

Methanol extract of mangosteen peel (*Garcinia mangostana* L.) increase activity acetylcholinesterase and glutathione peroxidase and reduce MDA in diazinon exposed rat



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ABSTRACT

Introduction: A study has been conducted on the methanol extract of mangosteen peel (MEMP) in rats exposed to diazinon pesticides (DZN). The purpose of this study is to prove that the methanol extract of mangosteen peel can increase the activity of AChE and GPx as well as decrease MDA concentration of rats that were exposed to DZN.

Method: Thirty healthy male Wistar rats divided into five groups. The control group (K-), group II was exposed to DZN (K+), group III was exposed to DZN and given 200 mg/kg MEMP (P1), group IV was exposed to DZN and given 400 mg/kg MEMP (P2) and group V was exposed to DZN and given 600 mg/kg MEMP (P3), and performed for three weeks. Blood samples were taken for analysis of acetylcholinesterase (AChE) activity, glutathione peroxidase (GPx) activity, and MDA levels.

Results: The results analyzed by ANOVA test followed by post hoc test. MEMP treatment showed significantly higher AChE activity ($p < 0.005$) than exposed without MEMP. Compared with control group, the greatest increase is in P2 (1105.26 ± 1.53 U/L); GPx activity was also significantly higher ($p < 0.005$) between the exposed treatment 990.00 ± 47.43 with P2 (1236.00 ± 12.76) and P3 (1530.00 ± 58.74). MDA levels were significantly lower ($p < 0.005$) among the three treatments were exposed to the P1, P2, and P3, treatment gave the highest decrease in MDA is P2.

Conclusions: The conclusion is MEMP can increase activity of AChE, GPx and decrease MDA concentration on rats exposed to DZN.

Keywords: AChE, DZN, MEMP, GPx, MDA

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INTRODUCTION

The use of pesticides cannot be avoided to get good results in quality and quantity, especially in highland areas that have high humidity and low temperatures. Farmers generally use pesticide by combining several types of pesticides and even used until the harvest.¹ As reported by Putra-Manuaba (2009) that there has been bioaccumulation of dichlorodiphenyl-trichloroethane (DDT) and chlo-rothalonil contamination on tilapia fish and carp fish in Lake Buyan. The average expected residues of DDT contamination in carp and tilapia respectively 16.6 and 9.6 ppb.²

The most widely used pesticides are organo-phosphates (OPs) and carbamates because OPs are strong, fast and the results are visible. OPs are also unstable and have short half-lives, making them better for the environment than organochlorines. Nevertheless, organophosphate compounds are toxic to vertebrate organisms.³⁻⁴ It can bind the active site of AChE enzyme activity that inhibits hydrolyze acetylcholine (ACh) into choline and

acetic acid. OPs pesticides are a source of free radicals to the body, while exposed to OPs may increase the number of free radicals. It can interfere with the activity of endogenous antioxidants such as glutathione peroxidase (GPx), catalase (CAT) and superoxide dismutase (SOD).⁵⁻⁷ Endogenous antioxidants are enzymes that play an important role in reducing the reactivity of free radicals, so that oxidative stress and lipid peroxidation can be prevented. Malondialdehyde (MDA) is a result of lipid peroxidation, so high free radicals cause high lipid peroxidation and high concentration of MDA.⁸⁻¹¹ Research of Misrha et al. (2013) found there was a significant increase in MDA concentration in pesticide sprayers compared to the control group.¹²

Secondary antioxidants are large compounds that contained in plants. One of the plants that have a high antioxidant in almost all of its parts is mangosteen, with the most numerous antioxidant content is in the skin of the fruit. Utilization of mangosteen

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peel is useful for the body because it contains various compound and preserving the environment with waste utilization. The chemical components that act as antioxidants are phenols and polyphenols. That compound is widely present in nature, especially in plants. This group of compounds can absorb free radicals. The methanol extract of dry mangosteen fruit has a phenol content and large antioxidant activity.¹³⁻¹⁴ The purpose of this study is to prove that the methanol extract of mangosteen peel can increase the activity of AChE and GPx as well as decrease MDA concentration of Wistar rats that were exposed to DZN.

MATERIAL AND METHODS

This research is an experimental study with randomized controlled method using 30 male Wistar rats, healthy, 2.5-3 months of age, weighing between 200-240 g and divided into a control group and four treatment group with six times treatment. The five groups are: controlled group (K-), exposure to DZN (K+), exposure to DZN and administration methanol extract of mangosteen peel with a dose of 200 mg/kg (P1), a dose of 400 mg/ kg (P2) and a dose of 600 mg/kg (P3). Mangosteen peel extract obtained by maceration method using methanol and evaporated in an evaporator vacuum. DZN exposure and administration of mangosteen peel extracts were performed daily for three weeks. The parameters determined in this study is the activity of AChE, GPx and MDA concentration, determined by a spectrophotometer. Data were statistically analyzed by ANOVA.

RESULTS

The mean analysis of the three parameters that observed can be seen in [Table 1](#).

AChE activity, GPx and MDA concentration were analyzed by ANOVA was significantly different ($p < 0.05$) between groups. Furthermore, a post hoc analysis was conducted to determine which treatment was significantly different. The results of the analysis are shown in [Table 2](#).

DISCUSSION

Mangosteen peel extract contains a variety of compounds having more than one hydroxyl group; in this study the exposure is given on the same day giving the extract of the skin of mangosteen fruit, then the mechanism that may occur is the phenol and polyphenol able to bind phosphorus of OPs (OPs blocked), so it can't phosphorylate AChE.

The result of mean analysis value of GPx activity showed a significant difference ($p < 0.05$) between P2 treatment (1236.00 ± 12.76) and P3 (1530.00 ± 58.74) U/L and significantly different with treatment K+ (990.00 ± 47.43) U/L. This difference indicates that the extract dose of 400 mg/kg mangosteen peel can increase blood GPx activity in Wistar rats that were exposed to OPs. The methanol extract of mangosteen peel enhances the activity of GPx through antioxidant gene triggers by activating nuclear factor erythroid 2-related factor 2 (Nrf2).

The result of MDA concentration analysis showed that three treatment of mangosteen peel extract on exposed rat were significantly different ($p < 0.05$) compared to exposed rat alone, as well as between P1 and P2 there were significant differences. The treatment of P2 (27.71 ± 7.22) μm was not significantly different compared to control group (23.84 ± 3.01) μm . It shows that a dose of 400 mg/kg MEMP is the most effective dose to decrease MDA concentration. High antioxidant compound of mangosteen peel extract can neutralize free radicals derived from OPs through free electron donor or the mechanism of the free radical scavenger. Thus the activity of the enzyme glutathione peroxidase in exposed Wistar rats that were given the extracts of mangosteen peel becomes higher and lower concentration of MDA.

CONCLUSION

The results of this study obtained several conclusions:

1. AChE activity increased in DZN exposed rat that given with MEMP.
2. GPx activity increased in DZN exposed rat that given with MEMP.

Table 1 Results of the mean activity analysis AChE, GPx and MDA concentration

Group	AChE activity U/L	GPx Activity U/L	MDA levels μm
K-	1073.68 \pm 66.11	1608.00 \pm 13.35	23.84 \pm 3.01
K+	498.246 \pm 21.00	990.00 \pm 47.43	45.66 \pm 4.45
P1	842.105 \pm 25.81	1084.00 \pm 60.66	36.44 \pm 6.32
P2	1105.26 \pm 15.41	1236.00 \pm 12.76	27.71 \pm 7.22
P3	946.636 \pm 13.06	1530.00 \pm 58.74	34.27 \pm 4.99

Table 2 Results of Post Hoc Analysis

Group Treatment	Mean Different			
	AChE activity	GPx activity	MDA levels	
K+	K-	575.44*	-618.00*	21.82*
	P1	-343.86*	-94.00	9.22*
	P2	-607.02*	-246.00*	12.95*
	P3	-448.39*	-540.00*	11.38*

3. MDA concentration decreased in DZN exposed rat that given with MEMP.

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