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Toxicity of Local Natural Ingredients from East Java, Indonesia Yam Bean *(Pachyrhizus erosus)* and Avocado *(Persea americana Mill)* on the Liver and Kidney Structure of *Sprague Dawley* Rats

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Authors' contributions

This work was carried out in collaboration among all authors. Author CNP designed the study, conceptualization, animal experiment, histology analysis. Author JW concept methodology, histology analysis. Author RCM managed manuscript, literature study, food analysis application. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The aim of the research was to test the toxicity of jicama (*Pachyrhizus erosus*) and avocado (*Persea americana* Mill) on the structure of liver and kidney tissue in Sprague Dawley rats.
Study Design: Male Sprague Dawley rats aged 5 months, 24 animals. Treatment of synthetic and natural ingredients. 6 treatment groups were given daidzein (P1), 6 treatment groups were given niacin (P2), 6 treatment groups were given jicama (*Pachyrhizus erosus*) (P3) and 6 treatment groups were given avocado (*Persea americana* Mill) (P4). Each treatment was carried out for 28 days. On the 29th day, surgery was performed and the liver and kidneys were removed, followed by HE staining.
Result: The results showed that the structure of liver and kidney tissue given daidzein and niacin experienced necrosis, increased vascularization, hemorrhage and fatty degeneration.
Conclusion: The use of natural ingredients does not produce toxic (harmful) effects in the body compared to synthetic substances. The percentage of kidney necrosis with daidzein administration is 24%, and with niacin administration, it is 29%. The percentage of liver necrosis with daidzein administration is 20%, and with niacin administration, it is 24%.

Keywords: Toxicity; natural ingridients; liver; kidney.

1. INTRODUCTION

Biodiversity is a wealth of Indonesia's natural resources and contributes to various aspects of life. Various plant species in each region originate from different countries or are native to Indonesia, thriving well in this tropical country. One aspect of biodiversity is medicinal plants. To date, medicinal plants have not been cultivated or utilized optimally. The utilization of medicinal plants as a potential local wisdom is declining due to the dominance of pharmaceutical developments in the health sector. Synthetic substances have dominated the pharmaceutical industry, leading to the extinction of local plants with medicinal potential due to underutilization.

Modern society views treatment with medicinal plants as unscientific and unreliable in terms of safety. People prefer treatment with synthetic substances over natural ingredients. The pharmaceutical field has significantly advanced with the production of synthetic compounds considered more effective and efficient for treatment. Modern society prefers treatment using synthetic compound formulations over medicinal plants.

Medicinal plants have very complex chemical compounds that interact with each other [1-3]. The use of medicinal plants as natural ingredients with multi-component compounds differs from the use of synthetic substances [2,4]. This is because synthetic substances are single compounds with one activity and one target [5,6]. Natural ingredients as medicines usually consist of one or more mixtures processed together, making the compounds more complex [7,8]. Additionally, their pharmacokinetics and pharmacodynamics become more complex due to interactions between multi-component compounds within the biological system of the body [9,10].

There is a growing trend of lifestyle changes towards 'back to nature,' utilizing natural ingredients as therapy for various diseases. Pachyrhizus erosus (yam bean) is one local plant that grows very well in tropical climates like Indonesia. In Indonesia, yam bean is usually consumed fresh in salads, fruit salads, and juices. Its development has reached the cosmetic industry. However, its utilization in the health sector in Indonesia has not yet been realized. Research findings indicate that yam bean tubers contain phytoestrogen compounds, such as daidzein and genistein, which are isoflavone compounds with a chemical structure similar to estrogen hormone [11-13]. These compounds can be used for estrogen replacement therapy [14,15,16].

Persea americana Mill (avocado) is another local plant that thrives in tropical climates. In Indonesia, avocados are usually consumed fresh in desserts and as a bread topping. The development of avocados in the cosmetic industry includes hand lotions, moisturizers, and face masks. Research findings indicate that avocados contain complex compounds beneficial for lowering cholesterol levels [17,18]. Avocados contain several active ingredients suspected to lower cholesterol levels, including pantethine, niacin (vitamin B3), beta-sitosterol, vitamin C,

vitamin E, vitamin A (beta carotene), pantothenic acid, oleic acid, folic acid, selenium, amino acids, and fiber [18,19].

Medicinal plants have complex compounds that can interact within the body's system [1,20]. The interaction of complex compounds in medicinal plants can provide physiological potential within the body's system. Long-term use of medicinal plants does not pose adverse effects on the body [21,22,23]. Medicinal plants contain various bioactive compounds that enhance physiological activity within the body, providing better effects [24,25,26].

The metabolism of plant compounds occurs in the kidneys and liver. One of the kidney's functions is to cleanse the body of waste products from digestion or metabolism [27,28]. The liver also functions as a detoxification organ [29,30]. Therefore, the effectiveness and safety of medicinal plants for health applications require toxicity testing. Toxicity tests are conducted to analyze the safety of treatments concerning liver and kidney necrosis. The purpose of this study is to examine the preclinical effects of yam bean and avocado consumption on test animals by observing changes in the histological structure of the kidneys and liver.

2. MATERIALS AND METHODS

2.1 Materials

Yam bean tubers were obtained from the plantations on the slopes of Mount Wilis in Madiun Regency, East Java, Indonesia. Avocado fruits were obtained from plantations in Dolopo, Madiun Regency, East Java, Indonesia. The yam bean tubers and avocado fruits were harvested when ripe. Male Sprague Dawley rats, 5 months old, 24 in total, were used. Rat feed included pellet milk A, 10% formalin, liquid paraffin, xylene, xylol, Hematoxylin-Eosin (HE), 70% alcohol, 80% alcohol, 96% alcohol, paraffin, physiological NaCl 0.9%, 50% alcohol, 70% alcohol, absolute alcohol, xylol, a mixture of xylol-alcohol with xylol ratios of 1:3, 2:2, and 3:1, Li2CO3 solution, 1% HCl, PBS, eosin, 3% formalin and haupt, 25 mg/kg daidzein, 10 mg/kg niacin, 1.5 ml yam bean tuber juice, and 1.5 ml avocado juice.

2.2 Methods

2.2.1 Maintenance and treatment of test animals

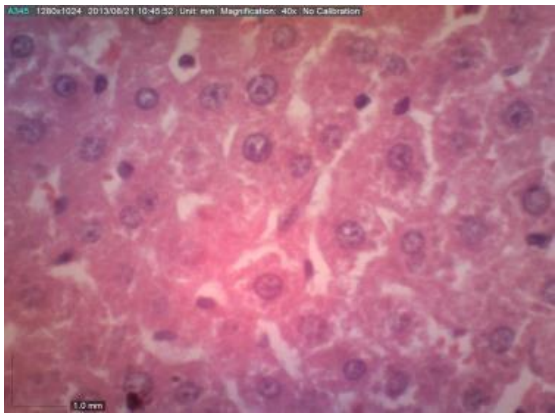
Male Sprague Dawley rats, 5 months old, were obtained from LPPT Gadjah Mada University. A total of 24 rats, weighing 250-350 grams, were kept in group cages and acclimatized for 7 days. The rats were divided into 6 treatment groups: daidzein administration (P1), niacin administration (P2), yam bean tuber juice administration (Pachyrhizus erosus) (P3), and avocado juice administration (Persea americana Mill) (P4). The treatment lasted for 28 days, and on the 29th day, surgery and organ (liver and kidney) removal were performed, followed by HE staining.

2.3 Data Analysis

Descriptive data analysis was conducted using an Optilab microscope to observe changes in the structure of hepatocyte and glomerular cells. The percentage of necrotic cells in the hepatocytes and glomeruli was calculated.

3. RESULTS AND DISCUSSION

A



B

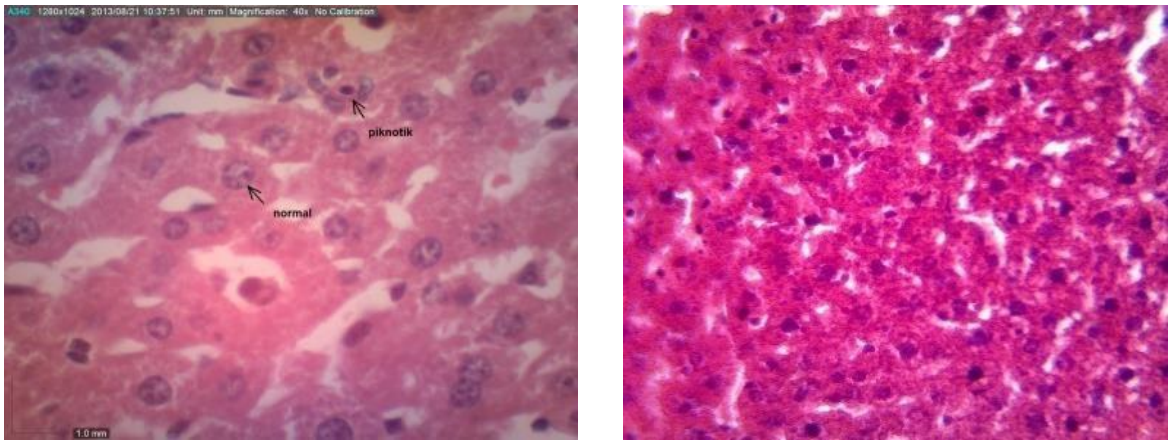


Fig. 1. HE staining rat kidney, 400X A) Necrosis and sinusoidal dilation in hepatocytes treated with daidzein, B) Normal hepatocytes in yam bean tuber treatment, C) Necrosis and sinusoidal dilation, pyknosis of nuclei in hepatocytes treated with niacin, D) Normal hepatocytes in avocado treatment

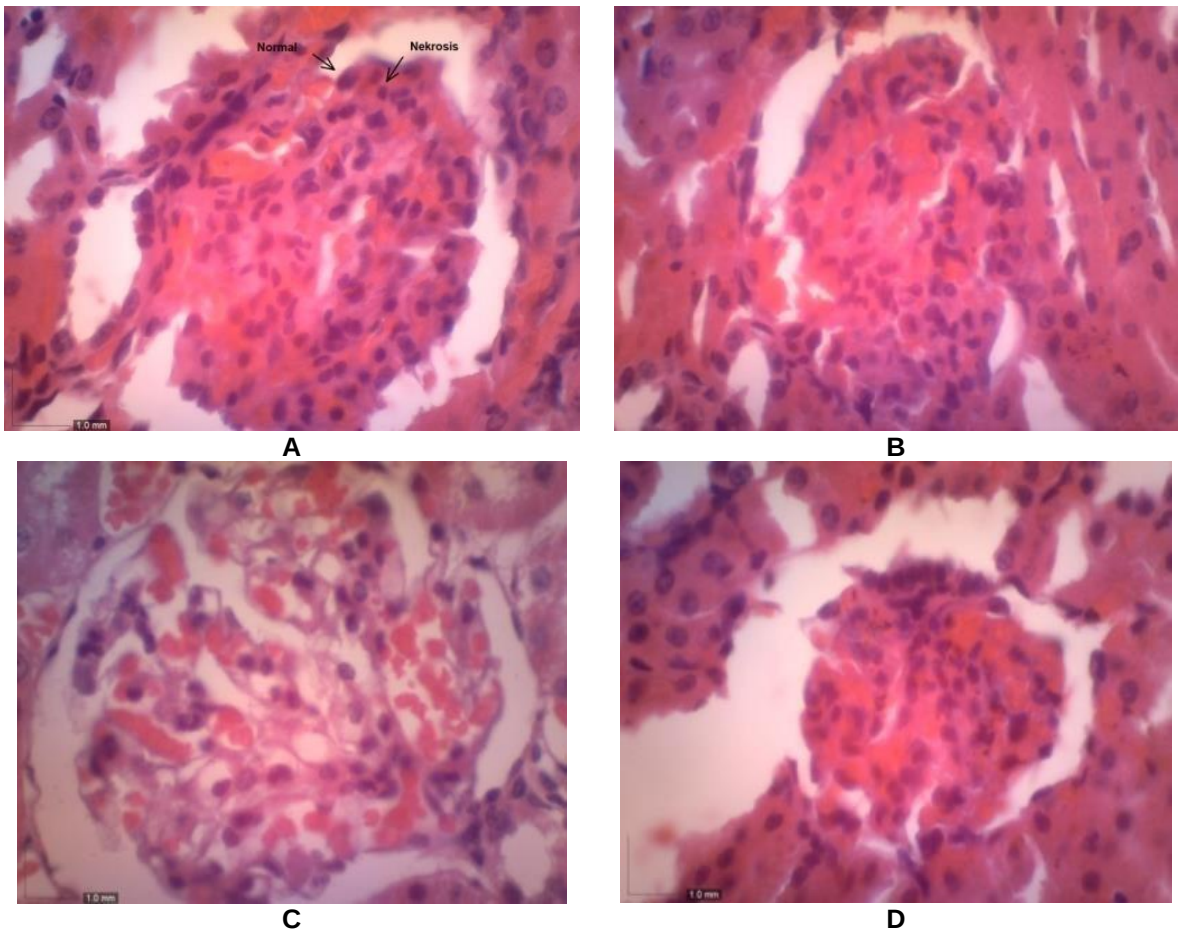


Fig. 2. HE staining rat glomerulus, 400X A) Necrosis and vascularization in treatment with daidzein; B) normal glomerulus in yam bean tuber treatment; C) Necrosis, fatty degeneration and vascularization in treatment with niacin; D) normal glomerulus in avocado treatment

Table 1. Percentage kidney and glomerulus necrosis in rats

No	Organ terdeteksi	Sel nekrosis (%)			
		P1	P2	P3	P4
1	Kidney	24	29	6	7
2	Heart	20	24	5	5

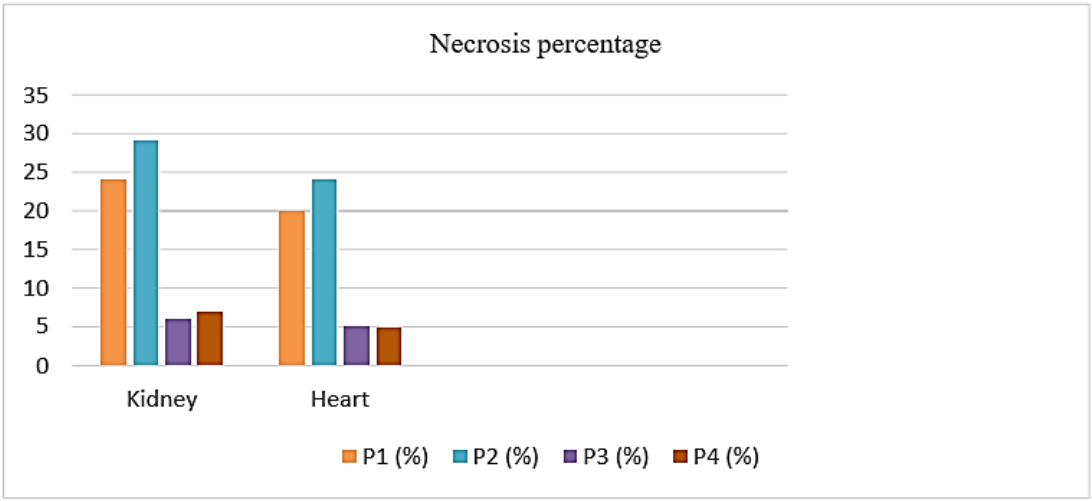


Fig. 3. Necrosis Percentage

The liver is an important organ in the body that functions to detoxify various substances ingested by the digestive tract. The functional unit of the liver is the liver lobule, which is cylindrical in shape, surrounding the central vein that flows into the hepatic vein, and then into the vena cava [31,32]. The liver is crucial in metabolism, detoxification, storage, and excretion of xenobiotics and their metabolites, and is particularly susceptible to damage [33]. Accumulation of toxic substances in the liver parenchyma can cause hepatocyte cell damage due to exposure. Histological changes vary depending on the dose, type, effects of the substance, or other diseases, and susceptibility [34]. Liver damage from toxic substances is influenced by several factors, such as the type of chemical involved, the dose given, and the duration of exposure [35,36].

The basic functional unit of the kidney is the nephron, which regulates water and solutes, especially electrolytes in the body, by filtering the blood [37,38]. It then reabsorbs fluids and molecules through the capillaries that are still needed by the body [39,40]. Chemicals entering the body through various administration routes generally undergo absorption, distribution, metabolism, and excretion [41,42]. The metabolism of medicinal plant compounds occurs in the kidneys [43,44]. The kidney is highly susceptible to the toxic effects of drugs and chemicals. Examination of glomerular and tubular necrosis is one way to demonstrate kidney cell damage [45].

Various phytochemicals in yam bean tubers and avocado fruits can work complexly within the body. Natural chemical compounds are complex and non-toxic compared to synthetic or isolated single compounds [46,47]. Daidzein in yam bean tubers, a compound similar to 17β- estradiol, has enantiomeric structures, including cis-tetrahydrodaidzein and trans- tetrahydrodaidzein, which have chiral structures [48]. This increases the number of daidzein- like compounds that can actively enter the bloodstream. Daidzein is followed into the bloodstream by genistein and quercetin, phytoestrogen compounds from yam bean tubers [49,50]. Avocado fruits contain potassium, phosphorus, calcium, magnesium, niacin, pyridoxine, riboflavin, thiamine, and biotin [51]. Niacin is a chemical compound that can lower cholesterol [52,53].

Consuming natural ingredients has better effects on the body than consuming isolated synthetic substances [54]. This is because natural ingredients have complex chemical compounds that interact with each other, creating beneficial

physiological effects [55,56]. All medicinal plants contain mixtures of active compounds with pharmacological activities [56].

Consuming fresh natural ingredients, without processing, shows beneficial effects on the body. This is because the compounds in plants have not been damaged during processing. Non-processed food is considered to have a better chemical composition compared to ultra-processed food, making the consumption of non-processed food in large quantities and over a long period safe and non-toxic. The complexity of natural compounds allows them to work in the body with the principle of balance metabolism, as some compounds enhance and others reduce effects, making complex compounds non-toxic. Based on this analysis, natural ingredients are more moderate compared to synthetic or isolated substances.

4. CONCLUSION

The use of natural ingredients does not produce toxic (harmful) effects in the body compared to synthetic substances. The percentage of kidney necrosis with daidzein administration is 24%, and with niacin administration, it is 29%. The percentage of liver necrosis with daidzein administration is 20%, and with niacin administration, it is 24%.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

ETHICAL APPROVAL

Animal Ethic committee approval has been collected and preserved by the author(s).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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