International Islamic Medical Journal
Journal Homepage ://journal2.unusa.ac.id/index.php/IIMJ

Effect of Kratom (*Mitragyna speciosa*) Hydrogel on Liver Function in Diabetic Burn Injury

Rosandhy Alifyah Pramesti[1]*, Muhammad Aqil Siroj Jazuli[1], Zainul Hadi Wildan Ismail[1], Khuzaimah Nur Juhanifah Rihhadatulays[1], Eka Satria Akbar Ferdinan Hanafi[1], Puspita Rahmatul Jinan[1], Hotimah Masdan Salim[2], Bastiana Bermawi[3]

[1]Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Indonesia
[2]Department Biochemistry and Biology Molecular Medicine, Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Indonesia
[3]Department Pathology Clinic, Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Indonesia
*Corresponding Author: rosandhyalifyah@gmail.com
DOI: 10.33086/iimj.v7i2.8239

ARTICLE INFO

Keywords:
Burns, Kratom, Hydrogel, Liver, Histopathology.

Submitted: Nov 2nd 2025
Reviewed: Nov 3rd 2025
Accepted: Dec 3rd 2025

ABSTRACT

Introduction: Burns are serious injuries that not only damage the skin but can also affect internal organs such as the liver. Severe inflammation following burn injury increases hepatocyte vulnerability, especially in diabetic conditions.
Objective: This study aimed to evaluate the effect of topical kratom (Mitragyna speciosa) hydrogel on liver histopathology in streptozotocin-induced diabetic mice with burn injuries.
Methods: An in vivo experimental study with a post-test-only control group design was conducted using 15 male mice (Mus musculus). Diabetes mellitus was induced prior to burn injury, and hyperglycemia was confirmed before further procedures. The diabetic mice were then randomly assigned into three groups: diabetic burn injury without hydrogel treatment (K), diabetic burn injury treated with 5% kratom hydrogel (T1), and diabetic burn injury treated with 15% kratom hydrogel (T2). The respective treatments were applied for four weeks. Following the intervention period, liver tissues were collected for histopathological analysis. Hepatocyte damage was quantitatively assessed and analyzed using one-way ANOVA followed by Dunnett's post hoc test.
Results: The diabetic burn injury control group exhibited the greatest extent of hepatocyte damage (66.5 ± 5.0%). Application of 5% kratom hydrogel (49.5 ± 4.0%) and 15% kratom hydrogel (52.5 ± 4.0%) resulted in a statistically significant reduction in hepatocyte injury compared with the diabetic control group ($p = 0.0043$ and $p = 0.0131$, respectively).
Conclusions: Topical administration of kratom hydrogel significantly attenuated hepatocyte damage in diabetic mice subjected to burn injuries, suggesting a hepatoprotective effect and potential benefits for preserving liver function under diabetic burn conditions.

Introduction

Type 2 diabetes mellitus is a chronic metabolic disease characterized by persistent hyperglycemia due to peripheral insulin resistance and pancreatic β-cell dysfunction. In Indonesia, diabetes mellitus is the third leading cause of death with a prevalence of approximately 10.3 million cases, and this number is estimated to jump to 21.3 million by 2030 (Nababan et al,

2023). In this context, complications of type 2 diabetes mellitus include both microvascular and macrovascular complications. In addition to microcellular and macrocellular complications, type 2 diabetes mellitus also causes complications in the skin, such as wound disorders (Lu et al., 2024).

When patients with type 2 diabetes mellitus suffer burns, the inflammatory response becomes much more complex. Burns trigger the massive release of proinflammatory cytokines and activate systemic inflammatory response syndrome (SIRS), which then develops into a systemic inflammatory and hypermetabolic process (Żwierełło et al. 2023). The systemic inflammatory response or Systemic Inflammatory Response Syndrome (SIRS) triggered by burns causes the massive release of proinflammatory cytokines such as TNF-α and IL-6, which serve to maintain the immune system but, when excessive, cause tissue damage. In addition, burns also increase the production of reactive oxygen species (ROS) in large quantities that exceed the body's antioxidant defense capacity. The combination of proinflammatory cytokines and ROS causes progressive hepatocyte damage through mechanisms of lipid peroxidation, DNA damage, and immune response dysregulation. In the long term, this condition leads to liver vulnerability to metabolic dysfunction and multiple organ failure (Siu, Ma, and Leung 2025).

In this context, a dual therapeutic strategy is needed: supporting wound healing in the skin while providing protection for internal organs. Topical hydrogels have been identified as one of the most promising drug delivery systems due to their ability to maintain wound moisture, provide an optimal environment for tissue regeneration, and serve as a reservoir for the controlled and sustained release of active substances (Siu et al. 2025). According to previous research, one potential bioactive candidate that can be formulated in hydrogels is Mitragyna speciosa Korth. (kratom), a plant from the Rubiaceae family that has anti-inflammatory and antioxidant activities. The content of indole alkaloids such as mitragynine, as well as polyphenols including flavonoids and phenolic acids, has been shown to provide a protective effect against tissue damage caused by chronic inflammation (Chen et al., 2022). Thus, the development of a topical kratom hydrogel formulation is expected to increase the bioavailability of active compounds while providing a protective therapeutic effect on the liver, which is susceptible to damage due to systemic inflammation in burn conditions with

comorbid diabetes (Tuntiyasawasdikul et al. 2024).

Methods

This study used an in vivo biomedical experimental design with a post-test only control group to assess liver function in mice using histopathological examination after administering a hydrogel made from kratom (Mitragyna speciosa) to skin burns in mice (Mus musculus) with streptozotocin-induced type 2 diabetes mellitus. This study also aims to evaluate the effects of topical drug administration on internal organs of mice as a potential innovation for type 2 diabetes mellitus therapy.

Materials and Reagents

Ethyl alcohol extract of kratom leaves (Mitragyna speciosa), Streptozotocin compound as an inducer, citrate buffer, 0.9% NaCl physiological solution, 10% neutral formalin solution, hematoxylin–eosin dye, 0.5% Na CMC suspension, glycerin, propylene glycol, methyl paraben as a preservative, distilled water, and ketamine and xylazine anesthetics.

Kratom Hydrogel Formulation

The hydrogel production process begins with the extraction of 500 g of kratom leaf powder. Extraction is carried out using the maceration method with 3500 mL of 96% ethanol (material:solvent ratio of 1:7). The mixture is soaked in a closed container protected from light for five days while being stirred periodically. After the maceration process is complete, the mixture is filtered to obtain the filtrate, then evaporated using a rotary evaporator at a temperature of 50 °C until a concentrated extract is formed. (Antaryani et al., 2019; Ningrum et al., 2020; Zhang et al., 2023).

Table 1. Kratom Hydrogel Formulation

Ingredient	**Function**	Concentration **(g)**	
		Kratom 5%	**Kratom 15%**
Ethanol Extract of Kratom Leaves	Active compound	1.5	4.5
Na-CMC	*Gelling Agent*	1.25	1.25
Gliserin	Humektan	3.0	3.0
Methylparaben	Pengawet	0.075	0.075
Propilen glikol	*Enhancer*	1.0	1.0
Etanol 96%	Pelarut. *Enhancer*	5	5
Aquades	Pelarut	ad 30 g	ad 30 g

In the manufacture of hydrogel, the first step is to prepare formula 1 by dissolving methylparaben in hot distilled water, then dispersing Na-CMC as a hydrophilic polymer and homogenizing it. Formula 2 is prepared by mixing propylene glycol and glycerin, then combining it with formula 1 (Table 1). The ethanol extract of kratom leaves is dissolved in 96% ethanol and added gradually to the mixture. Propylene

glycol and ethanol function as solvents and penetration enhancers (Purwasih et al., 2023). The final step is to add the remaining distilled water until homogeneous, and the mixture is left to stand for ±24 hours at room temperature before use.

Experimental Animals and Diabetes Mellitus Modeling

This study was a laboratory experimental study with a post-test only control group design. The subjects used were 15 male Swiss Webster mice (Mus musculus) aged 6–8 weeks with a body weight of 25–30 grams. All animals were obtained from the Animal Breeding Unit (UPHC), which has been certified as Specific Pathogen-Free (SPF) to ensure their health and quality. The mice were randomly divided into three treatment groups, namely the positive control group with burns without hydrogel (K), the group with 5% kratom hydrogel (T1), and the group with 15% kratom hydrogel (T2).

All procedures have been approved by the Health Research Ethics Committee of Nahdlatul Ulama University Surabaya (No.0251/EC/KEPK/UNUSA/2025). The study entitled "The Effect of Kratom Hydrogel (Mitragyna speciosa) Use on Liver Function in Burn Injuries" was conducted at the Integrated Research Laboratory 3 and the Animal Testing Laboratory of the Faculty of Medicine, UNUSA.

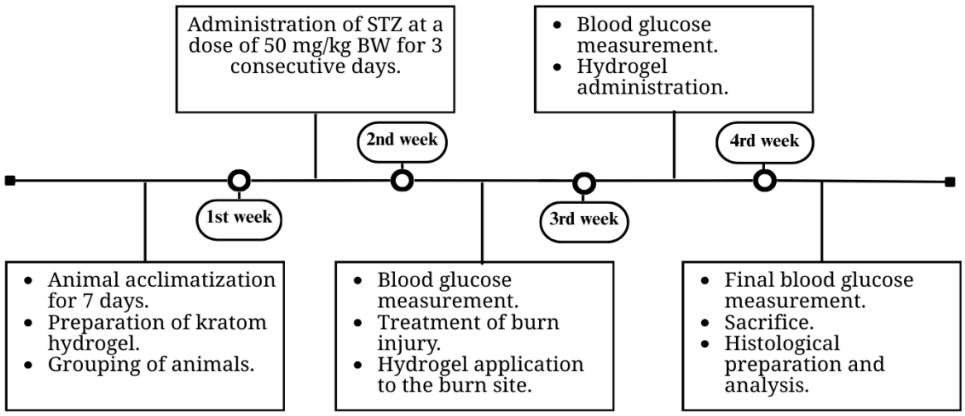

Figure 1. Experimental workflow showing acclimatization, diabetes induction, hydrogel treatment, and histological preparation and analysis.

Prior to treatment, all test animals underwent an acclimatization period of 4–7 days to adapt to the laboratory environment. Subjects were then randomly allocated into three treatment groups as follows:

- Group 1 (Positive Control) : Group induced with STZ and given a burn wound, but not given hydrogel treatment.

- Group 2 (Treatment 1) : Group induced with STZ and given topical kratom hydrogel with a 5% extract concentration every day for 4 weeks.
- Group 3 (Treatment 2) : The group that was induced with STZ and given topical kratom hydrogel with a 15% extract concentration every day for 4 weeks.

In the second week, diabetes was induced by intraperitoneal injection of Streptozotocin (STZ) at a single dose of 50 mg/kgBW three times over three consecutive days. Diabetes status was confirmed 72 hours after the last injection, with mice with fasting blood glucose levels above 200 mg/dL being declared hyperglycemic. In the following week, a second-degree burn was made on the back of the mice. The burn was administered using a 1 × 1 cm iron plate that had been heated to 98℃ with a Bunsen burner and placed on the back of the mice for 30 seconds (Afrianti et al., 2016; Gitafitri et al., 2023). Topical treatment with kratom hydrogel was initiated according to each group's allocation. Blood glucose levels were measured using a Gluco Dr GCU device three days after the STZ injection treatment. Subsequently, the mice were sacrificed and their blood glucose levels were rechecked. The examination process was carried out after the animals were anesthetized using a combination of ketamine 70 mg/kgBW and xylazine 10 mg/kgBW injected intraperitoneally with a volume of 0.03 mL.

Histopathological Analysis

After a four-week treatment period, the livers of the mice were removed and cleaned using a physiological solution. For preservation, the livers were immersed in a 10% Neutral Buffer Formalin (NBF) solution. Next, histological preparations were made using the paraffin embedding method, followed by staining with hematoxylin-eosin (HE) to visualize the cell structure (Dewhurst et al. 2020).

Morphological observation of liver tissue was performed under a light microscope at 100x and 400x magnification using Image Raster software with a light microscope (Nikon Eclipse type Ei) connected to a computer with the assistance of Optilab SIGMA MTN020. Data collection was performed on five different fields of view for each specimen. In each field of view, the total number of liver cells (hepatocytes) and the number of damaged cells (swelling or shrinkage indicating inflammation or necrosis) were counted (Agustini et al., 2019). This study was conducted with the assistance of the ImageJ application.

Mitragynine Bioinformatics Analysis

In silico analysis was conducted to assess the pharmacological potential of the mitragynine compound. The chemical structure of mitragynine was obtained from the PubChem database. Prediction of the compound's biological activity was performed using the Way2Drug platform (PASS Online), while protein target identification and prediction were performed using SwissTargetPrediction. Furthermore, the protein interaction network of the identified targets was analyzed using the STRING Database to evaluate functional relationships between proteins. All data used in this analysis was sourced from public databases and accessed in 2025.

Data Analysis

The research data consisted of the number of normal cells and damaged hepatocytes in five fields of view for each specimen. These values were added together to obtain the total number of normal cells, damaged cells, and total cells in each animal. The percentage of hepatocyte damage was calculated using the formula below (Agustini et al., 2019).

$$\text{Damages}(\%) = \frac{Total\ damages\ cell}{Total\ damages\ cell + Total\ normal\ cell} \times 100\%$$

Summary data for each group are presented as mean ± standard deviation (Table 3). Statistical analysis was performed using GraphPad Prism software version 9.0 (GraphPad Software, San Diego, CA, USA). Data distribution normality was tested using Shapiro–Wilk, while homogeneity of variance between groups was analyzed using Bartlett and Brown–Forsythe. If the data were normally distributed and the variances between groups were homogeneous, the parametric One-way ANOVA test was used to assess the differences between groups. The test was followed by a post-hoc Dunnett test to compare the treatment groups (T1 and T2) with the control group (K). The significance level was set at $p < 0.05$.

Results and Discussion

Protein Targets in Type 2 Diabetes

Table 2. Protein Targets in Type 2 Diabetes KEGG Pathways (STRING DB)

KEGG Pathways	ID	Protein Target
Type 2 Diabetes Mellitus	hsa04930	MTOR, MAPK8, JAK2, NOX4
Insulin Resistance	hsa04931	MTOR, JAK2, MAPK8
AGE–RAGE Signaling Pathway in Diabetic Complications	hsa04933	NOX4, MAPK8, JAK2

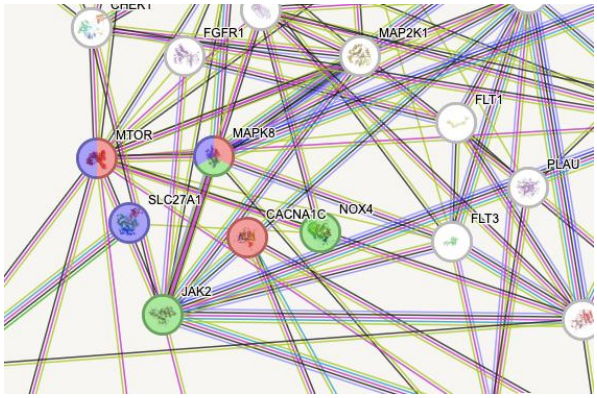

Figure 2. Protein–protein interaction (PPI) Molecular target prediction analysis using the Way2Drug approach via Swiss Target Prediction showed that mitragynine lacks high-probability direct targets for key proteins in type 2 diabetes mellitus.

Insulin regulates glucose metabolism by binding to insulin receptors (INSR) on the cell membrane, triggering the activation of IRS–PI3K–AKT–mTOR, which increases glucose uptake (through GLUT4 translocation), stimulates glycogen synthesis, and suppresses gluconeogenesis in the liver. This pathway is central to the metabolic effects of insulin. In addition, insulin also activates the RAS–MAPK pathway, which plays a role in cell proliferation and growth, as well as the JAK–STAT pathway, which regulates the expression of metabolic genes and growth hormones. In conditions of insulin resistance such as type 2 diabetes mellitus, IRS and AKT activation is disrupted so that GLUT4 does not move to the membrane, the liver continues to produce glucose, and blood glucose levels remain high even though insulin levels are high. Excessive mTOR activation triggers lipogenesis and oxidative stress, while hyperactive MAPK pathways increase inflammation and liver damage. Consequently, disruption of insulin signaling pathways leads to hyperglycemia, hepatic insulin resistance, and liver complications such as steatosis in DM.

Effects of hydrogel Mitragyana speciosa in Liver Function

Table 3. Summary of normal cells, damaged cells, total cells, and percentage of hepatocyte damage (Mean ± SD) per group

GROUP	Total N (Mean ± SD)	Total D (Mean ± SD)	Total Cell (Mean ± SD)	Damage % (Mean ± SD)
K	187.0 ± 5.0	224.0 ± 4.0	411.0 ± 5.0	66.5 ± 5.0
T1	212.0 ± 4.0	184.0 ± 4.0	396.0 ± 4.0	49.5 ± 4.0
T2	207.0 ± 4.0	190.0 ± 4.0	397.0 ± 4.0	52.5 ± 4.0

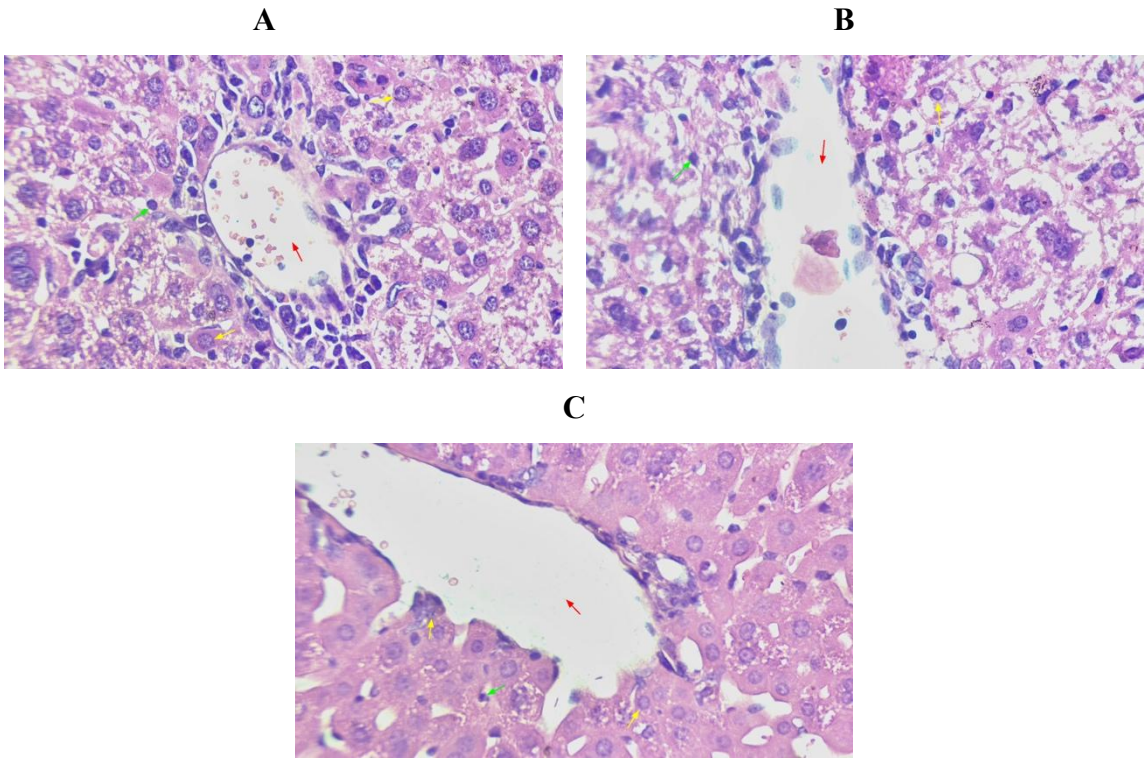

Figure 3. Histopathological image of mice liver stained with HE at 400x magnification. Colors indicate yellow (cell degeneration), red (central vein), and green (necrotic cells). (A) Group K (DM+BI) Severe liver damage with massive necrosis, inflammation, and cholangitis in untreated DM conditions; (B) Group T1 (DM+BI+K5%) A reduction in the degree of hepatocyte damage compared to the pure DM group, indicating the protective effect of 5% kratom hydrogel on the liver; (C) Group T2 (DM+BI+K15%) Kratom hydrogel 15% also reduces liver damage, but histological findings show that damage is still present (degeneration, necrosis) and appears less protective than the 5% dose.

Descriptive analysis of Table 3 shows that group K had the highest mean percentage of hepatocyte damage (66.5 ± 5.0%), while the 5% kratom hydrogel treatment group (49.5 ± 4.0%) and 15% kratom hydrogel treatment group (52.5 ± 4.0%) showed lower values. The total number of normal cells was also higher in the treatment groups than in the diabetic control group. This indicates that administration of kratom hydrogel, at both 5% and 15% concentrations, has the potential to reduce hepatocyte damage in a diabetic model.

Assumption tests showed that hepatocyte damage data in the three groups (K, T1, and T2) were normally distributed based on the Shapiro–Wilk test ($p>0.05$)

and had homogeneous variance according to the Bartlett (p=0.517) and Brown–Forsythe (p=0.244) tests. Thus, the analysis could be continued using the parametric ANOVA test.

The results of the one-way ANOVA test showed that there were significant differences between groups (F(2,9)=10.05; p=0.0051). Dunnett's post-hoc analysis showed that the control group (K) had a higher percentage of hepatocyte damage compared to the 5% kratom hydrogel treatment group (T1) and 15% kratom hydrogel treatment group (T2). These differences were significant with p=0.0043 for K vs T1 and p=0.0131 for K vs T2. Overall, these results indicate that administration of kratom hydrogel, at both 5% and 15% concentrations, was able to reduce the level of hepatocyte damage compared to the control group.

The mean percentage of hepatocyte damage (Mean ± SD) in groups K, T1, and T2. It can be seen that group K showed a higher percentage of hepatocyte damage compared to treatment groups T1 and T2 (Figure 4). The One-way ANOVA test showed a significant difference between groups (F(2,9) = 10.05; p = 0.0051). The Dunnett post-hoc test showed that hepatocyte damage in the T1 (p = 0.0043) and T2 (p = 0.0131) groups was significantly lower than in the K group.

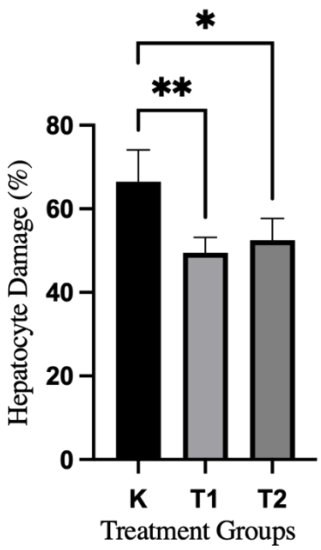

Figure 4. Comparison of the mean percentage of hepatocyte damage in three groups: K (diabetes without treatment), T1 (diabetes + 5% kratom), and T2 (diabetes + 15% kratom). Data are presented as mean ± SD. An asterisk indicates a significant difference between groups.

This study concluded that the administration of kratom hydrogel was able to reduce hepatocyte damage in a mouse model of diabetes mellitus with burns. The control group showed the greatest reduction in hepatocytes at 66.5%, while the treatment group with 5% kratom hydrogel showed a reduction of 49.5% and 15% showed a reduction of 52.5%, with both groups showing a significant decrease. These differences were statistically confirmed by ANOVA, which showed significant differences between groups, and by Dunnett's post-hoc test, which proved that

both concentrations of kratom hydrogel reduced hepatocyte damage compared to the control group.

The protective effects appear to be correlated with the bioactive components of Mitragyna speciosa, particularly the alkaloid mitragynine and several polyphenols such as flavonoids and phenolic acids. These compounds possess anti-inflammatory and antioxidant properties (Chen et al. 2022; Todd et al. 2020). Possible mechanisms include the reduction of reactive oxygen species (ROS), restoration of redox balance, and modulation of the release of inflammation-related cytokines (Pranantyo et al., 2024; Niu et al., 2023). Additionally, trimolecular hydrogels as a depot system for topical and controlled release contribute to wound moisture retention and, thus, enhance the penetration of active ingredients (Gounden & Singh, 2024; Alberts et al., 2025). Interestingly, a 5% concentration appears to provide better protective effects than 15%, which may indicate an optimal effect, where higher doses may cause mildly toxic or unbalanced pharmacodynamic effects.

Comparison with previous research indicates that kratom extract improves oxidative status and profiles in diabetic mice (Chen et al. 2022). Kratom also functions to strengthen its potential as a transdermal candidate (Tuntiyasawasdikul et al. 2024). Additionally, hydrogels are topical drug delivery systems that effectively maintain moisture for wound healing, accelerate tissue regeneration, and enable controlled release of bioactive compounds (Alberts et al. 2025; Gounden and Singh 2024).

Clinically, the results of this study indicate that kratom hydrogel has the potential to be developed as an adjunct therapy for diabetic patients with burns. The protective effect in group T1 is consistent with previous research findings showing that alkaloids, particularly mitragynine, along with other bioactive components such as flavonoids, phenolics, saponins, tannins, and glycosides, have antioxidant, anti-inflammatory, and antidiabetic activities (Raini, 2017; Salim et al., 2022; Limcharoen et al., 2022; Zhang et al., 2023). This mechanism occurs through the suppression of prostaglandin synthesis by inhibiting COX 2, decreasing iNOS activity, and reducing the formation of free radicals (ROS) (Zulhakim et al., 2025; Ramadhan et al., 2023). This is relevant to the pathogenesis of diabetes mellitus, where hyperglycemia and hyperlipidemia cause metabolic imbalances that lead to increased ROS (Galicia-Garcia et al., 2020). Additionally, kratom has the ability to inhibit the α-glucosidase enzyme, which can reduce glucose absorption and help

control glycemia (Wijayanti et al., 2023; Tuntiyasawasdikul et al., 2024). In silico findings also show the effect of kratom compounds on the modulation of inflammatory regulatory proteins such as MAPK and the control of mTOR activation, which plays a role in inflammatory and metabolic processes (Swaroop et al., 2024; Zhao et al., 2025).

This study has several limitations. The sample size used was relatively small, so the results should be generalized with caution. Liver damage was assessed based on histopathology alone, without involving biochemical biomarkers such as AST, ALT, cytokines, or ROS.

Conclusions

The application of kratom hydrogel on diabetic mice with burns significantly reduced hepatocyte cell damage. This protective effect is most likely due to the antioxidant and anti-inflammatory activities of bioactive compounds and the properties of hydrogel that support controlled release, along with tissue moisture. A 5% concentration had a better protective effect than 15%; therefore, further studies on the optimal dose are urgently needed. These findings reinforce the innovative topical application of kratom hydrogel aimed at protecting the liver from damage occurring during burns, especially in diabetic conditions. Further research is needed to validate the findings through biochemical analysis and long-term observation.

This study was conducted using a streptozotocin-induced diabetic mouse model, which may not fully reflect the complexity of diabetic burn injuries in humans. Liver function assessment was limited to histopathological evaluation without biochemical or molecular analyses, and the relatively small sample size and short treatment duration may limit the generalizability of the findings.

Acknowledgment

The authors would like to express their sincere gratitude to the Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya (UNUSA), for providing facilities and support for this study. Special thanks are extended to the all laboratories staff of the Integrated Research Laboratory, Faculty of Medicine UNUSA, for their technical assistance during the experimental procedures. The authors also appreciate all parties who contributed to the completion of this research.

References

Agustini, Rudiana, Erlix Rakhmad Purnomo, And Agus Widodo. 2019. Type 2 DM) After Red Rice Yeast Treatment.

Alberts, Adina, Andreea Gabriela Bratu, Adelina Gabriela Niculescu, And Alexandru Mihai Grumezescu. 2025. "New Perspectives Of Hydrogels In Chronic Wound Management." Molecules 30(3).

Afrianti, R., Nofiandi, D., Dira, D., & Ulfa, W. (2016). Pengujian Efektivitas Penyembuhan Luka Mencit Diabetes Melitus Yang Diberikan Sediaan Krim Ekstrak Etanol Daun Bandotan. Scientia: Jurnal Farmasi Dan Kesehatan, 6(1), 50-58.

Antaryani, D., Tandi, J., & Nobertson, R. (2019). Efek Ekstrak Biji Buah Pinang Terhadap Gambaran Histopatologi Pankreas Tikus Putih Diinduksi Streptozotocin. Farmakologika Jurnal Farmasi, 16(2), 135-144.

Chen, Lin, Shizao Fei, And Opeyemi Joshua Olatunji. 2022. "LC/ESI/TOF-MS Characterization, Anxiolytic And Antidepressant-Like Effects Of Mitragyna Speciosa Korth Extract In Diabetic Rats." Molecules 27(7). Doi:10.3390/Molecules27072208.

Dewhurst, Matthew R., Jin Rong Ow, Gözde Zafer, Noémi K. M. Van Hul, Heike Wollmann, Xavier Bisteau, David Brough, Hyungwon Choi, And Philipp Kaldis. 2020. "Loss Of Hepatocyte Cell Division Leads To Liver Inflammation And Fibrosis." Plos Genetics 16(11). Doi:10.1371/Journal.Pgen.1009084.

Farahanis Gitafitri, F., 2023. Pengaruh Gel Daun Jambu Mete (Anacardium Occidentale L.) Terhadap Perawatan Luka Bakar Grade II Pada Hewan Uji Mencit (Mus Musculus) (Doctoral Dissertation, Universitas Kusuma Husada Surakarta).

Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K.B., Ostolaza, H. & Martín, C., 2020. Pathophysiology Of Type 2 Diabetes Mellitus. International Journal Of Molecular Sciences, 21(17), P.6275.

Gounden, Varshan, And Moganavelli Singh. 2024. "Hydrogels And Wound Healing: Current And Future Prospects." Gels 10(1).

Limcharoen, T. Et Al., 2022. Inhibition Of A-Glucosidase And Pancreatic Lipase Properties Of Mitragyna Speciosa (Korth.) Havil. (Kratom) Leaves. Nutrients, 14(19), P.3909.

Lu, Xi, Qingxing Xie, Xiaohui Pan, Ruining Zhang, Xinyi Zhang, Ge Peng, Yuwei Zhang, Sumin Shen, And Nanwei Tong. 2024. "Type 2 Diabetes Mellitus In Adults: Pathogenesis, Prevention And Therapy." Signal Transduction And Targeted Therapy 9(1).

Nababan, Memo, Chatarina Umbul Wahyuni, And Fazidah Aguslina Siregar. 2023. "Factors Associated With Type 2 Diabetes Mellitus At Adam Malik General Hospital, Medan, Indonesia." Jurnal Berkala Epidemiologi 11(2):189–97. Doi:10.20473/Jbe.V11i22023.189-197.

Ningrum, A. M., Christina, M., Putri, T. R., & Simamora, C. J. K. (2021). Probability Induction Of Kratom Plant Bioactive Components In Antidiabetic And Antiobesity Studies. Bioeduscience, 5(3), 234-240.

Raini, M., 2017. Kratom (Mitragyna Speciosa Korth): Manfaat, Efek Samping Dan Legalitas. National Institute Of Health Research And Development, Indonesian Ministry Of Health, Pp. 175–184.

Ramadhan, F., 2023. Literature Review Artikel: Potensi Mitragyna Speciosa (Kratom) Sebagai Aktivitas Antioksidan, Antidiabetes, Antiinflamasi, Dan Antimikroba. An-Najat, 3(1), Pp.114–126.

Salim, H.M., Choirotussanijjah, C., Awwalia, E.S. & Alam, I.P., 2022. Anti-Inflammatory Effects And Potential Mechanisms Of Mitragyna Speciosa Methanol Extract On Λ-Karagenan-Induced Inflammation Model. Bali Medical Journal, 11(3), Pp.1172–1175.

Siu, Wing Sum, Hui Ma, And Ping Chung Leung. 2025. "Review On Current Advancements In Facilitation Of Burn Wound Healing." Bioengineering 12(4).

Swaroop, V., Ozkan, E., Herrmann, L., Thurman, A., Kopasz-Gemmen, O., Kunamneni, A. & Inoki, K., 2024. Mtorc1 Signaling And Diabetic Kidney Disease. Diabetology International, 15(4), Pp.707–718.

Todd, D. A., J. J. Kellogg, E. D. Wallace, M. Khin, L. Flores-Bocanegra, R. S. Tanna, S. Mcintosh, H. A. Raja, T. N. Graf, S. E. Hemby, M. F. Paine, N. H. Oberlies, And N. B. Cech. 2020. "Chemical Composition And Biological Effects Of Kratom (Mitragyna Speciosa): In Vitro Studies With Implications For Efficacy And Drug Interactions." Scientific Reports 10(1). Doi:10.1038/S41598-020-76119-W.

Tuntiyasawasdikul, S., Junlatat, J., Tabboon, P., Limpongsa, E. & Jaipakdee, N., 2024. Mitragyna Speciosa Ethanolic Extract: Extraction, Anti-Inflammatory, Cytotoxicity, And Transdermal Delivery Assessments. Industrial Crops And Products, 208, 117909.

Wijayanti, D.K., Masriani, M., Fadly, D., Muharini, R. & Rasmawan, R., 2023. Inhibition Of A-Glucosidase Enzyme By Ethanol Extract Of Kratom Leaf

Variant (Mitragyna Speciosa Korth.). Hydrogen: Jurnal Kependidikan Kimia, 11(3), P.286.

Zhang, P., Wei, W., Zhang, X., Wen, C., Ovatlarnporn, C., & Olatunji, O. J. (2023). Antidiabetic And Antioxidant Activities Of Mitragyna Speciosa (Kratom) Leaf Extract In Type 2 Diabetic Rats. Biomedicine & Pharmacotherapy, 162, 114689.

Zhao, H.L., Lai, F.M., Tong, P.C., Zhong, D.R., Yang, D., Tomlinson, B. & Chan, J.C., 2003. Prevalence And Clinicopathological Characteristics Of Islet Amyloid In Chinese Patients With Type 2 Diabetes. Diabetes, 52(11), Pp.2759–2766.

Zulhakim, I., Deswiaqsa, K. & Arantika, J., 2025. Formulation And Physical Evaluation Of Kratom (Mitragyna Speciosa Korth.) Leaf Extract Emulgel As An Analgesic In Mice (Mus Musculus). Jurnal Farmasi Dan Ilmu Kefarmasian Indonesia, 12(1), Pp.77–84.

Żwierełło, Wojciech, Krzysztof Piorun, Marta Skórka-Majewicz, Agnieszka Maruszewska, Jacek Antoniewski, And Izabela Gutowska. 2023. “Burns: Classification, Pathophysiology, And Treatment: A Review.” International Journal Of Molecular Sciences 24(4).