

Metformin and Its Removal From Water

Aragaw Delele Endeshaw (mantekiru09@gmail.com)
Injibara University, College of Social Science and Humanities, Ethiopia

Abstract

Metformin (MET) is an emerging pollutant that is frequently discovered in aquatic ecosystems because it is incompletely digested after absorption in the human body, with some dosages discharged in unaltered form through urine or feces. The study's goals are to investigate MET stability in water and to assess the possibility of pumice-based zeolite for treating MET pollutants. The hydrothermal process was used to create zeolites, which were then characterized using Fourier Transform Infrared (FTIR) and X-Ray Diffraction (XRD). A simple spectrophotometric approach for assessing the stability of MET in aqueous solution under various circumstances was proposed. The metformin solution was shown to be unstable in strong acid conditions (pH 2), as evidenced by the loss of the greatest absorption peak in the 220-250 nm range. The stable metformin conditions in this investigation were established at pH levels ranging from 6 to 10 and temperatures ranging from 14 to 40 degrees Celsius. Furthermore, MET stability can be maintained for up to three days of exposure. According to the adsorption results, zeolite absorption capacity (196 g/g) was greater than pumice uptake capacity (87 g/g) in reducing metformin concentration. Furthermore, the produced zeolite requires further modification to improve its adsorption ability.

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

Introduction

Metformin, also known as dimethyl-biguanide, is an anti-diabetic medication that has been proven to be beneficial in the treatment of type 2 diabetes, polycystic ovarian syndrome (PCOS), and certain cancers (Triggle et al., 2022). Metformin has become the most commonly prescribed medicine, with 150 million individuals using it each year as a result of its effectiveness (Bojani et al., 2023; Salovska et al., 2023; Sayedali et al., 2023). Because metformin is poorly absorbed in the human body, approximately 70% of doses are eliminated as an unaltered form through urine or feces (Rebecca et al., 2023). Oosterhuis et al. (2013) previously observed metformin concentrations in home wastewater ranging from 64 to 98 g/L, whereas its biodegradation product (guanyurea) was detected at 64 g/L.

Surface water concentrations were from 1.8 to 3.9 g/L. Kim et al. (2023) discovered metformin not only in wastewater effluents but also in surface waters in their research. Metformin has a substantial impact on aquatic ecosystems due to its potential as an endocrine disruptor, and it has emerged as an emergent pollutant in the aquatic environment (Adegoke et al., 2022; Gu et al., 2023; Sousa et al., 2023; Wu et al., 2023).

Adsorption, biological techniques using activated sludge, and advanced oxidation processes (AOPs) such as ozonation, Fenton reaction, and UV photocatalysis have all been utilized to remove metformin pollutants in wastewater (Balakrishnan et al., 2022). The biological method using activated sludge is incapable of completely removing active pharmacological chemicals (PACs).

Martinez-Alcala and colleagues (2017) Meanwhile, ozonation and UV photocatalysis require a lot of energy, which makes the process expensive (Fast et al., 2017; Liu et al., 2020). Adsorption, as an alternative, has been regarded as a reliable technology and is widely recommended by experts to remove PACs from surface waters due to its simple process, low cost, and convenience of operation (El-Fattah et al., 2023; Nuri et al., 2019). Because it is particularly effective for the treatment of PACs, including metformin, activated carbon is the most widely employed adsorbent (Ratnam et al., 2023; Kalumpha et al., 2020).

Depending on the raw material, activated carbon has a wide pore size, an amorphous structure, and many functional groups including various heteroatoms such as phosphorus, nitrogen, sulfur, hydrogen, and oxygen (Demiral et al., 2021). These functional groups contribute to activated carbon's adsorption characteristics for binding organic or inorganic materials. A fascinating study by Kalumpha et al. (2020) indicated that activated carbon generated from zea mays could be used for metformin elimination with up to 94% efficiency. Nonetheless, the restricted availability of raw material sources, as well as the high energy consumption for synthesis, activation, and regeneration, are the limitations of activated carbon as an adsorbent, making it difficult to apply on a broad scale (Wan Ibrahim et al., 2021; Moosavi et al., 2020). As a result, more research into the potential of natural materials with plentiful availability as adsorbents for removing metformin from water is required.

Pumice is a natural material that has the potential to be utilized as an adsorbent. Because of its location in the Pacific Ring of Fire, Indonesia has an abundance of pumice. According to earlier research, the principal components of pumice are SiO_2 and Al_2O_3 , which can be used as starting materials for zeolite synthesis (Toktamş, 2023; Prajaputra et al., 2021). Prajaputra et al. (2019) proved the capabilities of an Indonesian pumice-based zeolite as a methylene blue adsorbent, resulting in a high percentage removal when compared to pumice after adsorption and degradation procedures. To the best of our knowledge, no research has been conducted on the use of pumice-based zeolite to eliminate medication pollutants in water, such as metformin, particularly in Indonesia. As a result, the potential of this substance remains unknown. Thus, the efficiency of an Indonesian pumice-based zeolite for treating metformin in aqueous solution was studied in this study. Metformin stability was first assessed under a variety of circumstances, including pH, temperature, and exposure time..

Methods

Materials

Pumice samples were collected in Suwung, Bali, Indonesia. According to Prajaputra et al. (2021), pumice from Suwung includes up to 63.45% SiO_2 and 17.24% Al_2O_3 . The acquired sample was dried and crushed through a normal 100 mesh screen. It was then employed as a starting material for zeolite production using the schematic approach shown in Figure 1. Metformin ($\text{C}_4\text{H}_{11}\text{N}_5$) and sodium hydroxide (NaOH) were two compounds obtained at Universitas Syiah Kuala Lumpur's chemistry laboratory.



Figure 1 depicts a simplified zeolite synthesis technique

MET Solution and Stability Test Preparation

By dissolving up to 5 mg of metformin in 100 mL of distilled water, a 50 mg/L metformin stock solution was created. After then, the solution was diluted into numerous concentrations (2, 4, 6, 8, and 10 mg/L). The absorbance of a 10 mg/L metformin solution was scanned in the 220-400 nm range using a UV-Vis spectrophotometer to determine the maximum wavelength of metformin.

Metformin solution with a concentration of 10 mg/L was tested for stability in numerous test tubes under various settings, including pH (2, 6, and 10) and temperature (14, 28, and 40 oC) with a three-day exposure time. A UV-Vis spectrophotometer was used to measure the final concentrations for each condition. Metformin solution was judged stable if the maximum absorption peak created matched the maximum absorption peak before the treatment process and the concentration did not fluctuate considerably.

Pumice-Based Zeolite Synthesis

According to a prior study conducted by Prajaputra et al. (2021), the synthesis of pumice-based zeolite was carried out utilizing a simple hydrothermal treatment. In general, 10 g pumice was combined in a microwave container with 80 mL of 3.0 M NaOH solution. For 30 minutes, the liquid was vigorously mixed closed conditions, and then cooked for a day in a dried oven at 100 oC. After that, the solid phase was removed and the solution was washed many times with distilled water until the pH reached 8. The solid phase was heated again for 12 hours at 100 oC to generate zeolite crystals, which were subsequently analyzed using FTIR and XRD.

Adsorption Test MET

The adsorption test was performed to determine the ability of a pumice-based zeolite to remove metformin from an aqueous solution. A test tube containing 10 mL of metformin solution with varying concentrations (2, 4, 6, 8, and 10 mg/L) was filled with 50 mg of zeolite. The adsorption procedure took three hours. The mixture was then centrifuged at 4000 rpm for 5 minutes before being measured with a UV-Vis spectrophotometer. The zeolite uptake capacity (q_e , in mg/g) to remove metformin was estimated using Equation 1.

$$\alpha_e = \frac{C_0 - C_e}{m} v$$

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

Results and Discussion

pH and temperature effects on MET stability

The first metric we looked into was pH, which is significant in determining the stability of chemical compounds in solution. Metformin solution has an initial pH of 6 and a maximum wavelength of 233 nm, according to a UV-Vis spectrophotometer. We used this maximum wavelength to create the standard metformin curve using a linear correlation between absorbance and concentration, which produced good linearity with a correlation coefficient of 0.9979. The original pH of metformin was altered to 2 and 10 by adding a few drops of HCl or NaOH to investigate the influence of pH on metformin solution stability.

Figure 2 depicts metformin spectra at pH 2, 6, and 10. Metformin solutions at pH 6 and 10 displayed an absorption peak in the area of 220-250 nm, which was the characteristic peak of metformin, according to the spectra. After increasing the pH of the metformin solution to 10, the final metformin concentration remained consistent with the initial metformin concentration. Majithia et al. 2020 discovered a metformin absorption peak in the 220-250 nm region, with a maximal wavelength of 233 nm. However, when the pH was increased to a high acid state, particularly at pH 2, the absorption peak was lost. The metformin concentration reduced dramatically from 10 mg/L to 2.64 mg/L as a result of this situation. We predicted that the metformin structure would be protonated under highly acidic circumstances, beginning with the two amino groups, causing the metformin absorption peak to go undetected.

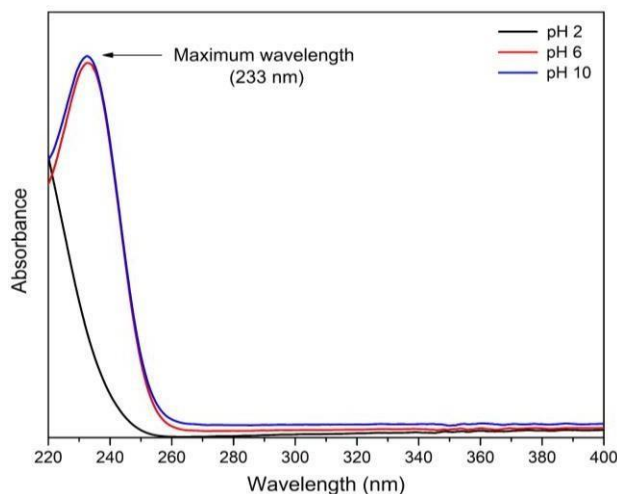


Figure 2. pH and temperature effects on MET stability ($C_0=10$ mg/L, $T=28$ °C, pH=6)

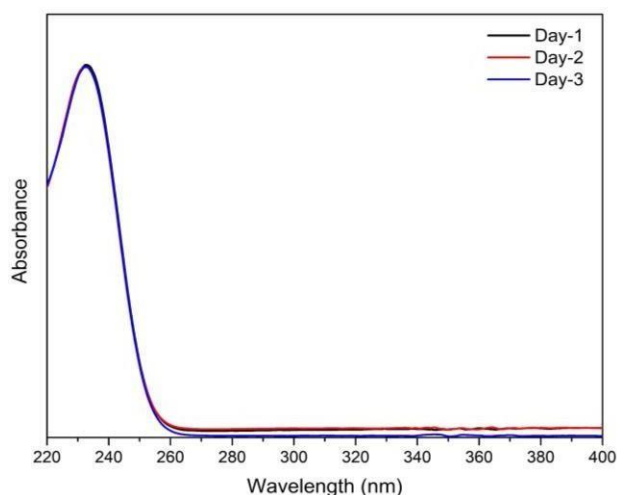


Figure 3. pH and temperature effects on MET stability ($C_0=10$ mg/L, $T=28$ °C, pH=6)

The next parameter to consider when determining metformin stability in solution is time exposure. The effect of time on metformin solution (pH 6) was studied at room temperature (28 °C) for 1, 2, and 3 days. Figure 3 depicts the absorption spectra of metformin over a period of many days. In general, the absorption peaks in all of the obtained spectra are comparable. It is reasonable to believe that the metformin solution stayed steady until the third day. Temperature is the final characteristic utilized to determine metformin stability. At room temperature, metformin solution has an initial temperature of 28 °C. This temperature was then altered to 14 degrees Celsius and 40 degrees Celsius by placing metformin solution in a refrigerator and a tiny oven, respectively. Each solution was allowed to sit for three days. Figure 4 depicts a comparison of metformin absorption spectra at 14 °C, 28 °C, and 40 °C. Because of the identical creation of absorption peaks, the data show that metformin solutions were stable at 14 to 40 °C. This finding was supported by Sharma et al. (2010), who discovered that metformin was stable in water at temperatures ranging from 30 °C to 80 °C and only degraded by 10% after more than eight days.

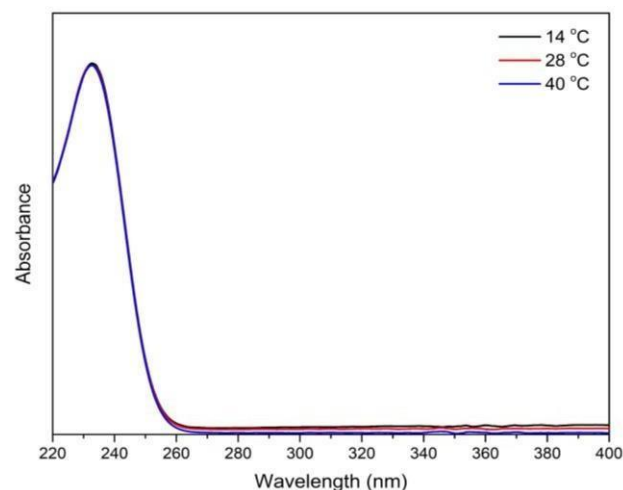


Figure 4. pH and temperature effects on MET stability ($C_0=10$ mg/L, $t=3$ days, $pH=6$)

Characterization of Materials

The XRD patterns for both samples are shown in Figure 5. These results revealed that the mineral phases of the pumice samples had been considerably changed by the alkaline addition. A pumice sample's XRD pattern reveals that it is primarily made of amorphous components with no discernible peaks. However, after being treated with alkaline solution and then subjected to a hydrothermal procedure, the pumice sample produced peaks at 12.46° , 17.66° , 21.67° , 28.10° , 33.38° , 38.01° , 42.2° , and 46.08° , which are typical of Na-P1 zeolite with a crystallinity percentage of 55.28%. For comparison and confirmation, Na-P1 zeolite phases with 2θ degree = 12.46° , 17.66° , 21.67° , 25.08° , 28.10° , 30.84° , 35.76° , 38.01° , 40.15° , 42.20° , 44.18° , 46.08° , and 49.72° from the International Zeolite Association (IZA) are utilized.

The FT-IR spectra of both materials from 500 cm^{-1} to $4,000\text{ cm}^{-1}$ are shown in Figure 6. Peaks in the pumice sample have been attributed to bending vibration of Si-O-Si bonds, symmetric stretching vibration of Si-O-Si in $(\text{SiO}_4)^{2-}$ groups as a characteristic peak, bending vibration of H-O-H bonds, and asymmetric stretching vibration of O-H bonds, respectively.

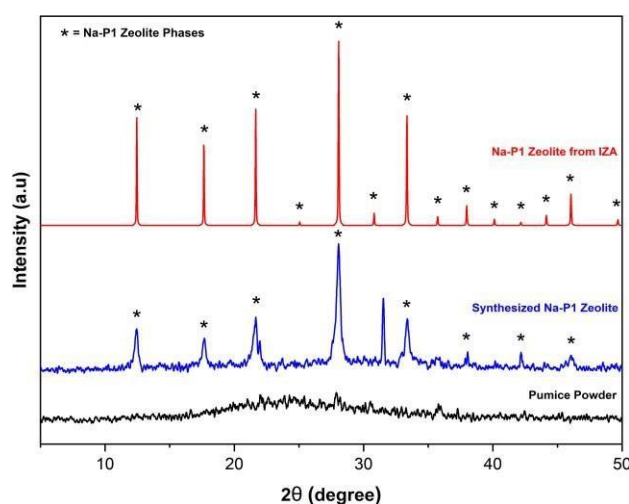


Figure 5. XRD patterns of Na-P1 zeolite and pumice

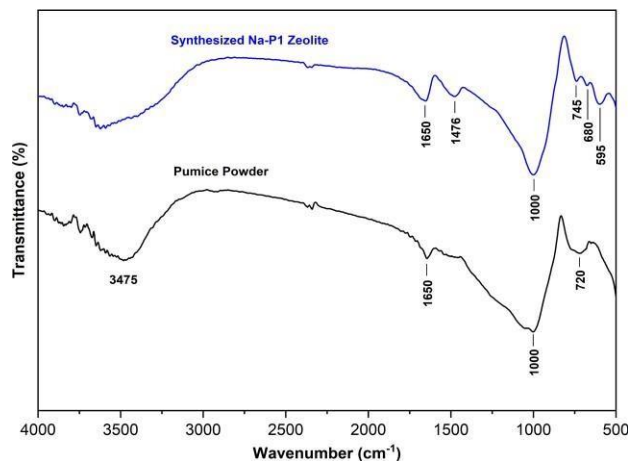
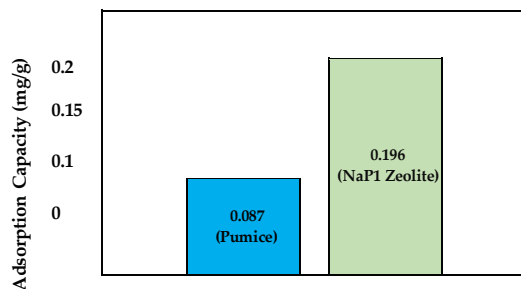


Figure 6: FTIR spectra of Na-P1 zeolite and pumice

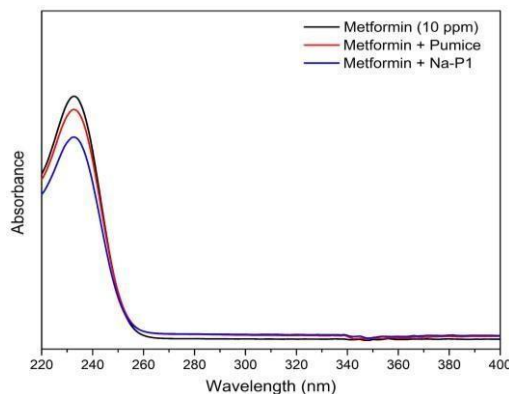
Adsorption Test MET

Pumice and zeolite were tested for their ability to remove 10 mL of metformin solution (pH 6) with a concentration of 10 mg/L for 3 hours at room temperature. Figure 7a depicts the adsorption capability of both materials, as well as their absorption spectra following adsorption (Figure 7b). The findings demonstrated that pumice has a lower adsorption capacity than zeolite for absorption of metformin from solution. It is possible that this is due to the presence of contaminants, which also affect the active side of pumices. This notion is corroborated by a prior investigation that found the original pumice to be impure and to have a low adsorption capability (Ersoy et al., 2010). Pumice was converted to zeolite, which resulted in the formation of additional silanol groups, which immediately enhanced the active side on its surface. As a result, zeolite outperformed pumice in terms of metformin elimination. Pumice and zeolite had adsorption capacities of around 0.087 mg/g and 0.196 mg/g, respectively.

(a)



(b)



(c)

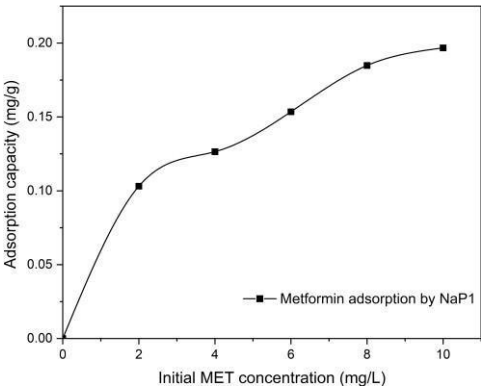


Figure 7. (a) the adsorption capacity of pumice and zeolite, (b) the change in absorption spectra, and (c) the influence of MET concentration on the adsorption capacity of Na-P1 zeolite.

The effect of initial metformin concentration was studied utilizing the synthesized zeolite in multiple metformin concentrations ranging from 2 to 10 mg/L. Figure 7c depicts the results. The figure shows that increasing the starting concentration enhanced the uptake capacity. In the concentration range of 8 to 10, there was a marginal improvement, with uptake capacities of 0.185 mg/g and 0.196 mg/g, respectively.

The Study of Equilibrium

To explore the metformin adsorption process on the adsorbent, two isotherm models, Freundlich and Langmuir, are used. The Freundlich isotherm model employs heterogeneous adsorbent surfaces, whereas the Langmuir isotherm model employs homogeneous surfaces. Both isotherm models can be used to describe whether or not the adsorption process Freundlich equation model:

(3) $\log q_e = 1 \log C_e + \log k_F$

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

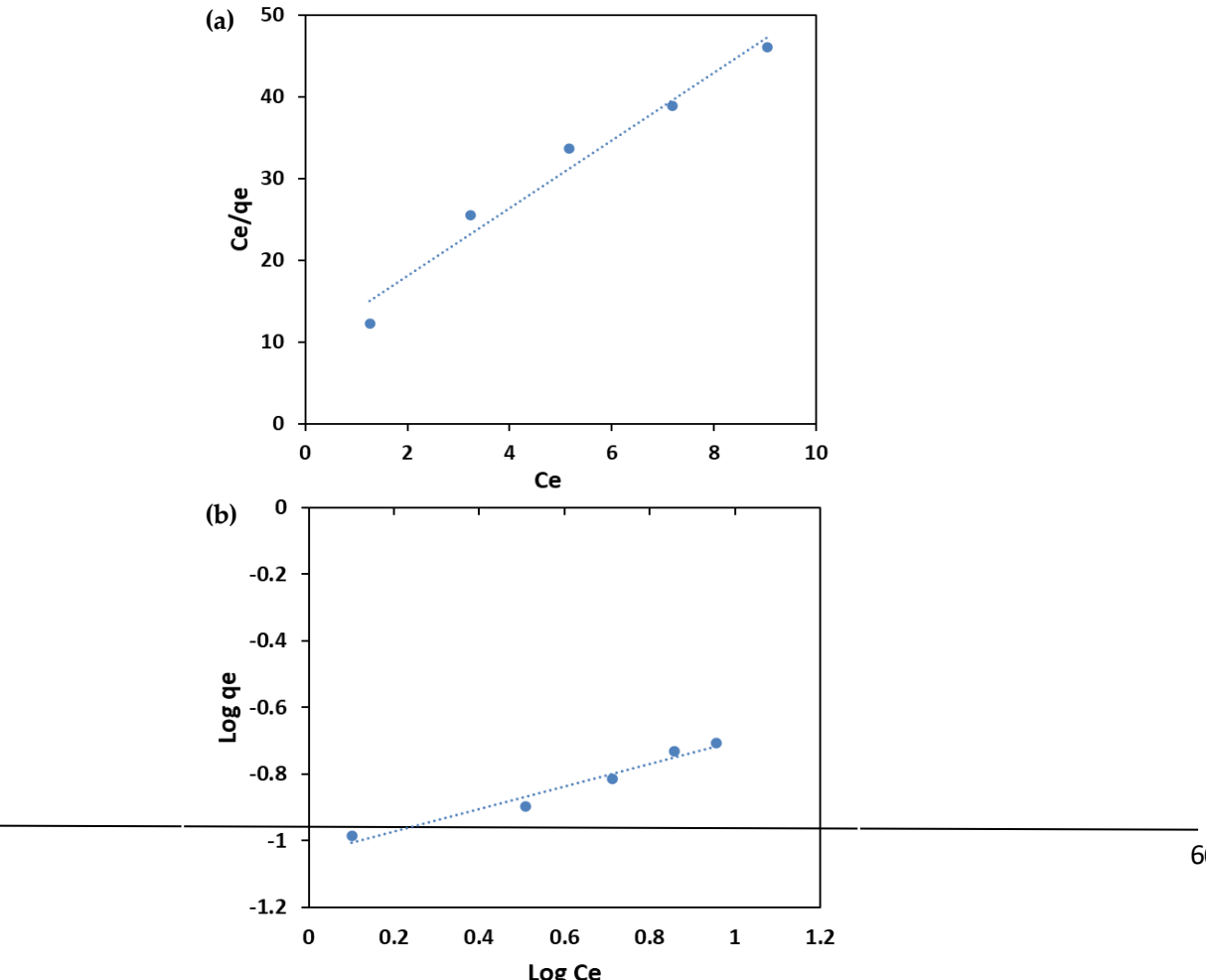


Figure 8: Langmuir and Freundlich adsorption isotherm models.

The equilibrium investigation of metformin adsorption onto pumice zeolite was performed by mixing 50 mg of zeolite in 10 mL of metformin solution with concentrations ranging from 2 to 10 mg/L (pH 6) at room temperature for 3 hours. The final metformin concentrations were then determined. The adsorption isotherm curves of the Langmuir and Freundlich models are shown in Figure 8. The correlation coefficient value (R^2) of the Langmuir equilibrium model (0.9682) was greater than that of the Freundlich equilibrium model (0.9648). The maximal adsorption capacity (q_m) was found to be around 241 g/g. This data suggested that metformin adsorption onto zeolite was caused by physical contact on homogenous surfaces. The effectiveness of zeolite in lowering metformin concentrations can still be enhanced, particularly by altering the pH, adsorbent dosage, and adsorption period in the adsorption test. As a result, the ability of zeolites to remove metformin needs to be explored further utilizing these parameters in order to reach the optimal circumstances with a significantly higher percentage of metformin removal.

Conclusion

Metformin stability in solution was determined using a UV-Vis spectrophotometer, and its adsorption onto pumice-based zeolite was examined. Metformin solution was shown to be stable at pH levels ranging from 6 to 10 and temperatures ranging from 14 to 40 degrees Celsius. Metformin solution stability can be maintained for up to three days; however, this medication proved unstable under high acid conditions. With an absorption capability of 196 g/g, zeolite was able to eradicate metformin from the solution, whereas pumice was only around 87 g/g. Although zeolite displayed superior adsorption to pumice, more modification was required to improve zeolite adsorption. The Langmuir model ($R^2=0.9682$) accurately characterized the equilibrium model and demonstrated that the adsorption process was a physical interaction on homogenous surfaces.

References

- Adegoke, K. A., Olagunju, A. O., Alagbada, T. C., Alao, O. C., Adesina, M. O., Afolabi, I. C., Adegoke, R. O., & Bello, O. S. (2022). Adsorptive removal of endocrine-disrupting chemicals from aqueous solutions: a review. *Water, Air, & Soil Pollution*, 233(2), 38. <https://doi.org/10.1007/s11270-021-05405-8>
- Balakrishnan, A., Sillanpää, M., Jacob, M. M., & Vo, D. V. N. (2022). Metformin as an emerging concern in wastewater: Occurrence, analysis and treatment methods. *Environmental Research*, 213, 113613. <https://doi.org/10.1016/j.envres.2022.113613>
- Bojanić, I., Bjerkeset, O., Williams, L. J., Berk, M., Bjørngaard, J. H., Sund, E. R., & Sletvold, H. (2023). Risk of antidepressant initiation among users of cardiovascular agents and metformin. Findings from the Trøndelag Health Study (HUNT) and Norwegian Prescription Database (NorPD), Norway. *Pharmacology Research & Perspectives*, 11(2), e01078. <https://doi.org/10.1002/prp2.1078>
- Demiral, İ., Samdan, C., & Demiral, H. (2021). Enrichment of the surface functional groups of activated carbon by modification method. *Surfaces and Interfaces*, 22, 100873. <https://doi.org/10.1016/j.surfin.2020.100873>
- El-Fattah, A., Maged, A., Kamel, R. M., & Kharbush, S. (2023). Recent Technologies for The Elimination of Pharmaceutical Compounds from aqueous solutions: A review. *Frontiers in Scientific Research and Technology*, 5(1). <https://doi.org/10.21608/FSRT.2023.173676.1074>
- Ersoy, B., Sariisik, A., Dikmen, S., & Sariisik, G. (2010). Characterization of acidic pumice and determination of its electrokinetic properties in water. *Powder Technology*, 197, 129-135. <https://doi.org/10.1016/j.powtec.2009.09.005>
- Fast, S. A., Gude, V. G., Truax, D. D., Martin, J., & Magbanua, B. S. (2017). A critical evaluation of advanced oxidation processes for emerging

- contaminants removal. *Environmental Processes*, 4, 283-302. <https://doi.org/10.1007/s40710-017-0207-1>
- Gu, Y., Zhang, Y., Jiang, C., Dong, Z., & Bai, X. (2023). Efficient metformin transformation in sulfite/UV process co-present with oxygen. *Frontiers in Environmental Science*, 10, 1071963. <https://doi.org/10.3389/fenvs.2022.1071963>
- Kalumpha, M., Guyo, U., Zinyama, N. P., Vakira, F. M., & Nyamunda, B. C. (2020). Adsorptive potential of Zea mays tassel activated carbon towards the removal of metformin hydrochloride from pharmaceutical effluent. *International journal of phytoremediation*, 22(2), 148-156. <https://doi.org/10.1080/15226514.2019.1652561>
- Kim, J. Y., Jeon, J., & Kim, S. D. (2023). Prioritization of pharmaceuticals and personal care products in the surface waters of Korea: Application of an optimized risk-based methods. *Ecotoxicology and Environmental Safety*, 259, 115024. <https://doi.org/10.1016/j.ecoenv.2023.115024>
- Liu, H., Wang, C., & Wang, G. (2020). Photocatalytic advanced oxidation processes for water treatment: recent advances and perspective. *Chemistry—An Asian Journal*, 15(20), 3239-3253. <https://doi.org/10.1002/asia.202000895>
- Majithia, R. H., Khodadiya, A., & Patel, V. B. (2020). Spectrophotometric method development and validation for simultaneous estimation of Anagliptin and Metformin HCl BY Q-Absorption ratio method in synthetic mixture. *Heliyon*, 6(5). <https://doi.org/10.1016/j.heliyon.2020.e03855>
- Martinez-Alcala, I., Guillén-Navarro, J. M., & Fernández-López, C. (2017). Pharmaceutical biological degradation, sorption and mass balance determination in a conventional activated-sludge wastewater treatment plant from Murcia, Spain. *Chemical Engineering Journal*, 316, 332-340. <https://doi.org/10.1016/j.cej.2017.01.048>
- Moosavi, S., Lai, C. W., Gan, S., Zamiri, G., Akbarzadeh
- Pivezhani, O., & Johan, M. R. (2020). Application of efficient magnetic particles and activated carbon for dye removal from wastewater. *ACS omega*, 5(33). <https://doi.org/10.1021/acsomega.0c01905>
- Nuri, O. S., Irannajad, M., & Mehdilo, A. (2019). Reagent adsorption on modified mineral surfaces: isotherm, kinetic and thermodynamic aspects. *Journal of Molecular Liquids*, 291, 111311. <https://doi.org/10.1016/j.molliq.2019.111311>
- Oosterhuis, M., Sacher, F., & Ter Laak, T. L. (2013). Prediction of concentration levels of metformin and other high consumption pharmaceuticals in wastewater and regional surface water based on sales data. *Science of the Total Environment*, 442. <https://doi.org/10.1016/j.scitotenv.2012.10.046>
- Prajaputra, V., Abidin, Z., Budiarti, S., & Suryaningtyas, D. T. (2021). Synergistic effect of adsorption and Fenton-like oxidation processes for methylene blue removal using Na-P1 zeolite prepared from pumice. *Desalination and Water Treatment*, 218(2021), 401-408. <https://doi.org/10.5004/dwt.2021.26976>
- Prajaputra, V., Abidin, Z., Budiarti, S., Suryaningtyas, D. T., & Isnaini, N. (2021). Comparative study of methylene blue adsorption using alkali-activated pumice from Bali and Banten. *Journal of Physics: Conference Series*, 1882(1), 012118. <http://doi.org/10.1088/1742-6596/1882/1/012118>
- Prajaputra, V., Abidin, Z., Suryaningtyas, D. T., & Rizal, H. (2019). Characterization of Na-P1 zeolite synthesized from pumice as low-cost materials and its ability for methylene blue adsorption. *IOP Conference Series: Earth and Environmental Science*, 399(1), 012014. <https://doi.org/10.1088/1755-1315/399/1/012014>
- Ratnam, M. V., Akilamudhan, P., Kumar, K. S., Reddy, S. N., Rao, K. N., Shaik, F., & Prasad, D. M. (2023). Carbon-Based Nano-adsorbents for the Removal of Emerging Pollutants. *Adsorption Science & Technology*, 2023. <https://doi.org/10.1155/2023/3579165>
- Rebecca, Y. M., Sudha, V., Bharathiraja, T., Kannan, T., Lavanya, J., & Kumar, A. K. H. (2023). Urinary excretion of metformin in diabetic patients with and without tuberculosis.

- Indian Journal of Tuberculosis*, 70(1).
<https://doi.org/10.1016/j.ijtb.2022.03.004> Salovska, B., Gao, E., Müller-Dott, S., Li, W., Cordon, C.
- C., Wang, S., Dugourd, A., Rosenberger, G., Saez- Rodriguez, J., & Liu, Y. (2023). Phosphoproteomic analysis of metformin signaling in colorectal cancer cells elucidates mechanism of action and potential therapeutic opportunities. *Clinical and Translational Medicine*, 13(2). <https://doi.org/10.1002/ctm2.1179>
- Sayedali, E., Yalin, A. E., & Yalin, S. (2023). Association between metformin and vitamin B12 deficiency inpatients with type 2 diabetes. *World Journal of Diabetes*, 14(5), 585-593. <https://doi.org/10.4239/wjd.v14.i5.585>
- Sharma, V. K., Nautiyal, V., Goel, K. K., & Sharma, A. (2010). Assessment of thermal stability of metformin hydrochloride. *Asian Journal of Chemistry*, 22(5), 3561. Retrieved from https://asianjournalofchemistry.co.in/User/ViewArticle.aspx?ArticleID=22_5_33
- Sousa, M., Rodrigues, S., Pretti, C., Meucci, V., Battaglia, F., Freitas, R., & Antunes, S. C. (2023). A forecast effects of climate change and anthropogenic compounds in *Gambusia holbrooki*: ecotoxicological effects of salinity and metformin. *Aquatic Toxicology*, 258, 106494. <https://doi.org/10.1016/j.aquatox.2023.106494>
- Toktamış, D. (2023). Thermoluminescence in pumice stone collected from the Mediterranean coast. *Luminescence*, 38(3), 318-325. <https://doi.org/10.1002/bio.4452>
- Triggle, C. R., Mohammed, I., Bshesh, K., Marei, I., Ye, K., Ding, H., MacDonald, R., Hollenberg, M. D., & Hill, M. A. (2022). Metformin: Is it a drug for all reasons and diseases? *Metabolism*, 133, 155223. <https://doi.org/10.1016/j.metabol.2022.155223>
- Wan Ibrahim, W. M. H., Mohamad Amini, M. H., Sulaiman, N. S., & Wan Abdul Kadir, W. R. (2021). Evaluation of alkaline-based activated carbon from *Leucaena Leucocephala* produced at different activation temperatures for cadmium adsorption. *Applied Water Science*, 11, 1-13. <https://doi.org/10.1007/s13201-020-01330-z>
- Wu, L., Lu, X., Wu, Y., Huang, C., Gu, C., Tian, Y., & Ma, J. (2023). An electrochemical sensor based on synergistic enhancement effects between nitrogen-doped carbon nanotubes and copper ions for ultrasensitive determination of anti-diabetic metformin. *Science of The Total Environment*, 878. <https://doi.org/10.1016/j.scitotenv.2023.163120>.