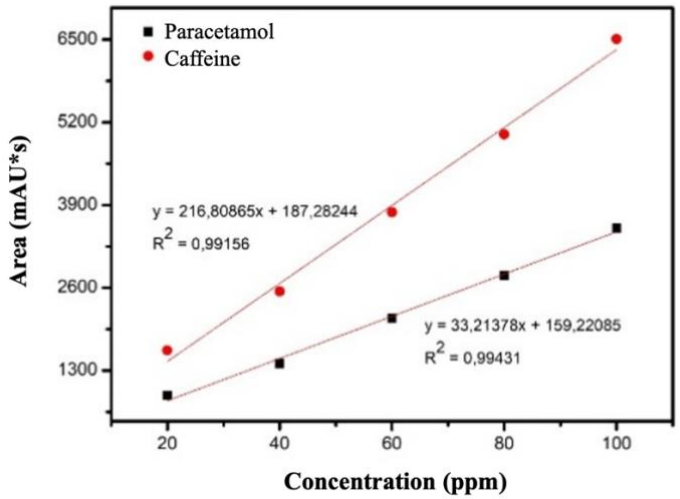


**Figure 15** Standard calibration curve for caffeine-paracetamol mixture; flow rate 1 mL/min; eluent methanol:water 1:99; column size 50 mm x 4.6 mm; DAD detector; λ = 274 nm

**Table 5** Comparison with previous research

| Analyte | Column | $t_R$ Paracetamol | $t_R$ Caffeine | Resolution | Selectivity | Ref. |
|---|---|---|---|---|---|---|
| **Paracetamol-caffeine** | C18 column (5 µm; 150 mm × 4.6 mm) | 2.63 | 3.49 | 4.73 | 1.32 | [20] |
| **Paracetamol-caffeine** | C18 column (5µm; 250 mm x 4.5 mm) | 3.13 | 3.83 | 7.2 | 1.22 | [21] |
| **Paracetamol-caffeine** | C8 column (5 µm; 250 mm x 4.6 mm | 4.480 | 5.84 | 6.433 | 1.54 | [22] |
| **Paracetamol-caffeine** | Vinyl column (2 µm; 50 mm x 4.6 mm) | 0.441 | 0.66 | 1.8 | 1.52 | This Work |

Based on **Table 5**, it is obtained information that the use of different column lengths will produce different retention time values. The longer the column used, the higher the retention time and resolution. Based on a comparison with previous studies, this study has good potential in the separation of paracetamol from caffeine because it has a selectivity that is almost similar to the use of commercial C-18 and C-8 columns.

## 4 Conclusion

The synthesis of silica and modified silica was successfully carried out. The synthesis of vinyl-modified silica gave good results based on the size and morphology of the silica particles. The synthesis of vinyl-modified silica was successful with the appearance of Si-O-Si absorption peak at wave number 1,095 $cm^{-1}$ and C-H vibrations at wave numbers 2,850 $cm^{-1}$ and 2,922 $cm^{-1}$ in the FTIR spectrum. SEM results show that the silica is spheric and homogeneous with a silica particle diameter size of 1.73 – 2.02 µm. However, this size still does not reach the target size. The synthesized silica-vinyl as column filler stationary phase can separate paracetamol and caffeine mixture with optimum conditions at MeOH:HOH = 1:99 eluent; flow rate of 1 mL/min; and column size of 50 mm x 4.6 mm.

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