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Assessment of Metformin Stability and Its Removal from Water by Pumice-Based Zeolite

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Abstract: Metformin (MET) is an emerging contaminant often found in aquatic environments due to incompletely metabolized after consumption in the human body, where some of its doses are excreted in unchanged form through urine or faeces. The research aims are to study MET stability in water and to evaluate the potential of pumice-based zeolite for treating MET contaminants. Zeolites were prepared from pumice via the hydrothermal treatment and characterized using Fourier Transform Infrared (FTIR) and X-Ray Diffraction (XRD). A simple spectrophotometric method was proposed for determining the stability of MET in aqueous solution with several different conditions. The result showed that the metformin solution was unstable under strong acid conditions (pH 2), marked by the loss of the maximum absorption peak in the 220-250 nm range. The stable metformin conditions in this study were obtained at the pH of solutions ranging from 6 to 10 and temperatures between 14 °C to 40 °C. Furthermore, the stability of MET can be maintained for up to 3 days of exposure time. Based on the adsorption result, zeolite uptake capacity (196 µg/g) was higher than pumice (87 µg/g) to reduce metformin concentration. In addition, the synthesized zeolite needs further modification to increase its adsorption performance.

Keywords: Adsorption; Environmental Sciences; Metformin; Pumice; Zeolite

Introduction

Metformin, known as dimethyl-biguanide, is one of the anti-diabetic drugs that have been shown to be effective in the treatment of type 2 diabetes mellitus, polycystic ovary syndrome (PCOS), and different types of cancer (Triggle et al., 2022). Due to its effectiveness, metformin became the most frequently prescribed drug consumed by 150 million people annually (Bojanić et al., 2023; Salovska et al., 2023; Sayedali et al., 2023). Approximately 70% of metformin dosages are excreted as an unchanged form through urine or faeces because of poorly absorbed in the human body (Rebecca et al., 2023). The previous research by Oosterhuis et al. (2013) reported metformin concentrations in domestic wastewater ranging from 64–98 µg/L, while its biodegradation product (guanylurea) was detected at concentrations of 1.8–3.9 µg/L in surface waters. Another research conducted by Kim et al. (2023) also found the presence of metformin not only in wastewater effluents but also in surface waters. Although in relatively small concentrations, metformin significantly impacts aquatic ecosystems due to its potential as an endocrine disruptor and becomes an emerging contaminant in the aquatic environment (Adegoke et al., 2022; Gu et al., 2023; Sousa et al., 2023; Wu et al., 2023).

Several conventional methods have been used for the treatment of metformin contaminants in wastewater, such as adsorption, biological processes using activated sludge, and advanced oxidation processes (AOPs), including ozonation, Fenton reaction, and UV photocatalysis (Balakrishnan et al., 2022). The biological process using activated sludge is unable to remove active pharmaceutical compounds (PACs) completely

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(Martinez-Alcala et al., 2017) meanwhile, AOPs by ozonation and UV photocatalysis consume high energy, which makes the process costly (Fast et al., 2017; Liu et al., 2020). As an alternative, adsorption has been considered a dependable method and is mostly recommended by experts to eliminate PACs from surface waters due to the simple process, inexpensive, and ease of operation (El-Fattah et al., 2023; Nuri et al., 2019). The most extensively used adsorbent is activated carbon because of is extremely effective for the treatment of PACs, including metformin (Ratnam et al., 2023; Kalumpha et al., 2020).

Activated carbon has a large pore size with an amorphous structure and several functional groups containing various heteroatoms, such as phosphorus, nitrogen, sulfur, hydrogen, and oxygen, depending on raw material types (Demiral et al., 2021). These functional groups contribute to the adsorption properties of activated carbon for binding organic or inorganic matters. A very intriguing study by Kalumpha et al. (2020) has demonstrated that activated carbon prepared from *zea mays* could be used for metformin removal with an efficiency of as much as 94%. Nevertheless, the limited availability of raw material sources and high energy consumption for synthesis, activation, and regeneration are the weaknesses of activated carbon as an adsorbent, making it difficult to be applied on a large scale (Wan Ibrahamin et al., 2021; Moosavi et al., 2020). Therefore, it is necessary to further explore the potential of natural materials with abundant availability as adsorbents for eliminating metformin from water.

One of the natural materials that has the potential to be developed as an adsorbent is pumice. The availability of pumice in Indonesia is abundant because of its location in the pacific ring of Fire region. The previous study has reported that the major compositions of pumice are SiO_2 and Al_2O_3, which can be used as starting materials for synthesizing zeolite (Toktamış, 2023; Prajaputra et al., 2021). A study by Prajaputra et al. (2019) has demonstrated the capability of pumice-based zeolite from Indonesia as a methylene blue adsorbent resulting in high percentage removal compared to pumice after adsorption and degradation processes. To the best of our knowledge, no study focused on using pumice-based zeolite to eliminate drug contaminants in water, such as metformin, especially in Indonesia. Hence, the potential of this material is still unknown. Thus, in the present study, the performance of pumice-based zeolite from Indonesia for treating metformin in aqueous solution was investigated. Metformin stability was evaluated first using several different conditions, including pH, temperature, and exposure time.

Method

Materials

Pumice samples were obtained from Suwung, located in Bali, Indonesia. According to Prajaputra et al. (2021), pumice from Suwung contains SiO_2 and Al_2O_3 as much as 63.45% and 17.24%, respectively. The collected sample was dried and crushed using a standard sieve of 100 mesh. It was then used as starting material for the synthesis of zeolite with the schematic procedure displayed in Figure 1. Metformin ($C_4H_{11}N_5$) and sodium hydroxide (NaOH) were two chemicals obtained from chemistry laboratory at Universitas Syiah Kuala.

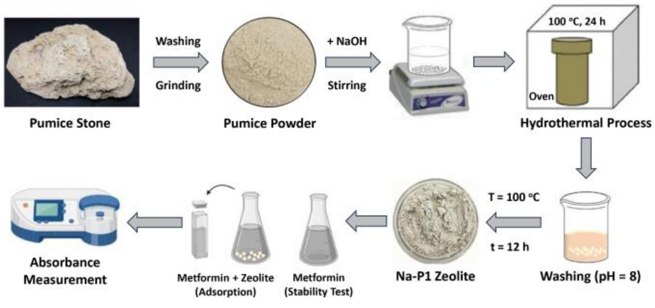

Figure 1. The schematic procedure of zeolite synthesis

Preparation of MET Solution and Stability Test

Metformin stock solution with a concentration of 50 mg/L was prepared by dissolving as much as 5 mg of metformin in 100 mL of distilled water. This solution was then diluted into several concentrations (2, 4, 6, 8, and 10 mg/L). The maximum wavelength of metformin was determined by scanning the absorbance of a ten mg/L metformin solution in the 220–400 nm range using a UV-Vis spectrophotometer.

The stability test of metformin solution with a concentration of 10 mg/L was carried out in several test tubes under different conditions, including pH (2, 6 and 10) and temperature (14 ^oC, 28 ^oC, and 40 ^oC) with exposure time for three days. The final concentrations for each condition were measured using a UV-Vis spectrophotometer. Metformin solution was considered stable if the maximum absorption peak formed was similar to the maximum absorption peak before the treatment process and the concentration was insignificantly changed.

Synthesis of Pumice-Based Zeolite

The synthesis of pumice-based zeolite was carried out using a simple hydrothermal treatment, according to the previous study conducted by Prajaputra et al. (2021). In general, a number of 10 g pumice was mixed with 80 mL of 3.0 M NaOH solution in a microwave container. The mixture was stirred for 30 minutes under tightly closed conditions and then heated using a dried oven at 100 ^{o}C for a day. After that, the solid phase was separated and rinsed several times with distilled water until the pH of the solution was 8. The solid phase was heated again at 100 ^{o}C for 12 hours to obtain zeolite crystals, then characterized using FTIR and XRD.

MET Adsorption Test

The adsorption test was conducted to evaluate the ability of pumice-based zeolite to eliminate metformin in an aqueous solution. About 50 mg of zeolite was put into a test tube containing 10 mL of metformin solution with different concentrations (2, 4, 6, 8, and 10 mg/L). The adsorption process was taken 3 hours. Then, the mixture was centrifuged at 4000 rpm for 5 minutes before measuring the final concentration with a UV-Vis spectrophotometer. Based on Equation 1, zeolite uptake capacity (qe, in mg/g) to eliminate metformin was calculated.

$$q_e = \frac{C_0 - C_e}{\mathrm{m}} \ v \qquad (1)$$

Where C_0 is the initial concentration of metformin (mg/L), C_e is the final concentration of metformin in equilibrium condition (mg/L), m is the adsorbent dosage (g), and v is the volume of solution (L).

Result and Discussion

Effect of pH and Temperature on MET Stability

The first parameter that we investigated is pH because it plays an important role in determining the stability of chemical compounds in solution. Metformin solution has an initial pH of 6 with a maximum wavelength at 233 nm which was determined using a UV-Vis spectrophotometer. We used this maximum wavelength to prepare the standard metformin curve through a linear correlation between absorbance and concentration, resulting in good linearity with a correlation coefficient value of 0.9979. For investigating the effect of pH on metformin solution stability, the initial pH of metformin was adjusted to 2 and 10 by adding a few drops of HCl or NaOH.

Metformin spectra at pH 2, 6, and 10 are shown in Figure 2. Based on the spectra, metformin solutions at pH 6 and 10 had an absorption peak in the region of 220–250 nm, which was the characteristic peak of metformin. After changing the pH of the metformin solution to 10, the final metformin concentration still exhibited a similar result to the initial metformin concentration. A study by Majithia et al. 2020 also found a metformin absorption peak in the range of 220–250 nm with a maximum wavelength of 233 nm. However, the absorption peak became unobserved when the pH was adjusted to a high acid condition, especially at pH 2. This condition affected the metformin concentration, which decreased significantly from 10 mg/L to 2.64 mg/L. We suspected that the structure of metformin would be in a protonated form under highly acidic conditions starting from the two amino groups so that the characteristic of metformin absorption peak became undetected.

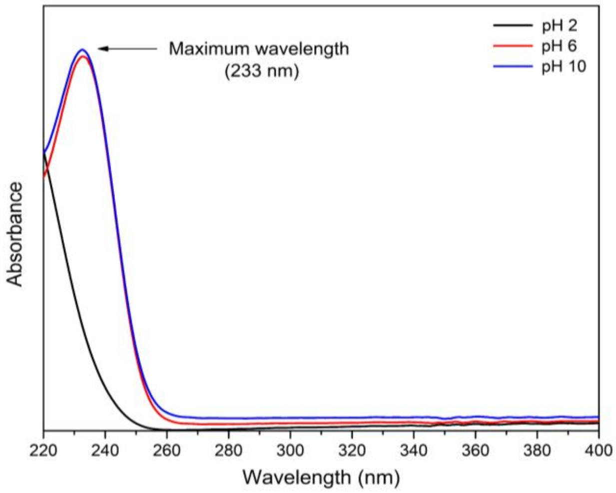

Figure 2. Effect of pH on MET stability (C_0=10 mg/L, T=28 ^{o}C, pH=6)

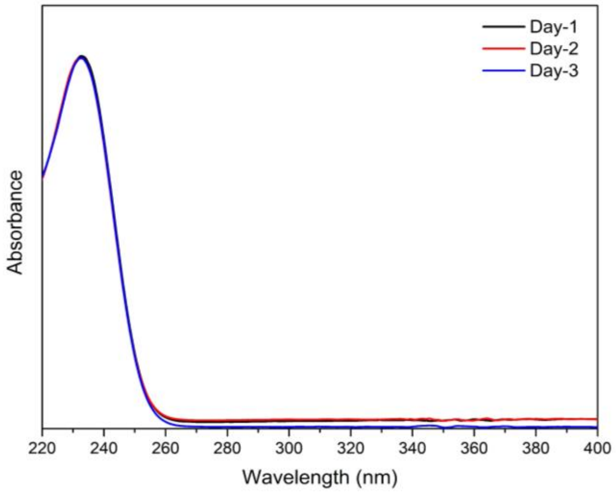

Figure 3. Effect of time exposure on MET stability (C_0=10 mg/L, T=28 ^{o}C, pH=6)

The next parameter to determine the stability of metformin in solution is a time exposure. The effect of time on metformin solution (pH 6) was investigated for 1, 2 and 3 days at room temperature (28 ^{o}C). Figure 3 displays the absorption spectra of metformin for several days. In general, all of the obtained spectra have similar absorption peaks. It can be assumed that the metformin solution remained in stable condition until the third day.

Temperature becomes the last parameter used to determine the stability of metformin. Metformin solution has an initial temperature of 28 ^{o}C at room condition. This temperature was then adjusted to 14 ^{o}C and 40 ^{o}C by entering metformin solution into a refrigerator and a small oven, respectively. Each solution was left for three days. The comparison of metformin absorption spectra at 14 ^{o}C, 28 ^{o}C and 40 ^{o}C is displayed in Figure 4. The results indicate that metformin solutions were stable at 14 to 40 ^{o}C because of the similar formation of absorption peak. This result was also supported by Sharma et al. (2010), which reported metformin was stable in water at temperatures between 30 ^{o}C to 80 ^{o}C and only degraded about 10% for more than eight days.

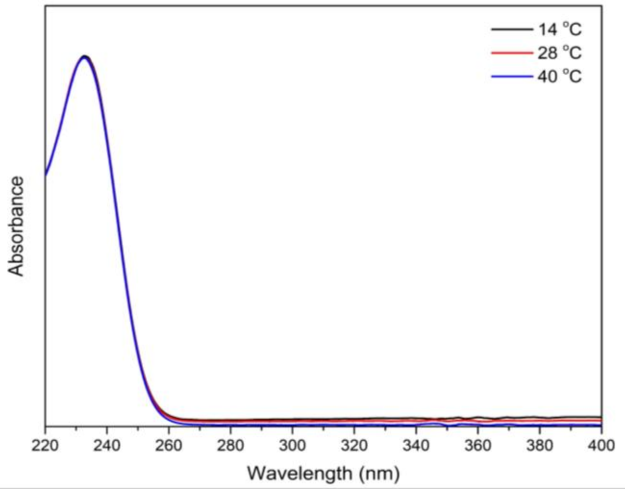

Figure 4. Effect of temperature on MET stability (C_0=10 mg/L, t=3 days, pH=6)

Material Characterization

Figure 5 shows the XRD patterns for both samples. These findings confirmed that the mineral phases of the pumice samples were significantly altered after the alkaline addition. The XRD pattern of a pumice sample shows that it is predominantly composed of amorphous elements with no obvious peaks. However, the pumice sample treated with alkaline solution and then subjected to a hydrothermal process successfully generated peaks at 12.46^{o}, 17.66^{o}, 21.67^{o}, 28.10^{o}, 33.38^{o}, 38.01^{o}, 42.2^{o}, and 46.08^{o}, which are characteristic of Na-P1 zeolite with a crystallinity percentage of 55.28%. Na-P1 zeolite phases with 2θ degree = 12.46^{o}, 17.66^{o}, 21.67^{o}, 25.08^{o}, 28.10^{o}, 30.84^{o}, 35.76^{o}, 38.01^{o}, 40.15^{o}, 42.20^{o}, 44.18^{o}, 46.08^{o}, and 49.72^{o} from the International Zeolite Association (IZA) are used for comparison and confirmation.

Figure 6 shows the FT-IR spectra of both materials from 500 cm^{-1} to 4,000 cm^{-1}. Peaks at 720 cm^{-1}, 1000 cm^{-1}, 1650 cm^{-1}, and 3475 cm^{-1} have been attributed to the bending vibration of Si-O-Si bonds, symmetric stretching vibration of Si-O-Si in $(SiO_4)^{2-}$ groups as a characteristic peak, bending vibration of H-O-H bonds, and asymmetric stretching vibration of O-H bonds, respectively, in the pumice sample.

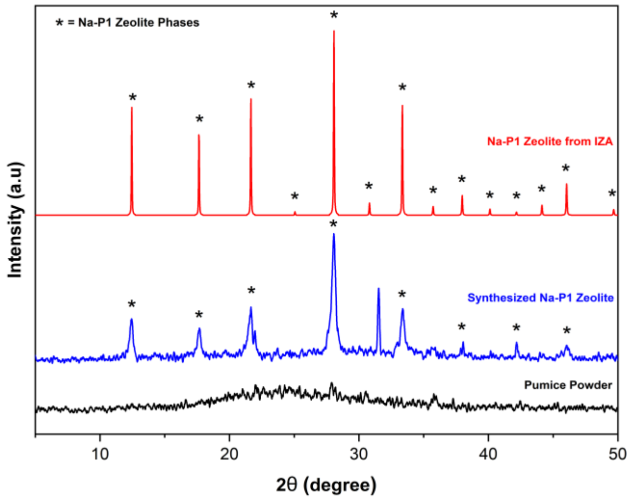

Figure 5. Na-P1 zeolite and pumice XRD patterns

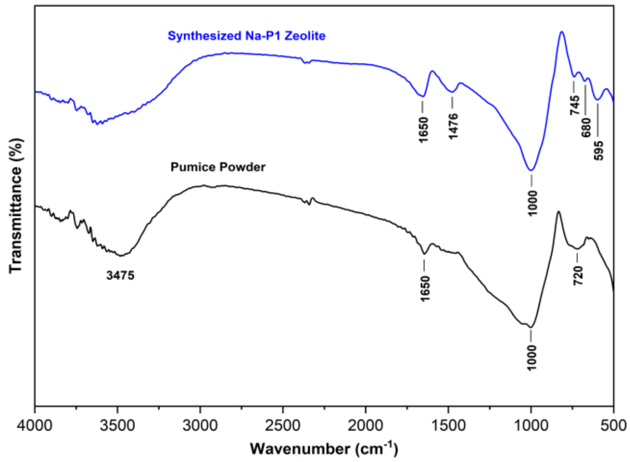

Figure 6. Na-P1 zeolite and pumice FTIR spectra

MET Adsorption Test

The ability of pumice and zeolite was tested to eliminate 10 mL of metformin solution (pH 6) with a concentration of 10 mg/L for 3 hours at room temperature. Figure 7a shows the adsorption capacity of both samples and their absorption spectra after the adsorption process (Figure 7b). The results proved that pumice has less adsorption capacity than zeolite to uptake metformin from the solution. It can be related to the presence of impurities which further affect the active side of pumices. This argument is supported by the previous study that reported the initial pumice containing some impurities and low adsorption capacity (Ersoy et al., 2010). When pumice was converted to zeolite, new silanol groups were formed and directly increased the active side on its surface. Therefore, zeolite was able to eliminate metformin better than pumice. The uptake capacities of pumice and zeolite were about 0.087 mg/g and 0.196 mg/g, respectively.

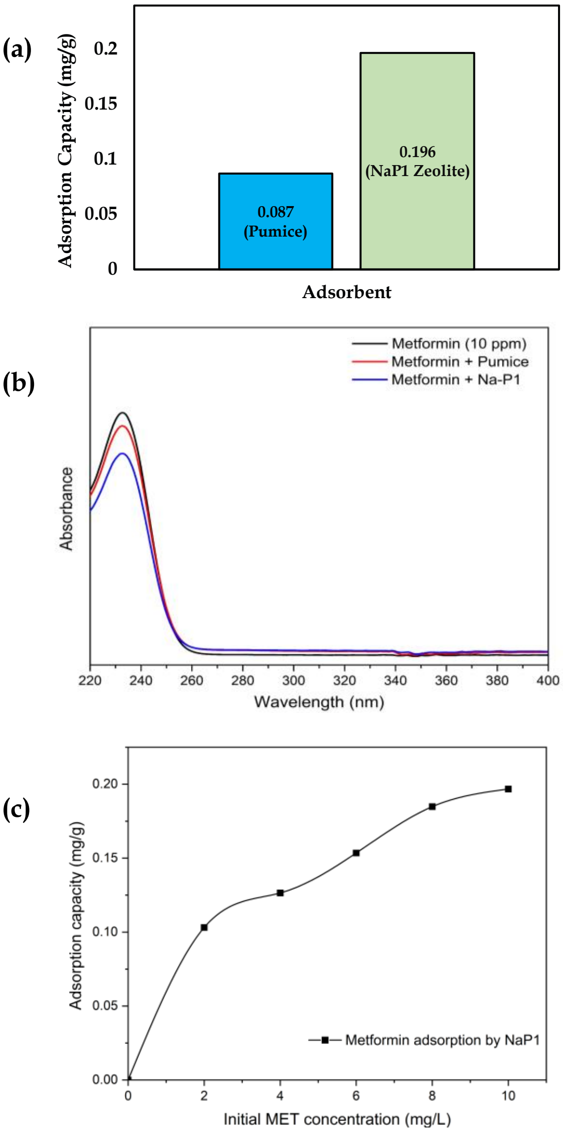

Figure 7. (a) the adsorption capacity of pumice and zeolite, (b) the change in absorption spectra, and (c) the effect of MET concentration on Na-P1 zeolite adsorption capacity

The effect of initial metformin concentration was carried out in several metformin concentrations from 2-10 mg/L using the synthesized zeolite. The results are shown in Figure 7c. From the figure, it can be seen that the uptake capacity increased with increasing the initial concentration. Insignificant improvement began to be seen in the concentration range of 8 to 10, with uptake capacities of 0.185 mg/g and 0.196 mg/g, respectively.

Equilibrium Study

Two isotherm models, such as Freundlich and Langmuir, are investigated to study the metformin adsorption process on the adsorbent. The Freundlich isotherm model uses the heterogeneous surfaces of adsorbent; in contrast, the Langmuir isotherm model uses homogeneous surfaces. Both isotherm models can also be used to describe whether the adsorption process occurs physically or chemically. The linear form of Langmuir and Freundlich models was expressed in Equations 2 and 3.

Langmuir equation model:

$$\frac{C_e}{q_e} = \frac{C_e}{q_m} + \frac{1}{k_L \cdot q_m} \tag{2}$$

Freundlich equation model:

$$\log q_e = \frac{1}{n} \log C_e + \log k_F \tag{3}$$

Where q_m is the adsorption capacity in maximum condition (mg/g), k_L is Langmuir equilibrium constant (L/g), k_F is Freundlich equilibrium constant (L/g), and n is Freundlich exponent.

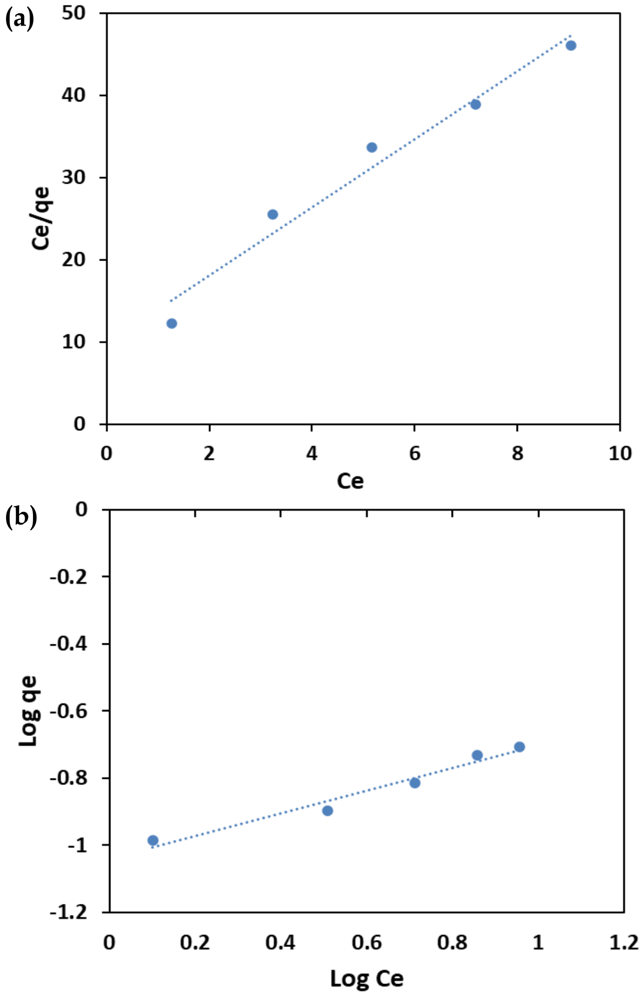

Figure 8. Adsorption isotherm models of (a) Langmuir and (b) Freundlich

The equilibrium study of metformin adsorption onto zeolite prepared from pumice was carried out by mixing 50 mg of zeolite in 10 mL of metformin solution with several concentrations of 2–10 mg/L (pH 6) at room temperature for 3 hours. After that, the final metformin concentrations were measured. Figure 8 shows the adsorption isotherm curve of the Langmuir and Freundlich models. It can be seen that the correlation coefficient value (R2) of the Langmuir equilibrium model (0.9682) was higher than the Freundlich equilibrium model (0.9648). The maximum adsorption capacity (qm) value was obtained at about 241 µg/g. This result suggested that the adsorption mechanism of metformin onto zeolite was physical interaction on homogeneous surfaces. The effectiveness of zeolite in reducing the concentration of metformin can still be improved, especially by varying the pH, adsorbent dose, and time in the adsorption test. Therefore, the ability of zeolites to remove metformin still needs to be studied further using these parameters so that the best conditions can be obtained with a much higher percentage of metformin removal.

Conclusion

A simple method for determining metformin stability in solution using a UV-Vis spectrophotometer and its adsorption onto zeolite prepared from pumice have been investigated. Stable conditions of metformin solution were obtained at the range pH of 6-10 and temperature between 14-40 °C. Metformin stability in a solution can be maintained up to 3 days of exposure time; however, this drug was unstable under high acid conditions. Zeolite was able to eliminate metformin from the solution with an uptake capacity of 196 µg/g, while pumice was only about 87 µg/g. Although zeolite exhibited a good adsorption ability compared to pumice, further modification was required to enhance the adsorption ability of zeolite. The equilibrium model was well described by the Langmuir model (R^2=0.9682) and proved that the adsorption process was physical interaction on homogeneous surfaces.

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Author Contributions

Vicky Prajaputra: Conceptualization, Methodology, Analysis and Drafting. Nadia Isnaini: Validation, Writing, Review and Editing.

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Conflicts of Interest

All authors state that they have no known competing personal relationships or financial interests that could have appeared to influence the work reported in this article.

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