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The National Seminar on Chemistry aimed to improve the quality of research in Chemistry and Chemical Education through skills of the 21st century in the 4.0 industrial revolution era. The Conference was held in Surabaya, Indonesia on October 5, 2019. The Conference was hosted by the Chemistry Department, Faculty of Mathematics and Natural Sciences, Universitas Negeri Surabaya, Indonesia.

Please click [here](#) for the conference website.

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National Seminar on Chemistry 2019 was dedicated to the topic “The Role of Chemistry and Its Learning to Improve Skills of the 21st Century in the 4.0 Industrial Revolution Era”. This conference was motivated by a variety of Indonesian natural resources, abundant, and demanding the development of innovation through material engineering produces the high quality materials known as smart materials. The conference took place in Surabaya, October 5, 2019. The success of this conference is supported by 85 presenters and more than 190 participants.

This conference had qualified keynote speakers, they are Prof. Dr. Didik Prasetyoko, M.Sc. from Institut Teknologi Surabaya, Prof. Dr. Suyanta, M.Si.

from Universitas Negeri Yogyakarta and Dr. Pirim Setiarso, M.Si. from Universitas Negeri Surabaya. They are expert at catalyst and energy, and expert in electrochemical and membrane technology, respectively.

The articles in this conference included the areas of Energy and Renewable Energy, Materials Chemistry, Computational Chemistry, Natural Product Chemistry, Synthesis of Organic Chemistry, Cosmetical Chemistry, Analytical Chemistry, Environmental Chemistry, Biochemistry, and Chemical Education. All the qualified papers had been selected through a strict reviewed process for Atlantis proceeding.

We would like to express our gratitude to keynote speakers, invited speakers, presenters, participants, organizing committee, members of scientific committee, reviewers, and sponsors for supporting the conference, Special thanks to Mr. Zeger Karssen from Atlantis Press for his support in publishing the proceedings.

Dr. Utiya Azizah, M.Pd
Chairman of Organizing Committee

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Utilization Of Nanogold And Nanosilver To Treat Herpes Disease: Case Study Of Herpes Transmission In Islamic

Cottage Schools

Titik Taufikurohmah, Djojok Supardjo, Rusmini Rusmini

This research aims to utilize nanogold and nanosilver to treat herpes disease which suddenly appeared in one of the Islamic cottage schools. How this happened is not a study this time. Nanogold has activity to increase cell proliferation and collagen biosynthesis. Nanogold also has antioxidant activity....

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Mucolytic Activity of Flavonol Isolated from The Silver Fern (*Pityrogramma calomelanos*)

Suyatno Sutoyo, Tukiran Tukiran, Nurul Hidajati, Nur Indah Kumalasari

The aim of study is to determine the mucolytic activity of flavonol compound namely 3,5, 7,3',4'-pentahydroxy flavone (quercetine), isolated from acetone extract of the silver fern (*P. calomelanos*). The mucolytic activity assay in vitro was based on the decreasing viscosity of intestinal mucus...

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The Effect of Concentration Calcium Alginate On Metformine Encapsulated

Sari Edi Cahyaningrum, Nuniek Herdyastuti, Amaria Amaria, Pupuh Findia

This research aimed to study the effect of concentration calcium alginate on metformine encapsulation processes and investigated characteristic of

metformine encapsulation. The encapsulation of metformine performed using chitosan and calcium alginate polymers with calcium chloride as crosslinking agent....

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Determination of Ellagic Acid Compound Activity as Anti Breast Cancer

I Gusti Made Sanjaya, Defitiana Wanita

This research was conducted to determine the activity of ellagic acid compounds as anti-breast cancer. The research was carried out through Molecular Docking in silico with several stages such as optimization of the structure of 3D ellagic acid compounds and docking between optimized ellagic acid compounds...

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Diversification of "NAJWA" Hijab Staining using Tie-Dye Method Based on Natural Dyes

Samik Samik, Agus Budi Santoso, Nita Kusumawati

Diversification of "Najwa" hijab staining has been carried out using a tie-dye method based on natural dyes. A number of natural dyes materials, which include turmeric, cherry and mango leaves and brazilwood bark, have been optimized for use. To obtain a stable color quality, staining is carried out...

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Histopathology of Kidney In Mice (*Mus musculus* L) Indicated By Pre-Diabetes Mellitus Type 2 (Pre-Type 2 DM) With a variation of Yeast Treatment

Rudiana Agustini, Erlix Rakhmad Purnama, Agus Widodo

A kidney is an organ that has many roles to survive. This organ can be damaged by type 2 diabetes mellitus which is marked by high glucose in the blood. Histological studies of kidney tissue in mice (*Mus musculus* L.) shown by type 2 pre-Diabetes Mellitus with variations in yeast treatment have been carried...

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Chemical and Physical Process Combinations: Microwave in Lignin Degradation of Pecan Shells as Alternative Fuel Raw Materials

Rini Kartika Dewi, M. Istnaeny Hudha, Anindita Rauda, Safarina Tsulusia

Pecan shell is an abundant amount of biomass waste and has the potential as one of the fuels, with a very hard texture and having holocellulose content of 49.22% and lignin 54.46%. Whereas the pecan shell composition after in the form of 100 mesh powder was 33% hemicellulose, 17% cellulose and 34% lignin....

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Isolation and Utilization of Protease Lactic Acid Bacteria as Meat Tenderizer

Prima Retno Wikandari, Diah Puri P. Panggayuh, I Gusti Ngurah Agung Oka Dhana

The objective of this research was to observe the potency of protease of Lactobacillus LBP 1 as meat tenderizer. The study included the proteolytic enzyme activity and the effect of the enzyme concentration to meat tenderizing. The isolation of protease used ammonium sulphate of 15%, 30%, 4%, and 60%,...

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Standardization of Herbal Tea Quality Production Baureno Bojonegoro Society

Pirim Setiarso, Rusijono Rusijono, Asrul Bahar, Samik Samik, Nita Kusumawati

In this study, standardization of ginger and curcuma tea produced by the Baureno Bojonegoro society was carried out. To get high quality products, standardization has been carried out in the washing, slicing and drying processes. Washing stages of raw materials carried out for 1 min, with a slice thickness...

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Production Of Working Electrodes Graphene Oxide For Phenol Analysis Voltammetrically

Pirim Setiarso

The working electrode in the voltammetry method is an electrode that responds to the current generated in a redox reaction. The working Electrode to response currents through the process of migration, convection and diffusion. Working electrodes can be made according to the needs for qualitative and...

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Antioxidant and Phytochemical Test of Ziziphus mauritiana Ethanol Extract

Nurul Hidajati, Siti Nafsiyah Rokhmania

Ziziphus mauritiana is one of the plants that can grow in Indonesia. Many of these plants have reported potential antioxidant compounds. Z. mauritiana ethanol extract was obtained through maceration of bark and continued with phytochemical screening and antioxidant activity testing using DPPH method....

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Adsorption of copper metal waste in prototypes on a laboratory scale

Nuniek Herdyastuti, Rusmini Rusmini, Sari Edi Cahyaningrum

Waste treatment has been carried out to reduce the presence of contaminants such as the content of copper (Cu) which is very dangerous for health. One of the efforts made is by adsorption using activated carbon. The purpose of this study was to determine the efficiency of activated carbon adsorption...

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Extraction and Application of Natural Dyes from Brazilwood and Water guava leaves

Nita Kusumawati, Samik Samik, Supari Muslim

The use of natural dyes for batik has some advantages because it produces a unique exotic color with exclusive imaging and is environmentally friendly due to the waste easily degraded. The purpose of this research was to obtain

textile dye extract from brazilwood (*Caesalpinia sappan* L) and water guava...

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Exploration of Natural Dyes by Using a Combination of *Caesalpinia sappan* and *Leucaena leucocephala* L. Leaves.

Nita Kusumawati, Anang Kristyanto, Samik Samik

In this research an exploration of the potential use of *Caesalpinia sappan* and *Leucaena leucocephala* L. has been carried out as an alternative to environmentally friendly dyeing. To optimize the quality of the shades produced, pre-treatment is done using Turkish Red Oil (TRO) (washing) as well as alum...

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Quality Improvement of ABBS Hand Writing Batik Production through Standardization of Natural Dyeing using Water Guava and Mango Leaves

Nita Kusumawati, Samik Samik, Anang Kristyanto

Dyeing standardization in the production of ABBS SMEs natural dye hand writing batik has been done. A series of stages of pre-treatment, dyeing and fixation have been determined to obtain the desired shades, color intensity and fastness. Optimizing the quality of dyeing is done by washing mori fiber...

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Increased Storage and Nutrition Content of Processed Foods through Vacuum Packaging

Niken Purwidiani, Pirim Setiarso, Nita Kusumawati

Food is a basic need for human survival. Various vegetable and animal sources are used to fulfill this. Through the production of potato donuts and beef meatballs, Auliya SMEs has played an active role as one of the providers to fulfill this need. Along with increasing public awareness of food health,...

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Morphometric and Nutrient Content of Endemic Solen sp. (Lorjuk) of Pamekasan Madura

Mirwa Adiprahara Anggarani, Erlix Rakhmad Purnama

The research was conducted on May to July 2019, in Pamekasan, Madura, East Java, Indonesia. The aim of this study was to know the content of *Solen sp.* (Lorjuk) the shellfish which live and consumed by local community in Madura. This is a descriptive quantitative research. Parameters that used in determining...

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Comparison of the method used for extraction chloramphenicol from its Molecularly Imprinted Polymer (MIP) using chloroform as porogen

Maria Monica Sianita, Ni Nyoman Tri Puspaningsih, Miratul Khazanah, Gaden Supriyanto

The synthesized of chloramphenicol – MIP (molecularly imprinted polymer) has been developed in many ways and many purposes. The purpose of this research was to compare the methods used for extracting chloramphenicol from its molecularly imprinted polymer (MIP) by calculating the percent of extraction...

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Effectiveness of Evodiamine and Evodone as Ovarian Anticancer In Silico

Erlix Rakhmad Purnama, Ghea Dionita Sanora, Elly Yana Mastura, Muhammad Ongky Muji Handoyo

Cancer is a disease that is still a global problem which ranked second leading cause of death, amounting to 13% after cardiovascular disease. Cancer of the ovaries are the second most common group of gynecologic cancers, and account for about 5% of all women's cancers. Chemotherapy (chemo) is the use...

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Synthesis and Characterization of Nano TiO₂ with Sol-Gel Method as Self-Cleaning Agent on Acrylic Paint

Dina Kartika Maharani, Pirim Setiarso, Mirwa Adiprahara Anggarani, Qurrota A'yun

Metal oxide TiO₂ has photocatalytic properties that make TiO₂ amphiphilic, that is, hydrophobic in the dark (without UV light) and hydrophilic in the light (there is UV light). The photocatalytic properties of TiO₂ can be utilized to develop self-cleaning materials in paints. Self-cleaning material is a...

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The Effect of Curing and Extraction Time against Yield and Quality of Type B Gelatin from Goat Bone

Asrul Bahar, Rusijono Rusijono, Nita Kusumawati

In this study evaluated the effect of preparation conditions (curing) and extraction time on the yield and quality (water and ash content, gel, and organoleptic properties) of type B gelatin from goat bone. In general, the yield of goat's gelatin (GBG) increases with increasing curing (10-50 days) and...

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The Effect Of Chitin Size And Soaking Time On Decreasing Cholesterol Levels On Quail Eggs

Nuniek Herdyastuti, Aisyah Vynkarini Daniar

Hypercholesterolemia is a symptom that shows an increase in cholesterol levels in the blood and can cause atherosclerosis which is a major factor for cardiovascular diseases such as coronary heart disease. Quail eggs are one of the foods that contain high cholesterol. Cholesterol content in quail eggs...

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The Development Of Anti Miskim Software To Reduce Misconception Of Students On Buffer Solution Matter Through Conceptual Change Text Strategy

Siti Agustyaningsih, Sukarmin Sukarmin, Utiya Azizah

The purpose of this study is to determine the feasibility of anti-miskim software with the conceptual change text strategy as a learning media to reduce misconceptions in buffer solution material. Feasibility of the software in terms of criteria validity, practicality, and effectiveness. This type of...

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The Development of Demische Software to Detect and Reduce Misconception in Chemical Equilibrium through Conceptual Change Text Strategy

Lifia Ramadhani, Sukarmin Sukarmin, Utiya Azizah

This research is used to obtain Demische (Decreasing misconception in chemical equilibrium) software that is proper through conceptual change text strategy that is developed as learning media to detect and reduce misconception in chemical equilibrium 11th grade. Software feasibility can be known by three...

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The Sorogan-Bandongan Model as Active Learning Model in Indonesia

Rinaningsih Rinaningsih, Asep Kadarohman, Harry Firman

Active learning is teaching and learning process its student centered. Exposure at this article bent on for to prove that Sorogan-Bandongan Model can be categorized as the active learning model that center on student. Method as used in exposure this article namely descriptive qualitative, use 52 students...

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Problem-Solving based Teaching Materials: an Important Role in Enhancing Undergraduate Students Thinking Skills

Utiya Azizah, Harun Nasrudin, Rusmini Rusmini

Problem-solving is an individual's cognitive process to achieve the goals and solutions to the problem at hand. Problem-solving is a serious concern of the government of the Republic of Indonesia to prepare graduates who have high competitiveness. This study aims to describe undergraduate students' thinking...

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Chemical Education Student Science Process Skills, in Specific and in General Content

Suyono Suyono, Harun Nasrudin, Bertha Yonata

This study aims to obtain the value of the estimated index of Science process skills (SPS) of students in the specific content (SPS-ISC) against the SPS score in general content (SPS-IGC). The SPS-ISC score is set based on the student's answer in answering questions developed based on the SPS indicator...

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The Role of Chemistry and its Learning to Improve 21st Century Skills in Revolutionary Industry 4.0 Era

Suyanta Suyanta

Technologies at the industrial revolution 4.0 (also referred to as Industry 4.0) which has grown exponentially and progressed at rapid pace largely take impact on many of other fields covering manufacturing, economy, health care,

and education. Therefore, Indonesia entails proper preparations to stay...

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Remediation Of Students' Misconception Based On Their Learning Style Through Guided Conceptual Change Strategies In The Concept Of Electrochemistry

Sukarmin Sukarmin, Suyono Suyono, Wasis Wasis

The problem of misconception in Chemistry is a very serious thing. Misconceptions that occur in the students' early learning, will become the source of misconceptions on the next material. This study will attempt to reduce or remedy such misconception through Guided Conceptual Change in the concept of...

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School Literacy Movement, Scientific Literacy, and Science Matter Inventory for Hearing Impaired Students

Sri Poedjiastoeti, Wagino Wagino, Dian Avina Turja Soffa

This paper aim to describe results of inventory school literacy movement, scientific literacy, and science matter in school for dissabilities especially hearing impairment students. This results used to design science multimedia was appropriate with hearing impairment students, especially for elementary...

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The Effect Of Using Atomic Models Interactive Multimedia Flash Based On Students Learning Outcomes

Sihaqqul Firdaus, Rusly Hidayah

The purpose of this study to determine the effect of using atomic models interactive multimedia flash based on students learning outcomes, student learning outcomes that will be measured is how much the value increases obtained by students and the minimum completeness criteria obtained by students. The...

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Theoretical And Empirical Validity Of Student Work Sheets To Train Eco Innovation In The Study Of Food Analysis

Rusmini Rusmini, Titik Taufikurohmah, Maria Monica Sianita

Research has been conducted on the development of Student Worksheets to practice eco innovation in the food analysis course. This development is motivated by the implementation of the FMIPA Unesa SD-Dikti curriculum based on ecopreneurship KKNI. Eco innovation is a part of ecopreneurship. The development...

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The Development of Chemtoon (Chemistry Cartoon) Comic as Chemistry Learning Media on Acid Base Matter for XI grade of Senior High School

Nurus Shobah Asmiarsih, Rusmini Rusmini

This study was intended to determine the feasibility of Chemtoon comic that was developed as a chemistry learning media on acid-base matter. It was conducted at SMAN 1 Wringinanom on 15 students in XI IPA 2 with heterogeneous abilities. The comic designed according to the criteria for learning media....

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The students' conception track of low-perception-students trough the conceptual change (CCM) module based on mental models on electron configuration concept

Nurina Kusuma Ayu Pratiwi, Suyono Suyono, Yuanita Leny

Misconception has a close correlation with mental models. The aim of this study is to know the track of student conceptions trough the misconception (MC) remediation using Conceptual Change Module (CCM) based on mental model in electron configuration concept. The research using one group pretest and...

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CHIBO Adventure Games a Learning Media on Chemical Bond

Matter for Senior High School

Nanik Mardiana, Achmad Lutfi, Dian Novita

The research aims to get the feasibility of CHIBO Adventure game as a learning media on chemical bond matter for senior high school. The research method uses Research and Development (R&D) done until limited testing phase. The test was conducted to 30 students of 10th grade of SMA Negeri 1 Manyar-Gresik....

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Chemmo Configuration Game As Learning Media On Periodic System Of Element Matter

Muslela Qona'atun, Achmad Lutfi, Rusly Hidayah

The aim of the research is to get the feasibility of Chemmo Configuration game as learning media in chemistry material, periodic system of element based on validity, practicality, and effectiveness of the game. This research use a Research and Development (R&D) method which consist of three stages,...

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Relationships Between Perception toward Assessment with Learning Result of Student

Muchlis Muchlis, Suhadi Ibnu, Subandi Subandi, Siti Marfuah

This research aim to describe relationships between perception toward

assessment with learning result of student. Perception toward assessment it means student perceps assessment as assessment of learning (AoL), assessment for learning (AfL) or assessment as learning (AaL). Subject research is 35 students...

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Utilization Of Colored Flowers as An Alternative Learning Media of Acid Base Indicator On Basic Chemistry Course With Green Chemistry Insight

Mitarlis Mitarlis, Utiya Azizah, Bertha Yonata

Using of natural product like colored plants or flowers as a medium for learning chemistry can realize of green chemistry principles by applying one or several of its principles. One of the principles of green chemistry that can be raised in basic chemistry learning is "use renewable feedstock". Chemistry...

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Analysis of Technological Pedagogical Content Knowledge (TPACK) Capabilities of Prospective Chemistry Teachers on Chemical Bonding Materials

Kusumawati Dwiningsih, Sri Poedjiastoeti, Muchlis Muchlis

The education of prospective Chemistry teachers is faced with the issue of integration of content knowledge, pedagogy and technology (TPACK

/ technological pedagogical content knowledge). Prospective teachers are expected to become teachers who are skilled in teaching effectively, mastering material...

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Train high order thinking skills at undergraduate students chemistry through concept map based learning

Ismono Ismono, Sri Poedjiastoeti, Suyono Suyono

This study aims to determine the role of concept map learning in studying organic chemical especially the matter of isomer. The subjects of this study were 58 chemistry education students with details of 24 PKU 16 students and 34 PKA16 students. Data acquisition was done by initial test, final test,...

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Validity of Interactive Multimedia with 3D Visualization to Practice the Spatial Visual Intelligence of Class X High School Students on Metallic Bonding Materials

Irvandar Nurviandy, Kusumawati Dwiningsih, Ahlan Riwahyu Habibi, Akhmad Fitriadi Akbar

This study aims to determine the validity of Interactive Multimedia with 3D Visualization to Train the Spatial Visual Intelligence of Class X High School Students on Metallic Bonding Materials. Validity is tested through quality of content and goals, instructional quality, and technical quality. Development...

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Reading, Questioning, and Answering (RQA) Strategies': an Alternative to Empowering Undergraduate Student Thinking Abilities

Harun Nasrudin, Utiya Azizah

Reading, Questioning, and Answering (RQA) is a constructivist based learning strategy. The implementation of RQA can motivate undergraduate students to read the assigned material and have an impact on improving the understanding of learning material. This study aims to describe undergraduate students'...

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Students' Misconceptions on Understanding Corrosion Topic by and without Analogy

Findiyani Ernawati Asih, Suhadi Ibnu, Suyono Suyono, Suhadi Suhadi

Redox reactions is spontaneous which can produce electrons flow. This condition can make corrosion of ferrum metal . The electrons flow is not observed (submicroscopic aspect), so requires visualization. Strategy for visualizing submicroscopic aspect is analogy learning. The electrons flow can be analogous...

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The Validity of Teaching Materials Oriented to Argument-Driven-Inquiry Model to Train Students' Science Literacy

Faridatur Rofi'ah, Tukiran Tukiran, Endang Susantini

Research related to the development of teaching materials using the Argument-Driven-Inquiry model to train Students' Science Literacy which seems not to have been done. Therefore, the purpose of this study is to produce a valid teaching materials. The developed teaching materials focused on the buffer...

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Enhancing Mastery Of Students' Concept Through Science Technology Society (STS) Approach On Chemical Equilibrium

Dwi Rahmi Putri, Leny Yuanita, Bambang Sugiarto

This study aims to determine the enhancement mastery of students' concepts after being given learning based on the Science Technology Society (STS) approach to Chemical Equilibrium. Students in class XI MIA 1 and XI MIA 2 of Senior High School 4 Sidoarjo be a subject. The data is obtained from concept...

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Interactive Multimedia and Kit Implementation on Chemistry

in Daily Life Topic with Writing-to-Learn Strategy for Hearing Impairment Students

Dian Novita, Sri Poedjiastoeti, Sukarmin Sukarmin, Achmad Lutfi

This research aims to describe the implementation of interactive multimedia and kits on Chemistry in Daily Life Topic. The kit consists of student activity sheet and tools and materials for experiment. Student activity sheet of chemistry on foods and chemistry on household theme each consist of four...

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The Effectiveness of Guided Discovery Based Learning Materials to Increase Students' Learning Outcomes

Devi Evylia Purmawanti, Utiya Azizah, Sari Edi Cahyaningrum

This research aimed to know the effectiveness of learning materials based on guided discovery to increase students' learning outcomes. The research model used in this study was Research and Development (R&D), but it is only limited to the development stage, namely by conducting a trial I. Trial I was...

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Effectiveness Of Learning Media Using Argument Driven Inquiry (ADI) Learning Model To Increase Students' Learning Outcomes And Self Efficacy

Ni'mah Tukiran, Nasrudin Choirun, Harun

This research aimed to find the effectiveness of a teaching instrument in

order to increase students' self efficacy and learning outcomes using Argument Driven Inquiry (ADI) teaching instrument on the electrolyte and non-electrolyte. The test was applied to the 30 students of grade X-3 and X-4 in Senior...

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Application Of Chemmo Configuration Play As A Learning Media Of Elements Periodic System

Achmad Lutfi, Rusly Hidayah, Muslela Qona'atun

This study aims to determine the effect of using the Chemmo Configuration game that has been developed based on pedagogical requirements and game requirements as a learning medium. The form of research used was Pre-Experimental Research with the design of a single group One Group Pretest-Posttest Design...

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Study of Surface Plasmon Resonance of Gold Nanoparticles Stabilized by L-arginine

Amaria Amaria, Dina Kartika Maharani, Maria Monica Sianita

Gold nanoparticles (AuNP) capped by L-arginine have been synthesized. In this research, gold nanoparticles were synthesized by reducing the solution of Au(III) to Au(0) using trisodium citrate and capping agent L-arginine as a stabilizer. The ratio of Au(III) ions to amino acids is optimized to obtain...

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Campesterol compound from Methanol Fraction of Brotowali (*Tinospora crispa*) Stem Bark

Weny A. J Musa, Suleman Duengo, Ahmad Kadir Kilo

Tinospora crispa is a plant of the Menispermaceae family which is one of the endemic plants in Indonesia, commonly called as Brotowali. *Tinospora crispa* have been used traditionally to treat fever, diabetes, rheumatism and sinusitis. The chemical components of the plant have not been reported so far....

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*Histopathology of Kidney In Mice (*Mus musculus L*) Indicated By Pre-Diabetes Mellitus Type 2 (Pre- Type 2 DM) With a variation of Yeast Treatment*

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Abstract— A kidney is an organ that has many roles to survive. This organ can be damaged by the type 2 diabetes mellitus which is marked by high glucose in the blood. Histological studies of kidney tissue in mice (*Mus musculus L.*) shown by type 2 pre-Diabetes Mellitus with variations in yeast treatment have been carried out. This study uses variations in the treatment of yeast planted in red rice (red yeast) and yeast extract produced by enzymatic hydrolysis (YHE-red rice) as a comparison. Mice as the experimental animals were induced obesity—using a high-fat and fructose diet, so they showed symptoms of Pre-DM type 2 and were then treated with red yeast rice and red YHE-rice. This study used a comparison of DM mice and treated mice with glibenclamide in CMC-Na 0.2% (positive control), DM mice and treated mice with CMC-Na 0.2% (negative control), and non-DM mice and treated mice with CMC -Na 0.2% (normal control). Observation of renal histopathology using a light microscope. Observed Parameters included cell necrosis, glomerular nephropathy performance, increasing of Bowman's space thickness, thickening of the distal and proximal tubules, thickening of the renal arteries, and leukocyte infiltration. The results showed that the kidneys of type-2 DM mice and Yeast-Red Rice and Yeast Extract-Red Rice as well as mice that indicated DM and were treated with glibenclamide in 0.2% CMC-Na for 1 week, did not show histological differences. Kidney when compared with non-DM mice and treated with 0.2% CMC-Na (normal control), as well as mice that were indicated by DM and treated with 0.2 CMC-Na. So to find out the effect of yeast treatment on the kidney of mice indicated by type -2 DM, it is necessary to induce obesity and treat yeast-red rice or YHE-red rice for longer periods.

Keywords—mice, pre-type 2 DM, yeast-red rice, histopathology of kidney

I. INTRODUCTION

A kidney is a pair of bean-shaped organs located in the dorsal left and right spine in the lumbar region. Kidney weight is estimated to be 0.5% of body weight, and its length is ± 10 cm. Every minute 20-25% of blood is pumped by the heart which flows into the kidneys. Just like other organs, the kidneys play an important role in the human body. The main function of the kidneys is to filter out wastes (waste) in the body, both those from food, drugs, or toxic substances. Another function is to control the balance

of body fluids and maintain proper electrolyte levels. The kidneys excrete nitrogenous metabolic waste such as ammonia, the result of protein degradation or deamination. Besides, the kidneys also function to excrete excessive substances, such as water-soluble vitamins; maintain extracellular fluid by releasing water when excessive; maintain acid and base balance, as well as endocrine function.

The kidney consists of three main parts, namely: cortex (outer part), medulla (kidney marrow), and renal pelvis (renal cavity). The renal cortex contains a lot of nephrons ± 1 million so that the surface of the kidney's capillaries becomes large. Each nephron consists of a long Malpighi body and tubules (channels). On Malpighi's body, there is Bowman's capsule, a layer that wraps the glomerulus. The glomerulus is in the form of arterial capillaries. The tubules in the Malpighi body are proximal tubules that roll near the Bowman's capsule where there are numerous mitochondria in the cell wall. The second tubule is the distal tubule.

In the kidney, a series of filtration, re-absorption, and augmentation processes occur. Filtrasi occurs in glomerular capillaries in Bowman's capsules. In the glomerulus, there are porous capillary endothelium cells (podocytes) making it easier for the filtering process. Several factors that facilitate the filtering process are high hydraulic pressure and permeability of the glomerulus. In addition to filtering, glomerulus also occurs in the re-binding of blood cells, pieces of blood, and most of the plasma protein. Small substances dissolved in the plasma, such as glucose, amino acids, sodium, potassium, chloride, bicarbonate, other salts, and urea pass through the filter and become part of the sediment. The result of filtering in the glomerulus is a glomerular filtrate (primary urine) whose composition is similar to blood but does not contain protein. Glomerulus filtrate can still be found in amino acids, glucose, sodium, potassium, and other salts. Human urine volume is only 1% of the glomerular filtrate. Therefore, 99% of the glomerular filtrate will be actively reabsorbed in the proximal contractile tubules and the addition of residual substances and urea in the distal contour tubules. Useful substances such as glucose and amino acids are returned to the blood.

The rest of the excess waste salt, and other ingredients in the filtrate removed in the urine. Every day the kidney tube reabsorbs more than 178 liters of water, 1200 g of salt and 150 g of glucose. Most of these substances are reabsorbed several times. After reabsorption, the tubules will produce secondary urine whose composition is very different from the primary urine. In secondary urine, substances that are still needed will not be found again. Conversely, the concentration of toxic metabolic waste products increases in secondary urine. The substance absorbs the tubules in two ways. Sugar and amino acid permeate through diffusion events, while water through osmosis events. Water reabsorption occurs in proximal tubules and distal tubules. Augmentation is the process of adding residual substances and urea that begin to occur in the distal tubule. The composition of urine excreted through the ureter is 96% water, 1.5% salt, 2.5% urea, and the rest of other substances, such as bile pigments that function to give warm and odor to the urine. Some disorders related to urine damage, including albuminuria (urine containing albumin due to kidney disease), nephritis (inflammation of the nephron's kidney that begins glomerular inflammation), hematuria (urine containing blood), kidney failure (increased blood urea levels, a substance that should be discharged by the kidney). The part of the kidney that plays a very important role in blood filtering is glomerulus, which is to filter proteins. This function can be disrupted if glomerular damage occurs.

Excessive drug use, obesity, and metabolic disorders can interfere with kidney function. The kidney is frequently affected in systemic diseases and, in some cases, the severity of the kidney damage is a determining factor for the survival of the patient. Diabetes mellitus is the most important by its frequency. Diabetes mellitus (DM) is a chronic metabolic disorder due to the pancreas not producing insulin or the body cannot use the insulin produced effectively. Insulin is a hormone that regulates blood glucose levels. Diabetes mellitus (DM) can be divided into 2 types, namely, type 1 DM and type 2. Type 2 DM is a disruption in the receptor (receiver) of the hormone insulin, in blood cells. In this condition the productivity of the insulin hormone works well, but is not supported by a sufficient quantity of receptor volume in blood cells, this condition is known as insulin resistance. The type -2 DM is known to be the most common type of DM found in the community, as many as 90% of DM cases globally. The detection of hemoglobin A_{1c} levels shows that 86 million people (37% of adults over age 20) suffer from pre-DM and thus are at high risk of developing diabetes [1]. Type 2 diabetes is characterized by blood glucose levels ≥ 150 mg/dL, whereas pre-DM blood glucose levels $> 126 < 150$ mg/dL.

Several studies have revealed that type 2 DM can be reduced by consuming chromium, one of the minerals needed by the human body. Chromium in food is in the form of Cr³⁺ (indicating the amount of oxidation), which is stable and safe [2]. Chromium serves to help the entry of glucose in body cells. Glucose can enter the cells of the body with the help of the hormone insulin. In this process, chromium interacts with the low-molecular weight chromium (LMWCr) substance which in turn activates insulin performance (Cefalu and HU, 2004). Foods that are known

to be rich in chromium include yeast. The results showed that red rice yeast can reduce blood glucose levels [3]. High glucose levels can lead to diabetic nephropathy is a loss of chronic kidney function that occurs in people with diabetes mellitus, protein in the urine due to glomerular damage [4]. Diabetes causes several changes in the body's metabolism and blood circulation. Chronic type -2 DM can cause diabetic nephropathy and lead to end-stage renal disease (ESRD) [5]. These changes damage the structure in the glomeruli known as glomerular filtration barrier (GFB)[6]. This barrier consists of three layers including endothelium, glomerular basement membrane, and epithelial podocytes. GFB is responsible for blood filtration that is very selective in entering the glomeruli of the kidneys and usually only passes through water, small molecules, and very small proteins (albumin does not pass through the whole GFB). [7]. The damage to the glomerular basement membrane allows protein in the blood to leak, causing proteinuria. Sedimentation of a large number of the mesangial matrix by protein causes positive nodules of Schiff acids called Kimmelstiel-Wilson nodules.

II. METHOD

1.1. The steps taken in describing the mice kidney histopathology include 1) pre-paration of test material, 2) obesity induction, treatment by giving test material, and 3) surgery and examination of mice kidneys.

1.2. Preparation Of treatment Material

Red yeast rice preamiceion was carried out in several stages. The initial stage was preparing of red rice flour as a raw material for yeast growth medium, with a size of 100 mesh. In the next step, rice flour is added with distilled water in the miceio of 5: 1 (w / v) and heated to form a gel and then cooled.. The gel was allowed to cool and then hydrolyzed using α -amylase and glucoamylase enzymes for 6 hours, at room tempemiceure ($28 \pm 5^\circ\text{C}$). The hydrolyzate formed was added with a commercial bakery yeast micecio of 5: 1 (v / w), then was fermented for 10 days. The fermentation results were then centrifuged at 6,000 rpm for 15 minutes and the obtained residue is the red rice yeast and will then be used as an ingredient for the production of YHE (yeast hydrolyzate enzymatic). Yeast-Red Rice was hydrolyzed using bromelain which was carried out at 37°C for 24 hours. The hydrolyzate obtained was YHE which was ready to be used as test material as well.

1.3. Induction of obesity

Mice were adapted for 10 days by giving a commercial food and drinking every day, and the blood glucose levels were measured using a Nesco multi check. Mice were induced by obesity using a high-fat and fructose diet of 1 ml/day for 10 days while was still given drink and the blood glucose levels were measured after 10 days. Mice that have glucose

levels of ≥ 140 mg/dL were declared indicated pre DM type 2 and subsequently, each treatment would be given.

1.4. The treatment of mice uses test material

The test material in this study is yeast red rice and yeast which have been enzymatically hydrolyzed (YHE). Positive, negative and normal controls are used as a comparison. Table 1 shows the formulation of the test material used in this study.

TABLE I. FORMULATION OF TEST MATERIAL

Treatment Group	Formulation
Red rice Yeast	Giving red rice yeast 1 mL/per day
Red rice YHE	Giving YHE red rice 1 mL/per day
Glibenclamide (Positive Control)	Control of diabetes, made diabetes and given glibenclamide (0.9 mg / 200 g bb mice) in Na-CMC 0.2%
Diabetic Control (Negetive Control)	Control of diabetes, made diabetes and only given 0.2% Na-CMC.
Normal Control	Non-diabetes, was given 0.2% Na-CMC.

Test material was given to male mice (*Mus musculus L.*) DDW strain aged 6 weeks, body weight 25-30 grams orally at a dose of 1 mL/day for 10 days.

1.5. Surgery and Observation of kidney histology

Mice that had been treated for 10 days are dissected and their kidneys were taken. The kidneys were stored in a physiological solution, put in a bouin's solution. The next step is to make histopathological prepamiceions from the kidneys using the paraffin method and staining hematoxylin and eosin. The prepamiceions were observed using a 400 X magnification light microscope with observations of five sub fields of view. The parameters observed included cell necrosis, glomerular nephropathy, increased thickness of Bowman's space, thickening of the distal and proximal tubules, thickening of the renal arteries, and leukocyte infiltmiceion.

III. RESULT AND DISCUSSION

DM is a metabolic disorder that affects life in the world leading to hyperglycemia [8]. This disorder is divided into 2, namely DM type 1 and DM type 2. DM type 2 is a chronic metabolic disorder due to the body cannot use the insulin that is produced effectively, which is a hormone that regulates blood glucose levels.

The research carried out aims to provide a histological picture of the kidney of mice that are indicated pre-DM type 2 using a variety of red rice yeast treatment. The research that has been carried out begins with the preparation of test materials in the form of red yeast-rice and red rice YHE as a comparison, in addition to that glibenclamide + CMC-Na (positive control), commercial feed + CMC-Na (normal control), and DM + CMC -Na (negative control). The results of the analysis of the chemical composition of yeast-red rice and YHE-red rice are presented in Table 1.

TABLE II. CHEMICAL COMPOSITION OF YEAST-RED RICE AND YHE-RED RICE AS A TEST MATERIAL

Test Material	Water Level (%)	Cr ³⁺	Cr ⁶⁺	% protein	% crude fiber	% starch
Red Rice Yeast	74,06	103 x 10 ⁻⁴	49 x 10 ⁻⁴	38	5,89	6,643
YHE Red Rice	58,29	37 x 10 ⁻⁴	17 x 10 ⁻⁴	38,48	13,15	5,149

Table 1 shows that the moisture content of Cr³⁺, Cr⁶⁺, and crude fiber of the two test materials was very different. Several studies have revealed that type -2 DM can be reduced by consuming chromium, one of the trace minerals needed by the human body. Chromium serves to help the entry of glucose in body cells. Glucose enter to the body cells with the helping of the insulin hormone. If the amount of insulin in a person's body is insufficient or if the body's cells do not respond to insulin, there will be a buildup of glucose in the blood (hyperglycemia).

Preparation of mice as experimental animals was also carried out with the stages of adaptation, then induction of obesity using a high-fat and fructose diet for 10 days and blood glucose levels were measured. Mice that showed symptoms of pre-DM type 2 marked by blood glucose levels > 140 were selected to be treated by giving test material for 10 days. The next step is to measure the glucose level of the mice after treatment. Table 2 shows a decrease in blood glucose levels and body weight of mice after treatment with the test material.

TABLE III. DECREASED BLOOD GLUCOSE LEVELS AND BODY WEIGHT OF MICE AFTER TREATMENT

No	Treatment	Weight loss (grams)	Decreased Blood Sugar Level (mg / dL)
1	Red Rice Yeast	3,0	130
2	YHE Red Rice	5,0	131
3	Glibenclamide	7,3	58
4	CMC-Na	5,0	90
5	Negative Control	7,5	97

The results of the study showed that treatment with the intake of red yeast rice and YHE (Yeast Hydrolyzate Enzymatic) on mice could reduce blood glucose levels for mice that indicated pre-DM type 2. Grouping glucose levels as follows: normal blood glucose is 100-126 mg/dL, pre-DM > 126 < 150 mg / dL type 2 DM is characterized by blood glucose levels ≥ 150 mg/dL. Decreased blood glucose levels of mice treated with red rice yeast showed a decrease in blood glucose of 130 mg/dL and YHE was 131 mg/dL. Decreased blood glucose levels of rats treated with red rice yeast showed a decrease in blood glucose of 130 mg / dL and YHE was 131 mg/dL. Red yeast rice is yeast that grows in red rice media, while YHE is a yeast extract from enzymatic hydrolysis. Treatment with YHE or enzymatically hydrolyzed yeast shows the highest decrease and the lowest glibenclamide reduction. Crude fiber, including carbohydrates, these compounds cannot be digested by gastrointestinal enzymes, but are useful and are known to reduce the risk of diabetes mellitus. Fiber can help slow down the absorption of sugar. Some studies explain that diabetics who consume a lot of fiber need less insulin than those who don't [3].

Red rice yeast is a yeast that is grown in red rice media, while YHE is a yeast extract from enzymatic hydrolysis. Treatment with YHE or enzymatically hydrolyzed yeast showed the highest decrease and the lowest glibenclamide reduction.

Kidney organs have vital functions that can experience various problems. Kidney disease is often associated with high blood pressure, diabetes mellitus (DM), and high cholesterol. Several studies have shown that high blood sugar levels is one of the triggers for kidney damage. DM can cause diabetic complications, such as nephropathy, structural abnormalities revealing hypertrophy of glomerular and tubular elements, increased thickness of the glomerular basement membrane, extracellular matrix accumulation [8].

Studies related to kidney damage can be approached in terms of its histology. The kidneys consist of functional units known as nephrons. The nephron consists of filter parts, namely the renal corpuscle and tubules. Both components are very sensitive to the process of absorbs and ion secretion. The renal tubule is divided into 3 parts, namely: the proximal tubule, the Loop Henle, and the distal tubule. This study illustration the kidney histology of mice and their parts (Figure 1).

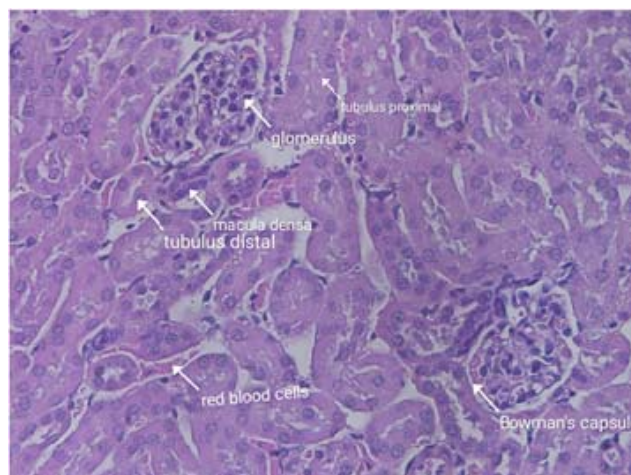


Fig. 1. Histology of the kidney of mice and their parts.

The observations of mice kidney tissue that indicated pre-DM type 2 with various treatments can be seen in Figure 2.

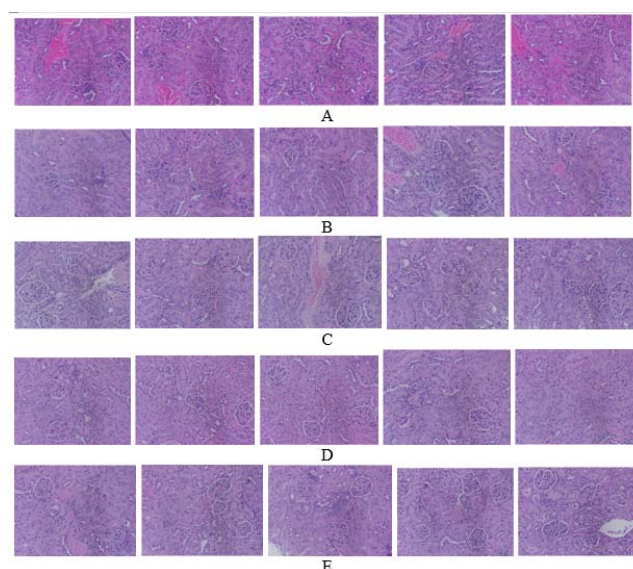


Fig. 2. Mice kidney tissue treated with: (A) yeast-red rice, (B) YHE-red rice, (C) glibenclamid and CMC-Na, (D) CMC-Na, and (E) DM and CMC-Na (Observation of a 400X light microscope, hematoxylin and eosin staining)

The very important part of the kidney is the glomerulus. This organ has the function of filtering blood. Figure 3 shows the renal glomerulus of mice in various treatments. Treatment A, B, C, D, and E were not found to be damaged. Glomerular atrophy is not visible. The basement membrane of the tubules, Bowman's capsule, and glomerular tuft can be seen as shown in Figure 3.

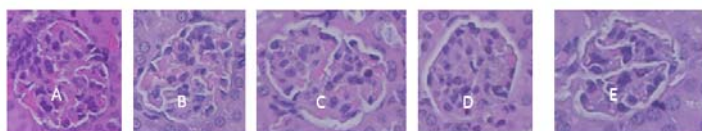


Fig. 3. Glomerulus of mice by treatment: (A) yeast-red rice, (B) YHE-red rice, (C) glibenclamid and CMC-Na, (D) CMC-Na, and (E) DM and CMC-Na (Observation of 400X light microscopy, staining of hematoxylin and eosin).

The kidney is composed of kidney cells, one of which is parenchyma cells. Figure 4 shows renal parenchyma in all treatments showing no de-generation and necrosis. Figure 4. mice parenchyma of mice by treatment: (A) yeast-red rice, (B) YHE-red rice, (C) glibenclamide and CMC-Na, (D) CMC-Na, and (E) DM and CMC-Na (Observation of 400X light microscopy, staining of hematoxylin and eosin).

The function of the kidneys is to filter blood, take what is needed by the body and throw out unnecessary materials outside the body. Every day blood passes through the kidneys through the arteries and one of the kidney abnormalities can be shown by the presence of thickening in the artery wall which results in narrowing of the arteries or known as renal artery stenosis. Many parents show symptoms of atherosclerosis (hardening of the arteries). Renal artery stenosis eventually causes hypertension (high blood pressure) and kidney damage. Blood that reaches the kidneys is very less. The results of this study showed that all treatments given to mice did not show any thickening of the renal artery wall (Figure 5).

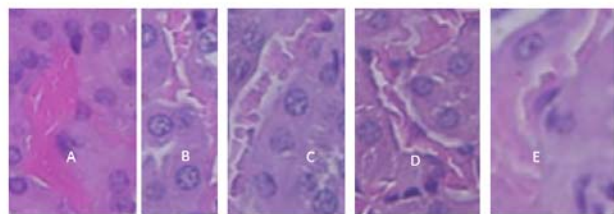


Fig. 4. Mice kidney arteries treated with: (A) yeast-red rice, (B) YHE-red rice, (C) glibenclamide and CMC-Na, (D) CMC-Na, and (E) DM and CMC-Na (Observation of 400X light microscopy, staining of hematoxylin and eosin).

Thickening of the distal tubule plays an important role in the homeostatic process, namely: sodium chloride reabsorbs, potassium secretion, calcium and magnesium handling [9]. This tubule can experience thickening which impacts the process of reabsorption and secretion. Figure 6 shows the results of histology observations of the distal tubules for all treatments and does not show the absence of thickening.

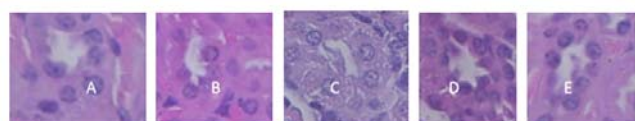


Fig. 5. Distal tubules of mice by treatment: (A) yeast-red rice, (B) YHE-red rice, (C) glibenclamide, and CMC-Na, (D) CMC-Na, and (E) DM and CMC-Na (400X light microscope observation, hematoxylin and eosin staining).

The other part of the kidney is the proximal tubule. The proximal tubule has a high reabsorption ability. The proportion of filtered substance reabsorption in the proximal tubule is sodium and water ($\pm 66\%$), organic compound e.g. glucose and amino acid (100%), potassium ($\pm 65\%$), urea ($\pm 50\%$), and phosphate ($\pm 80\%$) [10]. Interference with this tubule will affect its function in the process of reabsorption, one of which is the presence of thickening. Figure 6 shows the observations of proximal tubules in all treatments in this study that did not show any thickening.

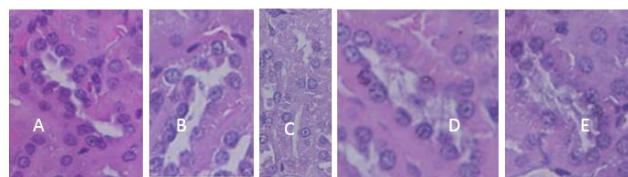


Fig. 6. Proximal tubules of mice treated: (A) yeast-red rice, (B) YHE-red rice, (C) glibenclamide and CMC-Na, (D) CMC-Na, and (E) DM and CMC-Na (400X light microscope observation, hematoxylin, and eosin staining).

Not all people with type 2 diabetes experience kidney dysfunction [11]. This research is preliminary. Induction of obesity using a diet high in fat and fructose for 1 week has not shown kidney damage in mice in all treatments, although glucose levels rose in mice. Then by giving treatment A, B, C, D, and E also has no effect on podocyte cells in the glomerulus. The other observation is the amount of glomerulus from each treatment as shown in Table 3.

TABLE IV. THE AMOUNT OF GLUMERULUS.

Treatment/test material	Amount of glomerulus
Red rice Yeast	111
Red rice YHE	88
Glibenclamide (Positive Control)	95
Normal Control (Normal Control)	117
Diabetic Control (Negatif Control)	129

Data Table 3 shows that the number of the glomerulus in negative controls (DM + CMC-Na) is the highest (129). The relationship between the amount of glomerulus and DM could not be revealed in this study.

The glomerulus is a ball of capillaries surrounded by the Bowman's capsule into which urine is filtered. This part is covered by the bowman capsule, and between the parietal and visceral layers, there is a Bowman space. The results of Bowman space thickness measurements are presented in Table 4.

TABLE V. BOWMAN SPACE THICKNESS DATA.

Observation	Treatment / Thickness of Bowman space (um)				
	A	B	C	D	E
1	0,278	0,208	0,182	0,243	0,311
2	0,288	0,473	0,314	0,103	0,258
3	0,300	0,416	0,336	0,157	0,288
4	0,273	0,427	0,457	0,081	0,474
5	0,383	0,208	0,258	0,103	0,258
6	0,383	0,310	0,369	0,093	0,369
7	0,300	0,393	0,315	0,208	0,157
8	0,288	0,283	0,109	0,232	0,220
9	0,388	0,222	0,244	0,186	0,284
10	0,215	0,208	0,294	0,387	0,388
11	0,212	0,215	0,290	0,199	0,288
Average	0,301	0,306	0,288	0,181	0,300

Note: Treatment (A) red rice yeast; (B) YHE red rice; (C) glibenclamide + CMC-Na; (D) CMC-Na; and (E) DM + CMC-Na

The data in Table 4 shows that the thickness of the Bowman space for normal control is the smallest compared to the given treatment, which is equal to 0.181 um, while other treatments have thicknesses ranging from 0.288 to 0.306 um. Thus it can be said that the treatment of red rice yeast, red rice YHE, glibenclamide + CMC-Na, and DM + CMC-Na on mice indicated by pre-diabetes affects the thickness of Bowman space.

IV. CONCLUSION

The kidney histology of mice indicated pre-DM type 2 after the administration of red yeast rice treatment for 10 days showed no kidney tissue damage. Likewise with other treatments (positive, normal and negative controls). These study conditions pre-DM type 2 using obesity induction, which is carried out for 10 days, therefore it is recommended that induction and treatment be carried out in a long time so that the effects on kidney histology are seen.

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