Salud, Ciencia y Tecnología. 2025; 5:2665
doi: 10.56294/saludcyt20252665

ORIGINAL

Antidiabetic Effect of Raru (*Vatica perakensis*) Bark Extract and Mocaf Activated Carbon in Streptozotocin-induced Diabetic Rats

Efecto antidiabético del extracto de corteza de raru (*Vatica perakensis*) y carbón activado Mocaf en ratas con diabetes inducida por estreptozotocina

Gunawan Pasaribu[1], Novitri Hastuti[2], Saptadi Darmawan[2], Gustan Pari[2], Lisna Efiyanti[2], Sigit Baktya Prabawa[2], Totok K. Waluyo[1], Yelin Adalina[1], Andianto[1], Soenarno[3], Agus Ismanto[4], Alfonsus H. Harianja[5]

[1]Research Center for Applied Botany, National Research and Innovation Agency of Indonesia. Cibinong, West Java, Indonesia.
[2]Research Center for Biomass and Bioproducts, National Research and Innovation Agency of Indonesia. Serpong, Banten, Indonesia.
[3]Research Center for Ecology, National Research and Innovation Agency of Indonesia. Cibinong, West Java, Indonesia.
[4]Research Center for Applied Zoology, National Research and Innovation Agency of Indonesia. Indonesia.
[5]Research Center for Behavioral and Circular Economics, National Research and Innovation Agency of Indonesia. Jakarta, Indonesia.

Cite as: Pasaribu G, Hastuti N, Darmawan S, Pari G, Efiyanti L, Baktya Prabawa S, et al. Antidiabetic Effect of Raru (*Vatica perakensis*) Bark Extract and Mocaf Activated Carbon in Streptozotocin-induced Diabetic Rats. Salud, Ciencia y Tecnología. 2025; 5:2665. https://doi.org/10.56294/saludcyt20252665

Submitted: 10-08-2025 **Revised:** 01-10-2025 **Accepted:** 25-12-2025 **Published:** 26-12-2025

Editor: Prof. Dr. William Castillo-González

Corresponding author: Gunawan Pasaribu

ABSTRACT

Introduction: the natural benefits of raru as a natural sweetness reducer. Batak people have practiced for generations, form the basis for exploring raru as a biomedicine ingredient for anti-diabetes.
Objective: this study aims to combine the raru's bark extract with tapioca-derived MAC (mocaf activated carbon) to assess its effectiveness and bioactivity as an anti-diabetic agent in male Sprague Dawley rats.
Methods: The carbonization technique used was inherently hydrothermal carbonization. For such, the modified tapioca flour was carbonized at a temperature of 250°C for 6 hours. Raru bark powder was extracted using ethanol 70 % by maceration for 72 hours. In vivo antidiabetic activity was used on Sprague Dawley rats, male, aged ± 12 weeks, with a weight of ± 250-350 grams.
Results: the result showed that the anti-diabetic activity of the combined raru's extract and MAC exposed to the rats brought about the declines in glucose levels in the rat's blood. The various treatments at different concentration ratios of raru's extract and MAC supposedly efficacious in the experiments showed that the levels of blood level reduction were slightly varied (14-21 %). The mixture of raru's extract and MAC with a 75:25 ratio was better than a 50:50 ratio in lowering the blood glucose level.
Conclusion: In vivo experiments can reduce blood sugar levels diabetic rats. The involvement of MAC in the alleged anti-diabetic agent did little to induce the glucose level decrease in the rat's blood. However, raru's extract and MAC indicate its potential utilization as an anti-diabetic agent.

Keywords: Antidiabetic; Extract; In-vivo; MAC; Raru.

RESUMEN

Introducción: los beneficios naturales del raru como reductor natural del dulzor, que el pueblo Batak ha practicado durante generaciones, constituyen la base para explorar el raru como ingrediente biomedicinal para la diabetes.
Objetivo: este estudio busca combinar el extracto de corteza de raru con MAC (carbón activado de mocafé) derivado de tapioca para estudiar su eficacia y bioactividad como antidiabético, probado en ratas macho

Sprague Dawley.
Método: la técnica de carbonización empleada fue esencialmente hidrotermal. Para ello, la harina de tapioca modificada se carbonizó a 250 °C durante 6 horas. El polvo de corteza de raru se extrajo con etanol al 70 % mediante maceración durante 72 horas. La actividad antidiabética in vivo se aplicó a ratas Sprague Dawley macho, de ± 12 semanas de edad y con un peso de ± 250-350 gramos.
Resultados: los resultados mostraron que la actividad antidiabética de la combinación de extracto de raru y MAC expuesta a ratas provocó la disminución de los niveles de glucosa en sangre. Los diversos tratamientos con diferentes concentraciones de extracto de raru y MAC, supuestamente eficaces en los experimentos, mostraron una ligera variación en la reducción de los niveles sanguíneos (14-21 %). La mezcla de extracto de raru y MAC en una proporción de 75:25 fue más eficaz que una proporción de 50:50 para reducir el nivel de glucosa en sangre.
Conclusión: los experimentos in vivo pueden reducir los niveles de azúcar en sangre en ratas diabéticas. La participación del MAC en el supuesto agente antidiabético tuvo poca influencia en la disminución del nivel de glucosa en sangre de la rata. Sin embargo, el extracto de raru y el MAC indican su potencial uso como agente antidiabético.

Palabras clave: Antidiabético; Extracto; In vivo; MAC; Raru.

INTRODUCTION

Diabetes is an alarming health problem today as nearly half a billion people worldwide have diabetes, including big countries such as China and the United States. Data from the International Diabetes Federation alleges that 1 in 11 people aged 20-79 years has diabetes and 1 in 2 adults is at risk of suffering undiagnosed diabetes.[1] Indonesia is one of the ten countries with the highest diabetes cases globally. Researchers have widely studied the effectiveness of natural extracts as anti-diabetic agents to manage the risk of diabetes, discovering several kinds of natural product compounds, such as indole alkaloids, which have been confirmed to afford specific anti-diabetic effectiveness in vitro and in vivo.[2]

Researchers are also developing the exploration of natural ingredients as anti-diabetic remedies by paying attention to the potential of locally available natural ingredients. Chinese researchers studied the Chinese *Sesbania cannabina* plant, and scientists in Africa studied the potential of *Ajuga remota* Benth leaf extract as anti-diabetic agent.[3,4] Furthermore, the Indian researcher reported several traditional medicinal plants as anti-diabetic agents, such as *Gymnema sylvestre, Momordica charantia, Trigonella foenum graecum, Tinospora cordifolia and Curcuma longa* in in-vivo and clinical studies.[5] In Sri Lanka, there are several medicinal plants for anti-diabetics, such as *Salacia reticulata, Coccinia grandis, Ipomoea aquatica*, and *Osbeckia octandra*. Researchers have subjected all of the plants to clinical trials.[6] Indonesia, as a country with high biodiversity, has several types of herbal plants that allegedly have anti-diabetic properties such as leaf extracts of consecutively *Annona muricata* (Soursop), *Andrographis paniculata* (*Sambiloto*), *Averrhoa bilimbi* (*Belimbing wuluh*), *Diospyros kaki* (Persimmon fruit/*kesemek*) and *Curcuma xanthorrhiza* (*Temulawak*).[7] The potential of Indonesia's natural resources as anti-diabetic medicine is not only limited to those commodities. It also has other unique local potentials in certain areas, such as *raru* (*Vatica perakensis*) bark extract from Sumatra.

Pasaribu, G. have identified several types of plants as *Raru* wood, which includes *Shorea maxwelliana*, and *Shorea faguetiana*. *Cotylelobium melanoxylon*, *Vatica songa* from the Dipterocarpaceae family, and *Garcinia* sp. from the Guttifera family.[8] Raru (*Cotylelobium* sp.) bark extract is known to have antioxidant properties. The Batak community usually uses this bark as a mixture for tuak (traditional drinks) in North Sumatra. It's important to note that local people strongly believe in the anti-diabetic properties of raru bark, which adds a cultural significance to the research. This belief is rooted in their traditional knowledge and practices, and it underscores the potential of indigenous knowledge in the development of anti-diabetic treatments.[9,10] In addition, extracts from the *Raru* stem bark of *Vatica pauciflora* Blume and *Cotylelobium* sp. have been tested in vitro and in vivo as antidiabetic agents.[2]

Researchers continue to investigate and develop the anti-diabetic potential of *Raru* extract especially with advancements in drug formulations to accelerate the effectiveness through the involvement of nanoparticles (NPs) loading techniques. Several research documentes the use of nanoparticles as antidiabetic loading agents, such as nano chitosan, nano Zinc oxide, nano solid lipids, and nanofibrous scaffold.[11,12,13] The use of polymeric NPs, which acted acts as a carrier of drugs to target sites by reducing the adverse side effects, and the entrapment of anti-diabetic ingredients brought about the ingredient release to more selectively reach the targeted diabetic cells.[14] The results revealed that the approach used in nanoparticles as anti-diabetic loaders seems to be a promising strategy to enhance the oral efficacy of oral antidiabetics. However, pore size and morphology of the carriers are the main factors affecting the drug loading and release, including the use of anti-diabetic agent nanoparticles.[15]

One of the materials with a porous structure and high adsorption capacity is activated carbon. Activated carbon is an amorphous carbon material possessing a large surface area. Activated carbon is considered inexpensive, commercially available, non-toxic and consists of a three-dimensional interrelated pore structure in a large amount with various sizes on a nanometer scale which is further classified as consecutive micropores (<2 nm), mesopores (2–50 nm) and macropores (>50 nm).[16] It has been employed as an adsorbent for removing the reaction mixture's smell, coloration, and impurities.[17]

The use of activated carbon as drug delivery was studied in 1997 as an anticancer drug and applied to digestive cancer in patients in whom the operation is contrarily indicated.[18] Recently, a drug-encapsulated carbon (DECON) has been developed as an enhancer of antiviral drug delivery of acyclovir (ACV). The results showed that the involvement of DECON reduced the dosing frequency, shortened treatment duration, and improved therapeutic efficacy more than topical or systemic antivirals alone.[19] Although the use of activated carbon has been extensively studied as a drug delivery agent, some studies have used carbon microparticles and have been tested to contain fever medications such as ibuprofen, paracetamol, and high blood pressure medication carvedilol.[18,20,21,22] However, a study that reported the effectiveness of activated carbon on the nanoscale and used as an anti-diabetic has not yet to be reported. Relevantly, in this study, we successfully elaborated the performance of *Raru* (*Vatica perakensis*) bark extract as the anti-diabetic agent, combined with a nano-activated carbon (i.e. mocaf activated-carbon/ MAC) as the agent carrier, which was tested *in vivo*. This study is expected to encourage the utilization of medicinal plants from Indonesia and enrich the oral drug formulation technology with high effectiveness, and all the related detailed results are the following. The combination of raru extract and MAC is intended to increase effectiveness and anti-diabetic bioactivity.

METHOD

Plants Materials

The bark of Raru (*Vatica perakensis*) was collected from the locality of Riau Province, Indonesia in June 2018 with GPS location: latitude 1°15'34.63" N and longitude 101°12'47.15" E. Mr. Abdurrahman Kartonegoro, a Botanist at Herbarium Bogoriensis, Indonesia, confirmed the plant's identity. A specimen coded as (BO-1273383) was deposited at the Herbarium Bogoriensis, Indonesia.

Activated carbon preparation and characterization

Nano-activated carbon was made from tapioca flour. Mocaf mass is 15 % of the water volume. Mocaf is cassava flour modified through fermentation using microbes. The carbonization technique used was inherently hydrothermal carbonization. For such, the modified tapioca flour was carbonized at a temperature of 250°C for 6 hours using water as media, which was placed as much as a third of the carbonizing digester volume. In this way, the hydrothermal carbonization brought out the product called modified carbonized tapioca flour (abbreviated as Mocaf).

The resultant hydrothermal-carbon (Mocaf) was then rinsed with hot water until the pH reached 7. Activation (of hydrothermal-carbon) was employed using a superheated water vapor at a temperature of 800°C for 30 minutes to obtain the mocaf-derived activated carbon. Afterwards, the resulting Mocaf activated-carbon (abbreviated as MAC) was rinsed using distilled water until the pH reached 6-7. The morphology of activated carbon was observed using a *Scanning Electron Microscope* (SEM) instrument of Type Zeiss EVO 50 (Zeiss, Germany) and was operated at 10 kV. Crystallite structure, porosity, particle size, and elemental analysis of activated carbon were observed using *X-Ray Diffractometer* (XRD); Surface Area Analyzer; Particle Size Analyzer (PSA), and X-Ray Fluorescence (XRF), respectively. The observed physical properties of activated carbon included moisture content, ash content, fixed carbon, volatile content, pH, and iodine adsorption capacity, and then were compared with the Indonesian National Standard (SNI).

Raru Bark Extraction

The barks of Raru (*Vatica perakensis*) were dried (under the shade). Afterward, the dried barks were ground to powder in a mechanical grinder (of *hammer mill* type) and sieved using a 40-60 mesh screener. Raru bark powder that passed through the sieve/screener was extracted using ethanol 70 % by maceration for 72 hours. Afterward, the bark extract liquid was filtered (to separate it from the extracted bark powder), then concentrated in a rotary vacuum evaporator (Buchi R-100) at 50°C temperatures. After evaporation, a dry extract will be obtained and used in the following experiment.

In vivo antidiabetic activity

Sprague Dawley rats, male, aged ± 12 weeks, with a weight of ± 250-350 grams were obtained from the Animal and Food Testing Center of the Food and Drug Supervisory Agency of Indonesia. The rat animals were placed in cages with 2-3 mice per cage at room temperature of 25°C with a humidity of 60-70 %. Animals were fed 15 gr of conventional diets/day and water *ad libitum*. The number of approvals of the Ethics Committee

in 019-2018 KEH TROP BRC. The procedures were performed accordance with principle of animal welfare, and the research procedures using experimental animals at SVMBS IPB University. Sprague Dawley rats were fasted 16 hours before induction using STZ streptozotocin (STZ) (Nacalai). Blood glucose levels of rat animals were checked using the Accu check ® test strip to determine the basal condition of the experimental animals. The animals were induced (infected) with streptozotocin (STZ) (Nacalai) at a dose of 45 mg/kg of the rat body weight and the route of injection (intraperitoneal is standard), previously dissolved in Citrate Buffer 0.05 M with pH 4.5, and then were injected intraperitoneally into the rats. After 48 hours, the rats' sugar (glucose) levels were observed using Accu Check ®, and then their serum was taken to check blood glucose levels. The rats were declared induced diabetes if the blood glucose level was ≥ 250 mg/dL,

Sprague Dawley rats were randomly divided into six groups (each containing seven rats), and the details were as follows:

- Group I: Normal group; the rats were orally administered with distilled water and a standard pellet diet (n= 7)
- Group II: Positive control group, the rats were orally administered (infected) with STZ and glibenclamide® **(n=7)**
- Group III: Negative control group, the rats were orally administered with STZ and distilled water (n=7)
- Group IV: Treatment 1, rats were orally administered with STZ and 350 mg of *Raru* extract/kg of rat body weight
- Group V: Treatment 2, rats were orally administered with STZ and 350 mg of *Raru* extract/kg of rat body weight of *Raru* extract and nano-activated carbon in a ratio of 75:25 (w/w).
- Group VI: Treatment 3, rats were orally administered with STZ and 350 mg of *Raru* extract/kg of rat body weight of *Raru* extract and nano-activated carbon in a ratio of 50:50 (w/w).

Initially, each treatment or group (I-VI) was employed to proceed for 4 weeks. At the end of 4-week treatments, the rats fasted for 16 h, and the fasted blood glucose (FBG) levels (in the fasted rats) were detected using Accu Check ® 6 times before STZ induction, 48 hours after STZ induction and at days 7, 14, 21, and 28 after 4-week treatments.

After 4 weeks of feeding, the rat animals (formerly in all 6 groups) were euthanized using the exsanguination method (anesthetized with ketamine as much as 80 mg/kg of rat body weight and with xylazine as much as 10 mg/kg of body weight, and the rat blood was taken as much as possible from the heart). Then, the rat pancreas was taken for histopathological examination.

Statistical analysis

To compare between groups, one-way ANOVA was used with $p<0.05$ considered significant. Data are presented as mean ± SD.

RESULTS

Characterization of Hydrothermal-Carbon and Activated-Carbon

The characterization includes the scrutinizing the physical properties of carbon generated from the hydrothermal carbonization on modified-tapioca flour (hydrothermal carbon or Mocaf); and of the Mocaf activated carbon (MAC), produced by the activation of hydrothermal carbon (Mocaf) using the high temperature of superheated water vapor. The results are described in table 1.

Table 1. Proximate analysis of initial hydrothermal carbon and activated carbon made of mocaf

Items	Yields (%)	Iodine adsorption (m^2/g)	Proximate (%)			
			Moisture content	Ash content	Volatile	Fixed carbon
Hydrothermal carbon	37,77	256	4,18	0,17	47,26	43,39
Mocaf activated carbon	24,00	834	3,48	1,57	5,43	89,52
Indonesian National Standards (SNI 06-3730-1995)	n.d	Min: 750	Max:15	Max: 10	Max: 25	Min: 65

Remarks: Min= minimum; Max= Maximum n.d= not determined

This result was incompatible with the resulting proximate analysis in table 1. However, hydrothermal carbon's hydrogen and oxygen contents were higher than those of activated carbon. The higher oxygen content of hydrothermal carbon can be attributed to the higher degree of surface oxidation.[23] The higher loss of

oxygen in activated carbon (final value = 13,55 %) is related to the aromatization process that continues when the temperature increases in the activation process and indicates that furans structures are consumed in the carbonization process.[24]

The results of XRD analysis also confirmed the structural changes that occurred during the carbonization process. The XRD diffractogram showed the differences among raw mocaf, hydrothermal, and activated carbon (figure 1-3). Hydrothermal carbonization has changed the structure of mocaf into amorphous hydrochar. The further process generated activated carbon with a hexagonal carbon structure, as shown in the peak at 2 thetas in angles around 24 and 43 degrees (figure 3). Observed diffraction peaks ranged from 20 to 46 two theta values, which corresponded to the Braggs reflective plane values and it is often used as an approach to analyzing the optical properties of carbon fiber composites.[25] There are two types of diffraction peaks at 2 theta values of 22,5 and 43,0, which could be ascribed to reflections from the (002) and (110) crystal planes.[26]

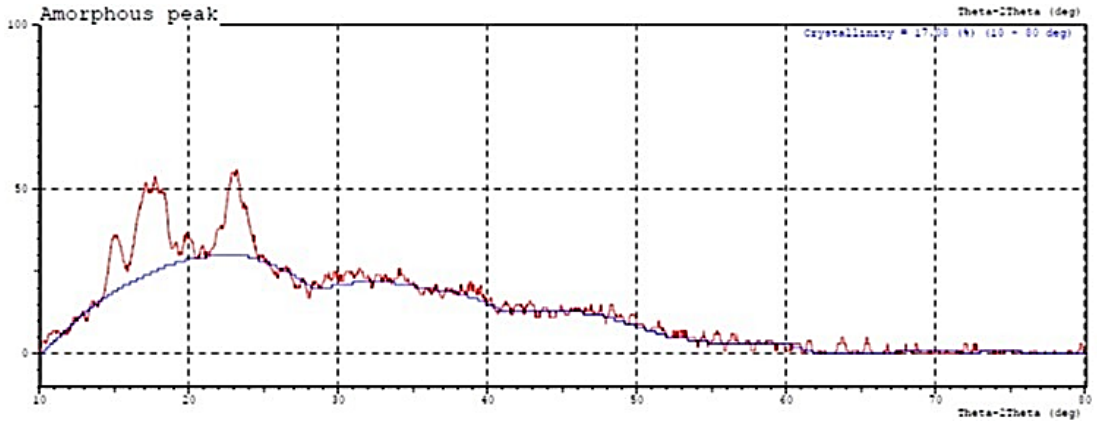

Figure 1. Diffractogram pattern of raw mocaf

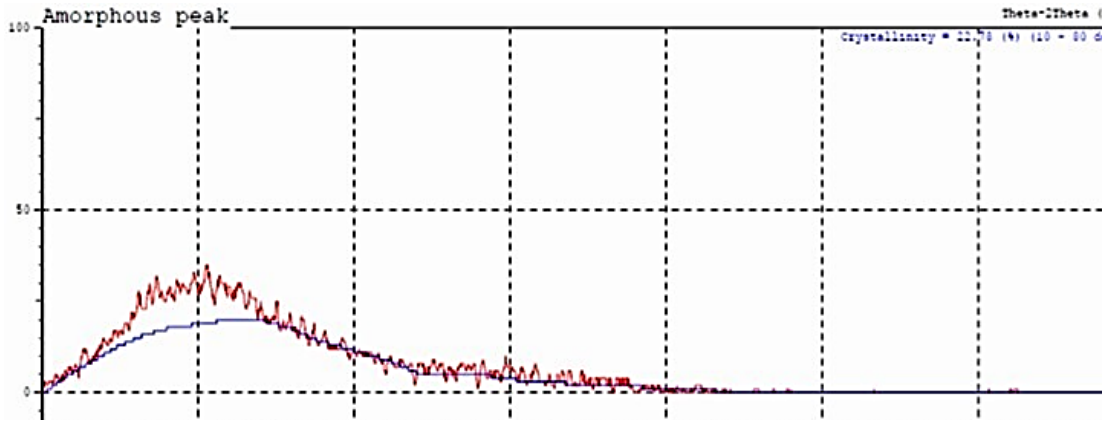

Figure 2. Diffractogram pattern of hydrothermal carbon

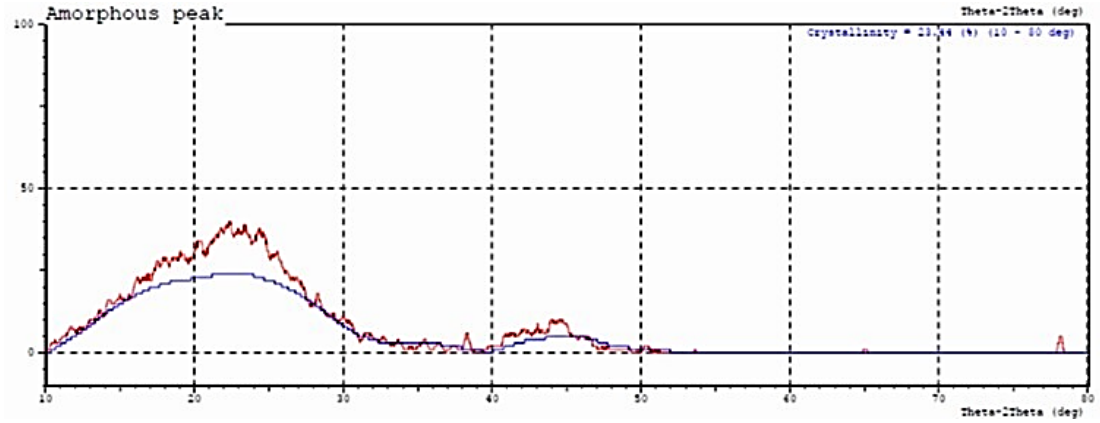

Figure 3. Diffractogram pattern of activated carbon

Isotherms of adsorption and desorption of N_2 gas were used to determine the surface area, pore volume, and

estimated pore diameter of hydrothermal carbon as well as activated carbon. Hydrothermal carbon revealed lower surface area, lower total pore volume, and higher pore diameter than activated carbon. Based on the classification of pores in solid materials, hydrothermal carbon had mesopores (2-50 nm), while activated carbon had supermicropores (0,7-2 nm).[17] The surface area of resultant activated carbon prepared by water vapor activation (690,451 m^2/g) was much lower than that of activated carbon produced by combining hydrothermal carbonization with NaOH activation, which showed a surface area of 1 282,49 m^2/g. The total pore volume and surface area of hydrothermal carbon were lower because, during hydrothermal carbonization, the pore development did not occur enormously due to the recondensation of volatile substances. However, in the hydrothermal process, the primary chemical components of lignocellulosic materials changed the cell wall structure and altered the surface properties.[27]

The volume of activated carbon micropores was higher than the volume range of micropores for activated carbon, which ranged from about 0,02-0,1 cc/g.[28] Accordingly, it can be assumed that superheated water vapor activation generated more micropore structures.

Hydrothermal and activated carbon pore structure formation could be observed from the isothermal adsorption/desorption curves of nitrogen (N2) gas. A slower adsorption/desorption rate indicated the least active sites formed on hydrothermal carbon during the hydrothermal carbonization process.[25] The type I/IV characteristics, with solid N_2 adsorption at low relative pressure (P/P_0) and slightly steep N_2 adsorption trend/curve at high relative P/P_0 indicating that micropores and mesopores/macropores coexisted in activated carbon.[22]

The pore distribution curves of Dubinin Astakov showed that activated carbon had a smaller pore size, which dominated over its surface when compared with the size of hydrothermal carbon. Based on the classification of pores in solid materials, hydrothermal carbon was predominantly mesoporous (2-50 nm), while activated carbon had supermicropores (0,7-2 nm) and ultra-micropores (< 0,7 nm).[17] Pore size distribution has been used to describe activated carbon's internal structures and adsorption capacities. The large number of micropores on activated carbon can be attributed to the development of mesopores from hydrothermal carbon formed during the activation process.

In-vivo antidiabetic activity

Mocaf activated carbon (MAC), derived from modified tapioca flour, was combined with *Raru*'s bark extract and then applied (as an antidiabetic agent) to reduce the blood glucose level in the experimented rats. The combination of raru extract and MAC is intended to increase effectiveness and bioactivity. Results indicate that the given treatments (expressed as Group IV-VI) positively lowered the blood glucose level in the experimented rats (table 2). The highest lowering value (blood glucose level) was found in pure rare extract, followed by 75:25 rare extract+MAC and 50:50 rare extract+MAC. It is indicated that there was no significant effect of the presence or involvement of activated carbon (MAC) in lowering the blood glucose levels in the rats (table 2).

Table 2. Blood glucose-lowering effect of raru extract and MAC in diabetic rat

Groups (Treatments)	Initial blood glucose level (mg/dl)	Final blood glucose level (mg/dl)	Blood glucose level decrease (%)
Group I (Normal)	126,24	154,42	(18,25)±3,47
Group II/ Positive control (C+)	356,10	322,05	34,05±4,36
Group III/ Negative control (C-)	383,68	467,75	(17,97)±8,32
Group IV/ Raru's extract, dosage 350 mg/kg BW	321,01	250,58	21,94±3,45
Group V/ Raru's extract +(MAC) =75:25, dosage 350 mg/kg BW	413,95	335,94	18,85±2,43
Group VI/ Raru's extract +(MAC) =50:50, dosis 350 mg/kg BW	354,59	301,50	14,97±2,54

MAC: Mocaf Activated Carbon

Table 3. Bodyweight (g) of diabetic rats induced with STZ before and after 28 days treatment of raru bark extract and MAC

Groups (Treatments)	Before (g)	After (g)	% change
Group I (Normal)	313,2	335,0	6,5±2,34
Group II/ Positive control (C+)	280,4	229,8	(22,0)±2,25
Group III/ Negative control (C-)	254,0	264,0	3,8±1,24
Group IV/ Raru's extract, dosage 350 mg/kg BW	374,8	210,8	(30,4)±2,68

Group V/ Raru's extract +(MAC) =75:25, dosage 350 mg/kg BW	278,2	200,4	(38,8)±3,76
Group VI/ Raru's extract +(MAC) =50:50, dosis 350 mg/kg BW	325,0	224,3	(44,9)±3,25
MAC: Mocaf Activated Carbon			

Table 3 presents the effects of raru extract and MAC on rats' body weights. The drastic weight loss cannot yet be explained whether it is due to the effect of the therapy used or a decrease in the appetite of the test animals.

DISCUSSIONS

During the hydrothermal carbonization process, the precursor derived from biomass (modified tapioca flour) was converted into valuable carbon materials using water as a reaction medium under self-generated pressures, bringing out the so-called hydro char.[29] Accordingly, the moisture content (MC) of hydrochar is relatively higher than that of regular/conventional char (without water involvement). The hydrothermal carbonization process has a low energetic impact. Using polysaccharides as raw materials (e.g., tapioca flour) will produce carbon microspheres with uniform sizes under very mild process conditions.[30] The yield of activated carbon was lower than that of hydrochar. This result was commensurate with the previous studies that used hydrothermal carbon as a precursor of activated carbon from tapioca and cassava flour.[26]

In general, the properties of activated carbon from mocaf could meet the Indonesian National Standards (table 1). Iodine adsorption and fixed carbon of activated carbon were higher than those of hydrochar. The high iodine adsorption value was related to the highly microporous activated carbon generated during the activation process.[31] This porous structure is formed from residual carbon atoms that have arranged themselves into flat aromatic sheets that are cross-linked randomly with each other, and the interstices in these irregularly aromatic sheets give rise to the porosity upon which the properties of activated carbon mostly depend.[32] The porosity development of activated carbon was extremely influenced by the temperature of the hydrothermal carbonization process, regardless of the different biomass parents (origins). Conversely, higher hydrothermal temperatures led to lower porosity development.[24]

The tendency of lower effectiveness/efficacy with larger doses of activated carbon (75:25 vs. 50:50) was likely due to the incorporation of *raru extract* on activated carbon. In this study, *raru* extract was arranged to be incorporated into activated charcoal pores, which was part of the passive delivery strategy, where the bark extract (presumed as the active compound) was physically incorporated into the internal cavity (in the active carbon) and then stabilized by non-covalent interactions between the extracts and nanocarriers, i.e., MAC.[31] The existing non-covalent bond between the activated carbon and the raru extract was fragile, affecting the extract-delivery process and the extract's effectiveness in the targeted diabetic cells.[31,33]

Furthermore, Mirilaya and co-authors mentioned that drug compounds loaded on activated carbon afforded faster drug release, which was influenced by the wettability of activated carbon and the melting process that occurred when the drug compounds interacted with the surface of activated carbon, which further could weaken the intermolecular bond between the drug compounds and activated carbon.[16]

The results of this study strengthened the previous research, where *Vatica perakensis*' bark extract with an in-vitro method could inhibit the activity of alpha-glucosidase enzyme up to 92,57 %.[8] However, this result differed from Anisah's study's results, in which the percentage decrease in glucose levels in rats treated with jabon extracts and jabon extract + hydro-activated carbon was 26,61 % and 30,85 %, respectively. There was an alleged effect of anti-hyperglycemic activity with the addition of hydro-activated carbon. The same thing concerning the glucose-level decrease was seen in the *samama* (different with raru extract) bark extract and the *samama* bark extract + hydro activated carbon, which were 25,82 % and 31,60 %, respectively.[34] This difference is caused by the different types of extract and characteristic of activated carbon used.

In accordance with previous research on antidiabetic activity using the alpha-glucosidase inhibition method, the compounds responsible for antidiabetic activity are phenolic compounds. This aligns with research conducted by Deka *et.al.*[35] The weight loss observed in the STZ-induced diabetes model indicates a significant decrease in body mass due to loss of pancreatic ß cells, hyperglycemia, and insulin deficiency leading to increased fat and protein catabolism for the body's energy supply.[36]

However, the limitations of this research are no pharmacokinetic data and no the investigation of mechanism of action. For the next, we will take concrete next steps: (a) optimize the loading and release profile of the extract onto MAC in vitro; (b) characterize the surface chemistry of MAC; (c) perform phytochemical analysis to identify the active compounds; (d) investigate other mechanisms (e.g., insulin secretion, insulin sensitivity.

The research's implication strengthens the findings obtained in previous in-vitro research, so the direction of development will be clear in further research. However, this research has limitations because it cannot explain the mechanisms occurring in the combination of raru extract and MAC.

CONCLUSIONS

The varying percentages in a particular mixture proportion between raru's extract and MAC were not significantly different from each other in lowering the blood glucose levels (18 %) in the experimented diabetic rats, where the levels were even slightly lower than those of solely raru's extract treatment (21 %).

The mixture of raru's extract and MAC with a 75:25 proportion ratio was better than a 50:50 ratio in lowering the blood glucose level. The porous structure of activated carbon has been suggested to be used as a potential carrier of drugs (i.e. raru's bark extracts). However, it is necessary to pay attention to the physical characteristics of activated carbon which could greatly affect its performance in lowering blood glucose levels.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas 2019. Brussel; 2019. (9th Edition).

2. Zhu Y, Zhao J, Luo L, Gao Y, Bao H, Li P. Research progress of indole compounds with potential antidiabetic activity. Eur J Med Chem. 2021;223:113665.

3. Li R, Tang N, Jia X, Xu Y, Cheng Y. Antidiabetic activity of galactomannan from Chinese Sesbania cannabina and its correlation of regulating intestinal microbiota. J Funct Foods. 2021;83:104530.

4. Tafesse TB, Hymete A, Mekonnen Y, Tadesse M. Antidiabetic activity and phytochemical screening of extracts of the leaves of Ajuga remota Benth on alloxan-induced diabetic mice. BMC Complement Altern Med. 2017;17:1–9.

5. Gaonkar VP, Hullatti K. Indian Traditional medicinal plants as a source of potent Anti-diabetic agents: A Review. J Diabetes Metab Disord. 2020;19(2):1895–908.

6. Wasana KGP, Attanayake AP, Jayatilaka KAPW, Weerarathna TP. Antidiabetic Activity of Widely Used Medicinal Plants in the Sri Lankan Traditional Healthcare System: New Insight to Medicinal Flora in Sri Lanka. Evidence-based Complement Altern Med. 2021;2021.

7. Firdausya H, Amalia R. Review Jurnal: Aktivitas dan Efektivitas Antidiabetes pada Beberapa Tanaman Herbal. Farmaka. 2020;18(1):162–70.

8. Pasaribu G. Inhibition Activity of Alpha Glucosidase from Several Stem Bark of Raru. J Penelit Has Hutan. 2011;29(1):10–9.

9. Pasaribu G, Setyawati T. Antioxidant and Toxicity Activity of Raru (Cotylelobium sp.) Stem Bark. J Penelit Has Hutan. 2011;29(4):322–30.

10. Situmorang ROP, Harianja AH, Silalahi J. Karo's Local Wisdom : The Use of Woody Plants for Traditional Diabetic Medicines. Indones J For Res. 2015;2(2):121–31.

11. Iqbal Y, Malik AR, Iqbal T, Aziz MH, Ahmed F, Abolaban FA, et al. Green synthesis of ZnO and Ag-doped ZnO nanoparticles using Azadirachta indica leaves: characterization and their potential antibacterial, antidiabetic, and wound-healing activities. Mater Lett. 2021;130671.

12. El-bagory I, Alruwaili NK, Elkomy MH, Ahmad J, Afzal M, Ahmad N, et al. Development of novel dapagliflozin loaded solid self-nanoemulsifying oral delivery system : Physiochemical characterization and in vivo antidiabetic activity. J Drug Deliv Sci Technol. 2019;54(August):101279.

13. Emin M, Ertas B, Alenezi H, Hazar-yavuz AN, Cesur S, Sinemcan G, et al. Accelerated diabetic wound healing by topical application of combination oral antidiabetic agents-loaded nanofibrous scaffolds : An in vitro and in vivo evaluation study. Mater Sci Eng C. 2021;119(April 2020):111586.

14. Ambalavanan R, John AD, Selvaraj AD. Nano-encapsulated Tinospora cordifolia (Willd .) using poly (D , L-lactide) nanoparticles educe effective control in streptozotocin- induced type 2 diabetic rats. IET Nanobiotechnology. 2020;14(9):803–8.

15. Avila MI, Alonso-Morales N, Gilarranz MA, Baeza A, Rodrıguez JJ, Gillaranz M. High load drug release system based on carbon porous nanocapsule carriers . Ibuprofen case study. J Mater Chem B. 2020;8:5293–304.

16. Tanemura K, Rohand T. Activated charcoal as an effective additive for alkaline and acidic hydrolysis of esters in water. Tetrahedron Lett. 2020;61(44):152467.

17. Hagiwara A, Takahashi T, Kitamura K, Sakakura C, Shirasu M, Ohgaki M, et al. Endoscopic local injection of a new drug delivery formulation , anticancer drug bound to carbon particles , for digestive cancers : Pilot study. J Gastroenterol. 1997;32:141–7.

18. Yadavalli T, Ames J, Agelidis A, Suryawanshi R, Jaishankar D. Drug-encapsulated carbon (DECON): A novel platform for enhanced drug delivery. Sci Adv. 2019;5:1–13.

19. Zhang Y, Zhi Z, Li X, Gao J, Song Y. Carboxylated mesoporous carbon microparticles as new approach to improve the oral bioavailability of poorly water-soluble carvedilol. Int J Pharm. 2013;454(1):403–11.

20. Inagaki M. Pores in carbon materials-importance of their control. New Carbon Mater. 2009;24(3):193–232.

21. Wang X, Liu P, Tian Y. Ordered mesoporous carbons for ibuprofen drug loading and release behavior. Microporous Mesoporous Mater. 2011;142(1):334–40.

22. Falco C, Morallo E, Titirici MM. Tailoring the porosity of chemically activated hydrothermal carbons : Influence of the precursor and hydrothermal carbonization temperature. Carbon N Y. 2013;2.

23. Falco C, Caballero FP, Babonneau F, Gervais C, Laurent G, Titirici M, et al. Hydrothermal Carbon from Biomass : Structural Differences between Hydrothermal and Pyrolyzed Carbons via 13 C Solid State NMR. Langmuir. 2011;14460–71.

24. Aravind M, Amalanathan M. Structural , morphological , and optical properties of country egg shell derived activated carbon for dye removal. Mater Today Proc. 2021;43:1491–5.

25. Yuan C, Lin H, Lu H-Y, Xing E, Zhang Y, Xie B. Synthesis of hierarchically porous MnO2/rice husks derived carbon composite as high-performance electrode material for supercapacitors. Appl Energy. 2016;178:260–8.

26. Islam A, Tan IAW, Benhouria A, Asif M, Hameed BH. Mesoporous and adsorptive properties of palm date seed activated carbon prepared via sequential hydrothermal carbonization and sodium hydroxide activation. Chem Eng J. 2015;270:187–95.

27. Promdee K, Chanvidhwatanakit J, Satitkune S. Characterization of carbon materials and di ff erences from activated carbon particle (ACP) and coal briquettes product (CBP) derived from coconut shell via rotary kiln. Renew Sustain Energy Rev. 2017;75(July 2016):1175–86.

28. Liu R, Xie Y, Cui K, Xie J, Zhang Y, Huang Y. Adsorption behavior and adsorption mechanism of glyphosate in water by amino-MIL-101 (Fe). J Phys Chem Solids. 2022;161:110403.

29. Pires E, García-bordej E. Parametric study of the hydrothermal carbonization of cellulose and effect of acidic conditions. 2017;123.

30. Pari G, Darmawan S, Prihandoko B. Porous Carbon Spheres from Hydrothermal Carbonization and KOH Activation on Cassava and Tapioca Flour Raw Material. Procedia Environ Sci. 2014;20:342–51.

31. Lu H, Wang J, Wang T, Zhong J, Bao Y, Hao H. Recent Progress on Nanostructures for Drug Delivery Applications. J Nanomater. 2016;2016.

32. **Çeçen** F. Activated Carbon. In: Kirk-Othmer Encyclopedia of Chemical Technology. John Wiley & Sons, Inc; 2014.

33. Patra JK, Das G, Fraceto LF, Vangelie E, Campos R, Rodriguez P, et al. Nano based drug delivery systems: recent developments and future prospects. J Nanobiotechnology. 2018;16(71):1–33.

34. Anisah LN, Syafii W, Pari G, Sari RK. Antidiabetic activities and identification of chemical compound from samama (Anthocephalus macrophyllus (Roxb) Havil). Indones J Chem. 2018;18(1):66–74.

35. Deka H, Choudhury A, Dey BK. An Overview on Plant Derived Phenolic Compounds and Their Role in Treatment and Management of Diabetes. 2022;25(3):199–208.

36. Ye L, Huang H, Zhang S, Lu J, Wu D, Chi P, et al. Streptozotocin-Induced Hyperglycemia Affects the Pharmacokinetics of Koumine and its Anti-Allodynic Action in a Rat Model of Diabetic Neuropathic Pain. 2021;12(May):1–12.

FINANCING

This study was funded by the Ministry of Environment and Forestry, Republic of Indonesia under letter of decree number 37/PE/VII/2021.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORSHIP CONTRIBUTION

Conceptualization: Gunawan Pasaribu, Novitri Hastuti, Totok K Waluyo.
Data curation: Lisna Efiyanti, Andianto, Agus Ismanto.
Formal analysis: Gunawan Pasaribu, Gustan Pari, Saptadi Darmawan.
Research: Gunawan Pasaribu, Novitri Hastuti, Saptadi Darmawan.
Methodology: Soenarno, Sigit Baktya Prabawa, Lisna Efiyanti.
Project management: Gustan Pari, Agus Ismanto, Totok K Waluyo.
Resources: Saptadi Darmawan, Yelin Adalina, Lisna Efiyanti.
Software: Soenarno, Agus Ismanto, Yelin Adalina.
Supervision: Alfonsus H Harianja, Soenarno, Totok K Waluyo.
Validation: Yelin Adalina, Alfonsus H Harianja, Sigit Baktya Prabawa.
Display: Agus Ismanto, Sigit Baktya Prabawa, Alfonsus H Harianja.
Drafting - original draft: Gunawan Pasaribu, Novitri Hastuti, Andianto.
Writing - proofreading and editing: Gunawan Pasaribu, Andianto, Gustan Pari.